TRIFLUMEZOPYRIM (303)

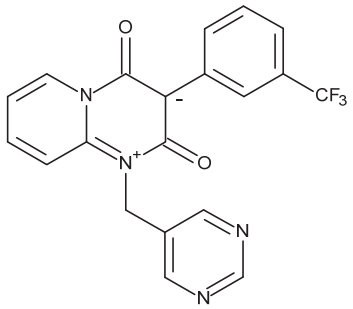
The first draft was prepared by Dr J Heidler, Federal Institute for Risk Assessment, Berlin, Germany

EXPLANATION

Triflumezopyrim is an insecticide used to control planthoppers in rice. Triflumezopyrim belongs to the class of mesoionic insecticides, binding to the orthosteric site of the nicotinic acetylcholine receptor. It has not been considered yet by the JMPR for toxicology and residues.

IDENTITY

ISO common name	Triflumezopyrim
Chemical name	2,4-dioxo-1-(pyrimidin-5-ylmethyl)-3-[3-(trifluoromethyl)phenyl]-3,4-dihydro-2H-pyrido[1,2-a]pyrimidin-1-ium-3-ide
IUPAC & CA	3,4-dihydro-2,4-dioxo-1-(pyrimidin-5-ylmethyl)-3-(α,α,α-trifluoro-*m*-tolyl)-2*H*-pyrido[1,2-*a*]pyrimidin-1-ium-3-ide
Synonyms	DPX-RAB55
CAS No.	1263133-33-0
CIPAC No.	Not yet listed
Structural formula	



Molecular formula	$C_{20}H_{13}F_3N_4O_2$
Molecular mass	398.3 g/mol
Specifications	Specifications for triflumezopyrim were not yet developed by FAO.

PHYSICAL AND CHEMICAL PROPERTIES

Table 1 Physical and chemical properties of pure triflumezopyrim

Property	Results		Method (test material)	Reference
Appearance	Physical state Odour	Solid, yellow (PAI & TGAI) No odour (PAI & TGAI)	OPPTS 830.6302 OPPTS 830.6303 OPPTS 830.6304 (Batch SG0311387, 98.8% purity; Batch SG0314011, 97.0% purity; Batch SG0313515, 95.0% purity; Batch SG0313524, 95.0% purity; Batch SG0313528, 95.0% purity; Batch SG0313536, 95.0% purity; Batch SG0313557, 95.0% purity)	Reddy M., 2013, TRIFLUMEZ_001 Siripriya G., 2014d TRIFLUMEZ_002

Property	Results	Method (test material)	Reference
Melting point	189.4 ± 0.6°C (PAI); 189.1 ± 0.3°C (TGAI)	OECD 102 OPPTS 830.7200 EEC A.1 (Batch SG0311387, 98.8% purity; Batch SG0314011, 97.0% purity)	Kumar S.V., 2013a TRIFLUMEZ_003 Siripriya G., 2014a TRIFLUMEZ_004
Boiling point & temperature of decomposition	Not measurable (decomposes) Decomposition starts to occur at about 205 210 °C (PAI) and 200-205 °C (TGAI)	OECD 103 OPPTS 830.7220 EEC A.2 (Batch SG0311387, 98.8% purity; Batch SG0314011, 97.0% purity)	Kumar S.V., 2013b TRIFLUMEZ_005 Siripriya G., 2014b TRIFLUMEZ_006
Relative density	1.4502 ± 0.0096 g/mL at 20 °C (PAI); 1.4235 ± 0.0007 g/mL at 20 ºC (TGAI)	OECD 109 OPPTS 830.7300 EEC A.3 (Batch SG0311387, 98.8% purity, Batch SG0314011, 97.0% purity)	Reddy M., 2013, TRIFLUMEZ_001 Siripriya G., 2014c TRIFLUMEZ_007
Bulk/tap density	Bulk density: 835 kg/m^3 (PAI); 565-705 kg/m^3 (TGAI) Tap density 913 kg/m^3 (PAI); 748-882 kg/m^3 (TGAI)	CIPAC MT186 (Batch SG0311387, 98.8% purity; Batch SG0314011, 97.0% purity; Batch SG0312442, 98.5% purity; Batch SG0312479, 97.6% purity; Batch SF14000066, 97.5% purity)	Livingston I., 2013a TRIFLUMEZ_008 Shanthaveerappa K.S., 2015 TRIFLUMEZ_009
pH	1% aqueous suspension of triflumezopyrim: 8.0 ± 0.05 (PAI); 6.3 ± 0.06 (TGAI)	CIPAC MT 75.3 OPPTS 830.7000 (Batch SG0311387, 98.8% purity; Batch SG0314011, 97.0% purity)	Reddy M., 2013, TRIFLUMEZ_001 Siripriya G., 2014f TRIFLUMEZ_010
Vapour pressure	2.65×10^{-8} Pa at 25 °C (by extrapolation) 2.88×10^{-8} Pa at 30 °C 3.37×10^{-8} Pa at 40 °C 3.95×10^{-8} Pa at 50 °C	OECD 104 OPPTS 830.7950 EEC A.4 (Batch SG0311387, 98.8% purity)	Manikandan K.N., 2013 TRIFLUMEZ_011
Henry´s Law Coefficient	4.19×10^{-8} Pa m^3 mol^{-1}	Calculation	Tessier D.M., 2014 TRIFLUMEZ_012
Partition coefficient n-octanol / water	Octanol-destilled water at 20 °C log P_{OW} = 1.24 ± 0.01 Octanol-aqueous buffer solutions at 20 °C log P_{OW} = 1.23 ± 0.01 (pH 4) log P_{OW} = 1.26 ± 0.01 (pH 7) log P_{OW} = 1.24 ± 0.02 (pH 9)	OECD 107 OPPTS 830.7550 EEC A.8 (Batch SG0311387, 98.8% purity)	Pushpalatha K.G., 2013 TRIFLUMEZ_013
Solubility in water	0.23 ± 0.01 g/L (20 °C)	OECD 105 OPPTS 830.7840 EEC A.6 (Batch SG0311387, 98.8% purity)	Kumar S.V., 2013c TRIFLUMEZ_014

<table>
<tr><th>Property</th><th>Results</th><th>Method
(test material)</th><th>Reference</th></tr>
<tr><td>Solubility in organic solvents</td><td>
<table>
<tr><th></th><th colspan="2">Solubility of triflumezopyrim (PAI) (g/L)</th></tr>
<tr><th>Solvent</th><th>Mean</th><th>Standard deviation</th></tr>
<tr><td>N,N-dimethylformamide</td><td>377.62</td><td>18.10</td></tr>
<tr><td>Acetonitrile</td><td>65.87</td><td>3.16</td></tr>
<tr><td>Methanol</td><td>7.65</td><td>0.45</td></tr>
<tr><td>Acetone</td><td>71.85</td><td>5.82</td></tr>
<tr><td>Ethyl acetate</td><td>14.65</td><td>1.04</td></tr>
<tr><td>Dichloromethane</td><td>76.07</td><td>4.34</td></tr>
<tr><td>o-Xylene</td><td>0.702</td><td>0.083</td></tr>
<tr><td>n-Octonol</td><td>1.059</td><td>0.023</td></tr>
<tr><td>n-Hexane</td><td>0.0005</td><td>0.0000</td></tr>
<tr><th></th><th colspan="2">Solubility of triflumezoyprim (TGAI) (g/L)</th></tr>
<tr><th>Solvent</th><th>Mean</th><th>Standard deviation</th></tr>
<tr><td>N,N-dimethylformamide</td><td>nd</td><td>nd</td></tr>
<tr><td>Acetonitrile</td><td>91.525</td><td>1.848</td></tr>
<tr><td>Methanol</td><td>19.748</td><td>0.536</td></tr>
<tr><td>Acetone</td><td>116.511</td><td>1.609</td></tr>
<tr><td>Ethyl acetate</td><td>18.267</td><td>0.547</td></tr>
<tr><td>Dichloromethane</td><td>64.656</td><td>1.418</td></tr>
<tr><td>o-Xylene</td><td>0.799</td><td>0.022</td></tr>
<tr><td>n-Octonol</td><td>1.153</td><td>0.023</td></tr>
<tr><td>n-Hexane</td><td>0.0002</td><td>0.00001 (<LOQ)</td></tr>
</table>
</td><td>OECD 105
OPPTS 830.7840
CIPAC MT 181
(Batch SG0311387, 98.8% purity; Batch SG0314011, 97.0% purity)</td><td>Moorthy M.S., 2016
TRIFLUMEZ_015

Revankar S.D., 2015
TRIFLUMEZ_016</td></tr>
<tr><td>Hydrolysis</td><td>No degradation of triflumezopyrim in buffer solutions was observed.
After 5 days at 50 ± 0.5 °C, the percentage of parent substance recovered was 98-101% at pH4, 99-101% at pH7 and 100-102% at pH9.</td><td>OECD 111
OPPTS 835.2120
([pyridine-2,6-^{14}C], 98.8% radiochemical purity; [pyrimidine-3-^{14}C, 99.3% radiochemical purity)</td><td>Anand, H.S., 2012
TRIFLUMEZ_017</td></tr>
<tr><td>Photolysis</td><td>At 25±1°C for up to 30 days (12 hours irradiation/12 hours dark)
Half-lives: 2.1 days (buffer pH 7); 2.8 days (natural water)
Identified degradation product: IN-RUB93 up to 85% in natural water after 30 days</td><td>OECD 316
OPPTS 835.2240
MAFF Guideline 12
Nousan-8147/2-6-2
([pyridine-2,6-^{14}C], 98.8% radiochemical purity; [pyrimidine-3-^{14}C], 99.3% radiochemical purity; [methylene-^{14}C], 99.9% radio-chemical purity)</td><td>McCorquodale G., 2015
TRIFLUMEZ_018</td></tr>
<tr><td>Dissociation constant</td><td>No dissociation in the range of pH 1.0 to 10.8 was observed</td><td>OECD 112
OPPTS 830.7370
(Batch SG0311387, 98.8% purity)</td><td>Shanthaveerappa K.S., 2013
TRIFLUMEZ_019</td></tr>
<tr><td>Stability</td><td>Stable at ambient storage for at least 12 month.
Stable at 54°C and to metal and metal ions for at least 2 weeks.</td><td>OPPTS 830.6317
OPPTS 830.6313
(Batch SG0311387, 98.8% purity; Batch SG0314011, 97.0% purity)</td><td>Anand H.S., 2014
TRIFLUMEZ_020

Siripriya G., 2015b
TRIFLUMEZ_021</td></tr>
</table>

Property	Results	Method (test material)	Reference
Flammability, Auto-flammability, Explosive properties, Oxidizing/reducing properties	Triflumezopyrim is not flammable, does not self-ignite, is not sensitive to thermal, friction, or impact stimuli and is not an oxidising or reducing agent.	EC Test A10 EC Test A14 EC Test A16 EC Test A17 (Batch SG0311387, 98.8% purity)	Livingston I. 2013b TRIFLUMEZ_022
Surface tension	69.35 dynes/cm at 20.23 °C of a 90% saturated aqueous solution. Triflumezopyrim is not considered a surface active agent.	OECD 115 EEC A.5 (Batch SG0314011, 97.0% purity)	Siripriya G., 2014e TRIFLUMEZ_023
UV/VIS absorption (max.) incl. ε	pH Wavelength [nm] molar extinction coefficient [l/mol cm] 1.8 190 37562 7.0 193 37479 10.5 190 40207	OECD 101 OPPTS 830.7050 (Batch SG0311387, 98.8% purity)	Shanthaveerappa K.S., 2016 TRIFLUMEZ_024

Formulations

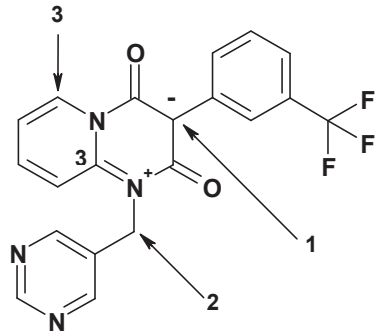
Triflumezopyrim is available as a water based formulation (SC).

Table 2 Examples of formulations registered containing triflumezopyrim as active ingredient

Formulation	Content of active ingredients	Trade names
SC	106 g ai/L	DuPont™ Pexalon™

METABOLISM AND ENVIRONMENTAL FATE

Metabolism studies were conducted using [pyrimidine-3-^{14}C]-triflumezopyrim (pyrimidine-label), [methylene-^{14}C]-triflumezopyrim (methylene-label) and [pyridine-2,6-^{14}C]-triflumezopyrim (pyridine-label). Moreover, [pyrimidine-3-^{13}C]-triflumezopyrim was used. The position of the label for the various test substances is presented in the following figure:



1 [pyrimidine-3-^{14}C]-triflumezopyrim

1 [pyrimidine-3-^{13}C]-triflumezopyrim

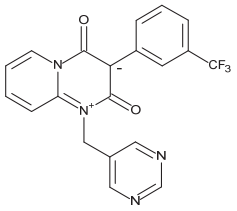
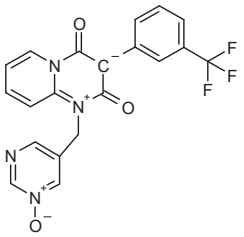
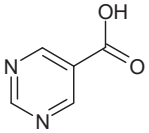
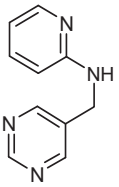
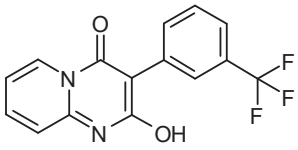
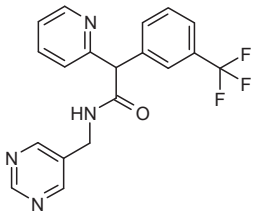
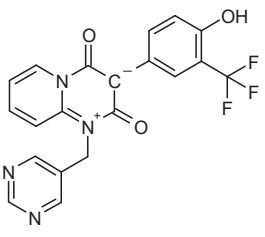
2 [methylene-^{14}C]-triflumezopyrim

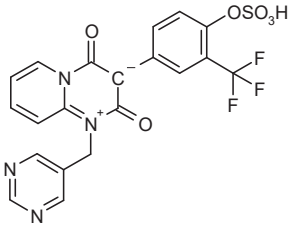
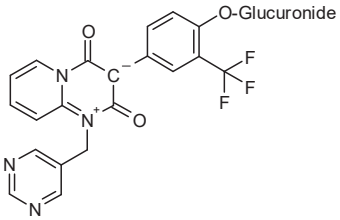
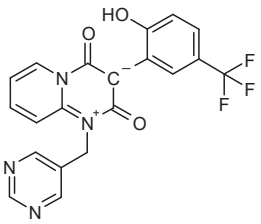
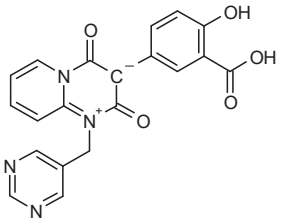
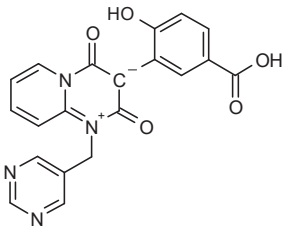
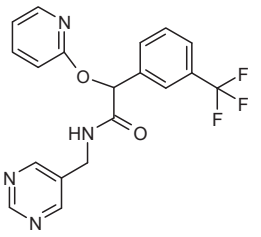
3 [pyridine-2,6-^{14}C]-triflumezopyrim

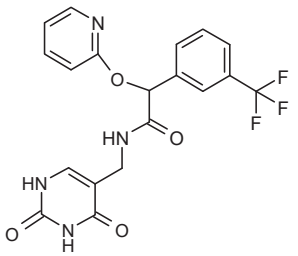
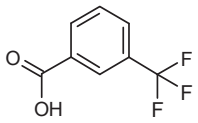
Figure 1 Structure of triflumezopyrim and position of radiolabels

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

Table 3 Known metabolites of triflumezopyrim

Code Names	Chemical Names (IUPAC)	Structure	Where found
Triflumezopyrim DPX-RAB55	2,4-dioxo-1-(pyrimidin-5-ylmethyl)-3-[3-(trifluoromethyl)phenyl]-3,4-dihydro-2*H*-pyrido[1,2-*a*]pyrimidin-1-ium-3-ide		Soil Water Plants (rice) Rotational crops (wheat) Livestock (hen, goat) Rat
IN-R3Z91 (N-oxide)	1-[(1-oxidopyrimidin-1-ium-5-yl)methyl]-3-[3-(trifluoromethyl)phenyl]pyrido[1,2-a]pyrimidin-1-ium-3-ide-2,4-dione		Plants (rice) Rotational crops (wheat) Livestock (hen, goat) Rat
IN-RPA16	pyrimidine-5-carboxylic acid		Soil Plants (rice) Livestock (goat)
IN-RPA19	N-(pyrimidin-5-ylmethyl)pyridin-2-amine		Soil, Plants (rice) Rotational crops (wheat) Rat
IN-RPD47	2-hydroxy-3-[3-(trifluoromethyl)phenyl]pyrido[1,2-a]pyrimidin-4-one		Soil Plants (rice) Rotational crops (wheat) Livestock (hen, goat) Rat
IN-RUB93	2-(2-pyridyl)-N-(pyrimidin-5-ylmethyl)-2-[3-(trifluoromethyl)phenyl]acetamide		Water (aqueous photolysis) Plants (rice) Rat
IN-R6U70	3-[4-hydroxy-3-(trifluoromethyl)phenyl]-1-(pyrimidin-5-ylmethyl)pyrido[1,2-a]pyrimidin-1-ium-3-ide-2,4-dione		Rotational crops (wheat) Plants (rice) Livestock (hen, goat) Rat

Code Names	Chemical Names (IUPAC)	Structure	Where found
R6U70 sulfate (sulphate conjugate of IN-R6U70)	[4-[2,4-dioxo-1-(pyrimidin-5-ylmethyl)pyrido[1,2-a]pyrimidin-1-ium-3-id-3-yl]-2-(trifluoromethyl)phenyl] hydrogen sulfate		Livestock (goat) Rat
R6U70 glucuronide (glucuronic acid conjugate of IN-R6U70)	6-[4-[2,4-dioxo-1-(pyrimidin-5-ylmethyl)pyrido[1,2-a]pyrimidin-1-ium-3-id-3-yl]-2-(trifluoromethyl)phenoxy]-3,4,5-trihydroxy-tetrahydropyran-2-carboxylic acid		Livestock (goat) Rat
IN-R6U71	3-[2-hydroxy-5-(trifluoromethyl)phenyl]-1-(pyrimidin-5-ylmethyl)pyrido[1,2-a]pyrimidin-1-ium-3-ide-2,4-dione		Plants (rice)
IN-R6U72 (hydroxy acid)	5-[2,4-dioxo-1-(pyrimidin-5-ylmethyl)pyrido[1,2-a]pyrimidin-1-ium-3-id-3-yl]-2-hydroxy-benzoic acid		Plants (rice) Livestock (goat) Rat
IN-R6U73 (hydroxy acid)	3-[2,4-dioxo-1-(pyrimidin-5-ylmethyl)pyrido[1,2-a]pyrimidin-1-ium-3-id-3-yl]-4-hydroxy-benzoic acid		Plants (rice) Livestock (goat)
IN-SBV06	2-(2-pyridyloxy)-N-(pyrimidin-5-ylmethyl)-2-[3-(trifluoromethyl)phenyl]acetamide		Soil Rotational crops (wheat) Plants (rice) Livestock (hen) Rat

Code Names	Chemical Names (IUPAC)	Structure	Where found
IN-SBY68	N-[(2,4-dioxo-1H-pyrimidin-5-yl)methyl]-2-(2-pyridyloxy)-2-[3-(trifluoromethyl)phenyl]acetamide		Soil
IN-Y2186	3-(trifluoromethyl)benzoic acid		Soil Rotational crops (wheat) Plants (rice) Rat

ENVIRONMENTAL FATE

For the investigation of the environmental fate of triflumezopyrim, the Meeting received studies on soil and aqueous photolysis, anaerobic and aerobic soil metabolism, aerobic and anaerobic degradation in water/sediment systems, mobility studies and the behaviour in confined rotational crops. According to the use pattern, degradation in anaerobic soil and water as well as mobility studies where not considered relevant here.

Environmental fate in water

Aqueous photolysis

The aqueous photolytic behaviour of triflumezopyrim was investigated by McCorquodale (2015, TRIFLUMEZ_018) using [pyridine-^{14}C]-, [methylene-^{14}C]- and [pyrimidine-^{14}C]-radiolabelled triflumezopyrim in sterilized buffer solution and natural water.

Sterile 0.01 M pH 7 phosphate buffer or sterile natural water was dosed with radiolabelled triflumezopyrim at 5.0 mg ai/L. The samples were subjected to a cycle of 12 hours irradiation and 12 hours darkness, using a xenon arc lamp (for approximately 15 days irradiation (30 days in total) at 25 ± 1 °C. The lamp was equipped with filters to eliminate emitted wavelengths of < 290 nm and reduce wavelengths greater than 800 nm to give a spectral distribution similar to natural sunlight. Dark control samples were prepared in parallel. Volatile organics and CO_2 were trapped with ethanediol and 1 M NaOH, respectively. Samples were taken and analysed at 0, 4, 8, 16, 20, 44, 116, 235 and 355 hours.

Samples were analysed by LSC for total radioactivity content and HPLC to determine the metabolite pattern. LC-MS/MS analysis was carried out as confirmatory analysis.

The percentage recovery of the applied radioactivity in sterile buffer solution and sterile natural water is presented in Tables 4 and 5, respectively. In sterile buffer solution, parent triflumezopyrim declined from 97–99% to 0.5–0.8% over the irradiation time, while IN-RUB93 went up from 0% to 68–76%. For sterile natural water, parent triflumezopyrim declined from 97–101% to 2–6% over the irradiation time. At the same time percentage recovery of metabolite IN-RUB93 increased from 0% to 66–85%, respectively. The recovery of triflumezopyrim in dark controls was between 92–98% after 355 hours.

Table 4 Phototransformation of triflumezopyrim, expressed as percentage of applied radioactivity, in sterile buffer solution

Degradate		Sampling interval (total hours irradiated)							
	0	4	8	16	20	44	116	235	355
[pyrimidine-^{14}C]-triflumezopyrim									
Triflumezopyrim	97.4%	94.8%	88.4%	77.8%	76.7%	53.8%	21.7%	6.8%	0.6%
IN-RUB93	<LOQ	3.9%	9.0%	18.4%	20.8%	43.1%	72.3%	82.4%	75.6%
Unidentified degradates[a]	1.9%	0.9%	2.1%	2.7%	2.3%	2.9%	3.7%	8.2%	16.4%
Volatiles organics	NS	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	0.12%
CO_2	NS	<LOQ	<LOQ	<LOQ	<LOQ	0.28%	0.04%	0.12%	0.03%
Apparatus wash	0.69%	1.0%	1.0%	1.6%	0.45%	0.99%	1.5%	1.1%	0.86%
Total	99.95%	100.6%	100.5%	100.5%	100.4%	101.0%	99.3%	98.6%	93.6%
[pyridine-^{14}C]-triflumezopyrim									
Triflumezopyrim	98.9%	91.5%	86.5%	80.1%	74.2%	58.4%	21.8	<LOQ	0.47%
IN-RUB93	<LOQ	4.4%	8.6%	16.7%	22.5%	39.2%	73.0%	78.4%	68.4%
Unidentified degradates[a]	0.37%	2.8%	3.8%	2.0%	2.3%	1.8%	4.6%	18.6%	27.8%
Volatiles organics	NS	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
CO_2	NS	<LOQ	<LOQ	<LOQ	<LOQ	0.02%	<LOQ	0.16%	0.24%
Apparatus wash	0.70%	0.74%	0.62%	0.89%	0.65%	0.79%	0.54%	1.5%	0.81%
Total	99.98%	99.4%	99.6%	99.8%	99.6%	100.1%	99.8%	98.8%	97.8%
[methylene-^{14}C]-triflumezopyrim									
Triflumezopyrim	99.4%	91.3%	87.2%	77.8%	78.9%	50.3%	14.2%	3.7%	0.80%
IN-RUB93	<LOQ	6.4%	10.5%	20.0%	18.6%	47.0%	78.5%	74.8%	69.0%
Unidentified degradates[a]	<LOQ	1.6%	1.8%	1.8%	1.9%	1.8%	7.2%	20.2%	27.3%
Volatiles organics	NS	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
CO_2	NS	<LOQ	<LOQ	<LOQ	<LOQ	0.11%	0.18%	<LOQ	<LOQ
Apparatus wash	0.81%	0.91%	0.69%	0.74%	1.0%	1.8%	0.80%	1.3%	1.0%
Total	100.2%	100.3%	100.2%	100.3%	100.4%	100.9%	100.9%	99.9%	98.1%

NS: no sample

[a] No individual unidentified component accounts for >3.97% AR

Table 5 Phototransformation of triflumezopyrim, expressed as percentage of applied radioactivity, in sterile natural water

Degradate		Sampling interval (total hours irradiated)							
	0	4	8	16	20	44	116	235	355
[pyrimidine-^{14}C]-triflumezopyrim									
Triflumezopyrim	96.8%	91.8%	89.7%	82.8%	76.6%	63.1%	31.9%	5.4%	5.7%
IN-RUB93	<LOQ	3.3%	6.5%	12.8%	19.6%	32.5%	56.2%	73.6%	66.2%
Unidentified degradates[a]	1.9%	4.0%	1.9%	2.6%	2.2%	3.3%	6.6%	15.1%	22.3%
Volatiles organics	NS	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
CO_2	NS	<LOQ	<LOQ	<LOQ	<LOQ	0.44%	0.02%	<LOQ	0.10%
Apparatus wash	0.72%	1.1%	1.6%	0.94%	1.1%	0.72%	1.3%	1.6%	0.75%
Total	99.4%	100.2%	99.8%	99.1%	99.6%	99.7%	96.1%	95.7%	95.0%
[pyridine-^{14}C]-triflumezopyrim									
Triflumezopyrim	101.2%	95.9%	92.6%	80.0%	80.5%	62.6%	33.8	6.4%	3.3%
IN-RUB93	<LOQ	4.2%	7.4%	18.4%	17.9%	35.9%	59.8%	82.0%	84.7%
Unidentified degradates[a]	<LOQ	1.1%	1.6%	3.0%	2.3%	2.6%	6.7%	10.6%	9.0%
Volatiles organics	NS	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
CO_2	NS	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	0.21%	0.19%
Apparatus wash	0.69%	0.55%	0.66%	0.88%	1.1%	1.0%	0.97%	2.2%	1.9%
Total	101.9%	101.7%	102.2%	102.3%	101.9%	102.1%	101.2%	101.4%	99.1%
[methylene-^{14}C]-triflumezopyrim									
Triflumezopyrim	99.6%	92.7%	88.5%	78.8%	80.4%	62.4%	28.5%	3.7%	1.9%
IN-RUB93	<LOQ	4.1%	7.9%	18.6%	17.7%	33.2%	66.1%	73.3%	76.0%
Unidentified degradates[a]	<LOQ	2.6%	2.2%	0.9%	1.1%	3.4%	4.0%	22.2%	19.9%
Volatiles organics	NS	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
CO_2	NS	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	0.03%	<LOQ
Apparatus wash	0.41%	1.1%	1.1%	1.6%	0.60%	0.63%	0.61%	0.91%	1.4%
Total	100.0%	100.5%	99.6%	99.9%	99.8%	99.7%	99.2%	100.2%	99.1%

NS: no sample

[a] No individual unidentified component accounts for >3.64% AR

Based on the decline rate observed for triflumezopyrim under intermittent irradiation, a half-life time of 2.1 and 2.8 days (single 1st order kinetics) was estimated for sterile buffer solution and natural water, respectively.

Outdoor aerobic aquatic metabolism

The degradation of triflumezopyrim was studied outdoors by Cochrane (2015, TRIFLUMEZ_052) in two irradiated water/sediment systems (silt loam and sand) using [pyridine-^{14}C]- and [pyrimidine-^{14}C]-radiolabelled triflumezopyrim at a nominal application rate of 0.5 µg ai/g water. Irradiated buffer controls and dark buffer controls were carried along as well.

Water/sediment samples were incubated outdoors for 30 days under natural sunlight at 22.3 ± 4.7 °C. The experimental setup consisted of two traps filled with 1 M NaOH to collect CO_2. Samples were taken at 0, 1, 2, 3, 4, 7, 10, 14 and 30 days after application.

Sediment and water were separated by decanting the water. The water samples were directly analysed by HPLC and LSC. The sediment samples were extracted twice with acetonitrile (day 2-day 30 samples additionally once with acetonitrile:0.1% formic acid (9:1, v/v)), followed by analysis by LSC for total radioactivity and by HPLC against reference standards to identify metabolites. Confirmation of the identity of triflumezopyrim and metabolites was performed by TLC and LC-MS analysis. The sediment remaining after extraction was combusted followed by LSC.

The concentration of triflumezopyrim in the water phase of the silt loam system declined from 98% AR at Day 0 to 9–10% AR at Day 30 via a combination of degradation and transfer into the sediment. Similar, triflumezopyrim declined in the surface water of the sand system from 97% AR at Day 0 to 13–22% AR at Day 30. Of the identified metabolites, only IN-RUB93 was observed at > 5% AR at two consecutive sampling intervals. The recovery of triflumezopyrim after 30 days in irradiated and dark buffer controls was between 46–47% and 78–88%, respectively.

Table 6 Degradation of triflumezopyrim, expressed as percentage of applied radioactivity in natural sunlight irradiated silt loam water/sediment systems

Degradate	Matrix	% AR at sampling time (days)								
		0	1	2	3	4	7	10	14	30
[pyrimidine-^{14}C]-triflumezopyrim										
Triflumezopyrim	Water	98.2	69.1	49.3	51.0	46.6	38.1	29.9	15.1	9.4
	Sediment	NA	13.7	25.1	25.8	35.6	39.2	39.4	44.0	46.9
	Total	98.2	82.8	74.4	76.8	82.2	77.3	69.3	59.1	56.3
IN-RUB93	Water	ND	2.8	3.9	5.5	2.6	3.6	2.7	4.2	3.2
	Sediment	NA	0.5	1.3	1.7	0.8	1.5	2.3	4.6	4.2
	Total	NA	3.3	5.2	7.2	3.4	5.1	5.0	8.8	7.4
IN-RPD47	Water	ND	ND	ND	ND	ND	0.7	2.0	0.2	3.2
	Sediment	NA	ND	ND	ND	ND	ND	0.3	ND	1.6
	Total	NA	NA	NA	NA	NA	0.7	2.3	0.2	4.8
IN-SBV06	Water	ND	ND	0.7	0.5	ND	0.8	0.7	1.1	1.2
	Sediment	NA	ND	ND	ND	0.9	0.4	1.2	2.1	0.9
	Total	NA	NA	0.7	0.5	0.9	1.2	1.9	3.2	2.1
Unidentified radioactivity	Water	0.5	2.0	4.6	2.3	1.5	1.7	1.8	6.1	10.6
	Sediment	NA	ND	ND	ND	ND	ND	1.3	1.2	1.5
	Total	0.5	2.0	4.6	2.3	1.5	1.7	3.1	7.3	12.1
Total extracted radioactivity	Water	98.7	73.9	58.5	59.3	50.7	44.9	37.1	26.7	27.6
	Sediment	NA	14.2	26.4	27.5	37.3	41.1	44.5	51.9	55.1
CO_2		NS	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	0.2
Unextracted		<LOQ	2.7	5.2	2.7	8.5	7.3	6.3	9.9	12.9
%AR not analysed		0.8	7.2	9.2	2.0	3.5	3.1	3.2	7.1	0.2
Total		99.5	98.0	99.3	91.5	100.0	96.4	91.1	95.6	96.0
[pyridine-^{14}C]-triflumezopyrim										
Triflumezopyrim	Water	97.5	67.9	60.9	49.1	45.6	30.2	28.9	19.3	9.9
	Sediment	NA	15.6	23.2	31.6	32.9	41.2	36.1	47.6	40.3
	Total	97.5	83.5	84.1	80.7	78.5	71.4	65.0	66.9	50.2
IN-RPA16	Water	ND	ND	ND	0.9	0.7	1.2	0.5	0.7	ND
	Sediment	NA	ND	ND	ND	ND	ND	ND	ND	ND

Degradate	Matrix	% AR at sampling time (days)								
		0	1	2	3	4	7	10	14	30
	Total	NA	NA	NA	0.9	0.7	1.2	0.5	0.7	NA
IN-RPA19	Water	ND	ND	ND	ND	ND	ND	ND	ND	ND
	Sediment	NA	0.1	0.2	0.3	0.4	0.3	0.6	0.6	1.2
	Total	NA	0.1	0.2	0.3	0.4	0.3	0.6	0.6	1.2
IN-RUB93	Water	ND	0.8	3.6	5.0	5.0	2.5	4.7	3.9	5.0
	Sediment	NA	0.4	0.5	1.4	1.9	1.8	2.1	3.3	6.0
	Total	NA	1.2	4.1	6.4	6.9	4.3	6.8	7.2	11.0
IN-RPD47	Water	1.0	ND	ND	ND	ND	0.2	2.2	2.2	1.0
	Sediment	NA	ND	ND	ND	0.2	ND	0.4	ND	ND
	Total	1.0	NA	NA	NA	0.2	0.2	2.6	2.2	1.0
IN-SBV06	Water	ND	ND	ND	0.5	0.2	1.2	0.9	0.7	1.8
	Sediment	NA	ND	0.3	1.8	0.4	0.9	ND	0.6	1.8
	Total	NA	NA	0.3	2.3	0.6	2.1	0.9	1.3	3.6
Unidentified radioactivity [a]	Water	0.9	2.2	1.9	1.9	1.7	4.3	0.8	4.8	3.5
	Sediment	NA	NA	ND	ND	0.6	ND	0.8	NA	1.1
	Total	0.9	2.2	1.9	1.9	2.3	4.3	1.6	4.8	4.6
Total extracted radioactivity	Water	99.4	70.9	66.4	57.4	53.2	39.6	38.0	31.6	21.2
	Sediment	NA	16.1	24.2	35.1	36.4	44.2	40.0	52.1	50.4
CO_2		NS	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Unextracted		<LOQ	3.0	4.5	3.4	4.5	8.4	7.1	8.2	18.0
%AR not analysed		0.2	7.2	4.4	2.1	7.6	3.2	9.3	3.7	7.7
Total		99.6	97.2	99.5	98.0	101.7	95.4	94.4	95.6	97.3

[a] Consists of multiple components none of which are >5% AR at two consecutive sampling intervals, >10% AR at any sampling interval or >5% and increasing at the end of the study.

NS: no sample

NA: not applicable

ND: not detected

Table 7 Degradation of triflumezopyrim, expressed as percentage of applied radioactivity in natural sunlight irradiated sand water/sediment systems

Degradate	Matrix	% AR at sampling time (days)								
		0	1	2	3	4	7	10	14	30
[pyrimidine-^{14}C]-triflumezopyrim										
Triflumezopyrim	Water	96.7	81.2	69.5	68.3	63.4	49.7	42.4	31.8	22.2
	Sediment	NA	6.8	13.7	15.5	20.5	21.3	31.1	33.4	32.6
	Total	96.7	88.0	83.2	83.8	83.9	71.0	73.5	65.2	54.8
IN-RUB93	Water	ND	0.6	4.0	5.3	5.7	5.0	6.5	7.1	5.9
	Sediment	NA	0.1	0.5	0.5	1.2	1.4	2.1	2.8	5.6
	Total	NA	0.7	4.5	5.8	6.9	6.4	8.6	9.9	11.5
IN-RPD47	Water	ND	ND	ND	ND	0.2	0.7	1.0	1.2	3.0
	Sediment	NA	ND	ND	ND	ND	ND	ND	ND	ND
	Total	NA	ND	ND	ND	0.2	0.7	1.0	1.2	3.0
IN-SBV06	Water	ND	0.9	0.6	0.3	1.1	1.0	1.3	0.9	2.2
	Sediment	NA	ND	ND	ND	0.6	ND	0.5	1.0	2.1
	Total	NA	0.9	0.6	0.3	1.7	1.0	1.3	1.9	4.3
Unidentified radioactivity	Water	1.3	1.1	1.6	2.6	2.6	3.2	2.9	5.4	4.9
	Sediment	NA	NA	ND	ND	ND	0.7	0.5	ND	0.9
	Total	1.3	1.1	1.6	2.6	2.6	3.9	3.4	5.4	5.8
Total extracted radioactivity	Water	98.0	83.8	75.7	76.5	73.0	59.6	54.1	46.4	38.2
	Sediment	NS	6.9	14.2	16.0	22.3	23.4	34.2	37.2	41.2
CO_2		NS	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	0.3
Unextracted		<LOQ	1.4	1.4	1.9	2.4	4.3	5.7	6.6	14.2
%AR not analysed		0.5	4.1	1.0	3.5	1.6	5.7	2.8	3.3	0.3
Total		98.5	96.2	92.3	97.9	99.3	93.0	96.8	93.5	94.2
[pyridine-^{14}C]-triflumezopyrim										
Triflumezopyrim	Water	96.7	78.6	66.3	64.5	57.1	51.0	36.8	21.6	12.9
	Sediment	NA	6.3	19.7	17.4	15.6	25.8	31.1	44.8	33.5
	Total	96.7	84.9	86.0	81.9	72.7	76.8	67.9	66.4	46.4
IN-RPA16	Water	ND	ND	ND	1.0	1.0	0.8	0.7	0.9	ND

Degradate	Matrix	% AR at sampling time (days)								
		0	1	2	3	4	7	10	14	30
	Sediment	NA	ND	ND	ND	ND	ND	ND	ND	ND
	Total	NA	NA	NA	1.0	1.0	0.8	0.7	0.9	NA
IN-RPA19	Water	NA	ND	ND	ND	ND	ND	ND	ND	ND
	Sediment	NA	0.1	ND	0.2	0.3	0.8	ND	1.0	0.6
	Total	NA	0.1	NA	0.2	0.3	0.8	NA	1.0	0.6
IN-RUB93	Water	ND	3.7	4.7	7.9	8.6	5.2	4.6	2.9	10.4
	Sediment	NA	0.2	0.8	1.0	1.5	0.9	1.7	2.1	5.0
	Total	NA	3.9	5.5	8.9	10.1	6.1	6.3	5.0	15.4
IN-RPD47	Water	0.9	ND	ND	ND	ND	0.8	1.1	1.1	4.6
	Sediment	NA	ND	ND	ND	ND	ND	0.6	0.8	0.7
	Total	0.9	NA	NA	NA	NA	0.8	1.7	1.9	5.3
IN-SBV06	Water	NA	1.7	1.3	0.5	0.5	1.0	1.1	1.1	2.7
	Sediment	NA	ND	0.5	0.3	0.5	0.4	1.0	2.0	1.9
	Total	NA	1.7	1.8	0.8	1.0	1.4	2.1	3.1	4.6
Unidentified radioactivity [a]	Water	0.7	1.1	1.9	2.3	2.1	2.9	2.0	3.5	6.6
	Sediment	NA	ND	ND	ND	ND	0.2	ND	1.8	0.8
	Total	0.7	1.1	1.9	2.3	2.1	3.1	2.0	5.3	7.4
Total extracted radioactivity	Water	98.3	85.1	74.2	76.2	69.3	61.7	46.3	31.1	37.2
	Sediment	NA	6.6	21.0	18.9	17.9	28.1	34.4	52.5	42.5
CO_2		NS	<LOQ	<LOQ	<LOQ	<LOQ	0.2	0.2	0.2	0.4
Unextracted		<LOQ	2.3	2.5	2.9	2.9	4.8	7.9	12.3	12.6
%AR not analysed		0.9	4.1	1.5	1.5	4.1	2.2	9.9	0.2	0.4
Total		99.2	98.1	99.2	99.5	94.2	97.0	98.7	96.3	93.1

[a] Consists of multiple components none of which are >5% AR at two consecutive sampling intervals, >10% AR at any sampling interval or >5% and increasing at the end of the study.

NS: no sample

NA: not applicable

ND: not detected

Based on the decline rates observed for triflumezopyrim in the water phase and the total system, the following half-lives (single 1st order kinetics) were determined:

Silt loam sediment/water system: 5 days (water); 36 days (total system)

Sand sediment/water system: 9 days (water); 33 days (total system)

Aerobic degradation in water and water/sediment systems

The rate of degradation of triflumezopyrim in two aerobic water/sediment systems (sand/water and silt loam/water) was studied by Andrews & Cleland (2013, TRIFLUMEZ_051) using [pyridine-^{14}C]- and [pyrimidine-^{14}C]-radiolabelled triflumezopyrim at a nominal application rate of 5 µg ai/g total water.

Test systems were maintained in darkness at a nominal temperature of 20 ± 2°C for 100 days. Volatile organics and CO_2 were trapped with ethanediol and 1 M KOH, respectively. Samples were taken at 0, 1, 14, 28, 60, 75 and 100 days after application.

Sediment and water were separated by decanting the water. The water samples were filtered and directly analysed by HPLC and LSC. The sediment samples were extracted twice with acetonitrile, followed by analysis by LSC for total radioactivity and by HPLC against reference standards to identify metabolites. Confirmation of the identity of triflumezopyrim and metabolites was performed by LC-MS analysis. The sediment remaining after extraction was combusted followed by LSC.

In the sand sediment/water system, the amount of parent declined from 104–105% AR to 83–87% AR after 100 days, while triflumezopyrim in the silt loam sediment/water system declined from 103–107% AR to 77–79% AR. Several unidentified degradation products were observed over the course of the study, but none of them accounted for more than 5% AR.

Table 8 Biotransformation of triflumezopyrim, expressed as percentage of applied radioactivity in an aerobic sand sediment/water system

Degradate	Matrix	Sampling time (days)						
		0	1	14	28	60	75	100
[pyrimidine-^{14}C]-triflumezopyrim								
Triflumezopyrim	Water	103.8%	97.6%	70.6%	59.2%	46.0%	41.6%	38.6%
	Sediment	NS	6.6%	30.4%	36.9%	43.7%	47.2%	48.1%
	Total	103.8%	104.1%	101.0%	95.6%	89.5%	88.7%	86.7%
Unidentified polar components	Water	ND	ND	ND	0.61%	ND	ND	0.74%
	Sediment	NS	0.30%	1.1%	0.28%	ND	ND	ND
	Total	ND	0.30%	1.1%	0.89%	ND	ND	0.74%
Unidentified non-polar components	Water	ND	ND	0.40%	3.4%	4.8%	4.0%	5.2%
	Sediment	NS	0.21%	0.52%	1.4%	1.5%	3.5%	2.2%
	Total	ND	0.21%	0.92%	4.8%	6.3%	7.5%	7.4%
Total extracted radioactivity	Water	103.8%	97.6%	71.0%	63.2%	50.8%	45.6%	44.6%
	Sediment	1.6%	7.1%	32.6%	38.8%	46.6%	51.5%	51.5%
	Total	105.5%	104.6%	103.6%	102.0%	97.3%	97.0%	96.1%
CO_2		NS	< 0.01%	0.02%	0.05%	0.13%	0.18%	0.24%
Volatiles organics		NS	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Unextracted		0.30%	1.3%	3.1%	5.1%	7.9%	7.7%	8.1%
Total		105.8%	105.9%	106.7%	107.2%	105.3%	105.0%	104.4%
[pyridine-^{14}C]-triflumezopyrim								
Triflumezopyrim	Water	104.8%	97.7%	70.1%	54.4%	49.2%	41.1%	37.3%
	Sediment	NS	6.0%	31.3%	35.4%	41.8%	46.8%	45.8%
	Total	104.8%	103.7%	101.4%	87.8%	91.0%	87.8%	83.1%
Unidentified polar components	Water	ND	ND	ND	4.1%	ND	ND	4.7%
	Sediment	NS	0.72%	0.36%	ND	0.23%	0.87%	1.1%
	Total	ND	0.72%	0.36%	4.1%	0.23%	0.87%	5.8%
Unidentified non-polar components	Water	ND	ND	0.60%	3.5%	3.5%	2.7%	2.8%
	Sediment	NS	ND	ND	2.4%	1.9%	2.3%	1.9%
	Total	ND	ND	0.60%	6.0%	5.4%	5.0%	4.6%
Total extracted radioactivity	Water	104.8%	97.7%	70.7%	60.0%	52.8%	43.8%	44.8%
	Sediment	0.98%	6.8%	32.2%	38.6%	44.9%	50.8%	50.1%
	Total	105.8%	104.4%	102.87%	98.6%	97.7%	94.5%	94.9%
CO_2		NS	0.01%	0.14%	0.36%	0.79%	0.92%	1.37%
Volatiles organics		NS	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Unextracted		0.17%	1.5%	3.39%	6.8%	7.1%	9.5%	9.4%
Total		105.9%	105.9%	106.40%	105.7%	105.6%	104.9%	105.6%

NS: no sample

ND: not detected

Table 9 Biotransformation of triflumezopyrim, expressed as percentage of applied radioactivity in an aerobic silt loam sediment/water system

Degradate	Matrix	Sampling time (days)						
		0	1	14	28	60	75	100
[pyrimidine-^{14}C]-triflumezopyrim								
Triflumezopyrim	Water	107.3%	98.8%	61.6%	50.1%	39.9%	35.9%	23.2%
	Sediment	NS	6.3%	40.3%	51.2%	58.4%	58.2%	56.1%
	Total	107.3%	105.1%	101.9%	101.2%	98.4%	94.1%	79.3%
Unidentified polar components	Water	ND	ND	0.91%	0.73%	ND	ND	3.9%
	Sediment	NS	ND	0.15%	ND	ND	ND	0.6%
	Total	ND	ND	1.1%	0.73%	ND	ND	4.5%
Unidentified non-polar components	Water	ND	ND	0.38%	1.3%	1.0%	1.6%	5.1%
	Sediment	NS	0.07%	0.84%	1.00%	1.5%	2.4%	6.0%
	Total	ND	0.07%	1.2%	2.3%	2.6%	4.0%	11.1%
Total extracted radioactivity	Water	107.3%	98.8%	62.9%	52.0%	41.0%	37.6%	32.2%
	Sediment	0.92%	6.4%	41.6%	52.5%	60.0%	60.6%	64.1%
	Total	108.2%	105.1%	104.4%	104.5%	101.0%	98.1%	96.3%
CO_2		NS	< 0.01%	0.02%	0.05%	0.09%	0.13%	0.21%
Volatiles organics		NS	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ

Degradate	Matrix	Sampling time (days)						
		0	1	14	28	60	75	100
Unextracted		0.22%	1.8%	3.3%	5.4%	8.8%	10.3%	11.2%
Total		108.4%	107.0%	107.7%	110.0%	109.8%	108.6%	107.7%
[pyridine-^{14}C]-triflumezopyrim								
Triflumezopyrim	Water	103.4%	94.0%	59.7%	45.8%	28.7%	33.1%	20.8%
	Sediment	NS	10.3%	40.1%	54.0%	60.9%	60.0%	56.1%
	Total	103.4%	104.3%	99.8%	99.8%	89.6%	93.2%	76.9%
Unidentified polar components	Water	ND	ND	0.61%	0.17%	0.72%	ND	2.0%
	Sediment	NS	0.04%	0.15%	0.13%	ND	ND	ND
	Total	ND	0.04%	0.76%	0.30%	0.72%	ND	2.0%
Unidentified non-polar components	Water	1.3%	ND	0.44%	0.54%	1.4%	1.4%	3.5%
	Sediment	NS	0.07%	0.64%	0.58%	3.2%	1.0%	4.8%
	Total	1.3%	0.07%	1.1%	1.1%	4.6%	2.4%	8.3%
Total extracted radioactivity	Water	104.6%	94.0%	60.8%	46.5%	30.8%	34.5%	26.3%
	Sediment	1.4%	10.4%	41.7%	55.5%	64.1%	61.0%	63.4%
	Total	106.0%	104.4%	102.5%	102.0%	94.9%	95.6%	89.7%
CO_2		NS	0.01%	0.07%	0.28%	0.60%	0.81%	1.2%
Volatiles organics		NS	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Unextracted		0.39%	2.9%	3.2%	5.57%	10.6%	9.9%	14.9%
Total		106.4%	107.3%	105.7%	107.8%	106.2%	106.3%	105.8%

NS: no sample

ND: not detected

Based on the decline rates observed for triflumezopyrim alone and the total system, the following half-lives (total system: single 1st order kinetics; water only: double 1st order in parallel kinetics) were determined:

Sand sediment/water system: 41 days (water); 320 days (total system)

Silt loam sediment/water system: 23 days (water); 283 days (total system)

Environmental fate in soil

Soil photolysis

The soil surface photolytic behaviour of triflumezopyrim was investigated by Wardrope (2013, TRIFLUMEZ_030) using [pyridine-^{14}C]-, [methylene-^{14}C]- and [pyrimidine-^{14}C]-radiolabelled triflumezopyrim on both, dry and moist soil surfaces.

Thinly-layered (*ca* 2 mm) soil (Tama, Illinois, USA, silty clay loam) was dosed with radiolabelled triflumezopyrim at 5.0 mg ai/kg soil. The samples were subjected to intermittent irradiation (target 12–14 hours light and 10–12 hours dark cycles) for approximately 15 days at 20 ± 1 °C using a xenon irradiation source with filters to eliminate wavelengths of < 290 nm. Dark control samples were prepared in parallel. Volatile organics and CO_2 were trapped with ethanediol and 2 M NaOH, respectively. The moist irradiated soil samples were analysed at 0, 4, 8, 16, and 24 hours and 2, 5, and 15 days total irradiance, while the dry soil samples were analysed at 0 and 24 hours and 5 days total irradiance.

The soil samples were extracted three times with acetonitrile. Select samples were further extracted where extraction efficiency remained < 90% of the applied radioactivity after three acetonitrile extracts. Extracts were analysed by HPLC to determine the metabolite pattern. Identification of the degradation products was performed by LC MS/MS analysis. The soil remaining after extraction was combusted followed by LSC.

The percentage recovery of the applied radioactivity in moist and dry soil is presented in Tables 10 and 11, respectively. In moist soil, parent triflumezopyrim declined from 95–96% to 43–47% over the irradiation time. At the same time percentage recovery of metabolites IN-Y2186 and IN-RPA19 increased from 0–12% and < 1–11%, respectively. For dry soil, parent triflumezopyrim

declined from 97–99% to 68–74% over the irradiation time. At the same time percentage recovery of metabolites IN-Y2186 and IN-RPA19 increased from 0–15% and < 1–7%, respectively.

Table 10 Phototransformation of triflumezopyrim, expressed as percentage of applied radioactivity, on moist irradiated soil samples

Degradate	Incubation period								Dark controls
	0 hours	4 hours	8 hours	16 hours	24 hours	2 days	5 days	15 days	
[pyrimidine-^{14}C]-triflumezopyrim									
Triflumezopyrim	95.2%	90.2%	93.0%	82.2%	86.8%	70.3%	60.2%	43.6%	90-96%
IN-Y2186	<LOQ	0.47%	<LOQ	4.9%	0.63%	10.4%	20.6%	12.0%	-
Unidentified degradates[a]	1.0%	2.3%	1.7%	<LOQ	4.4%	5.6%	6.6%	11.1%	<1.1%
CO_2	NS	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	0.53%	0.75%	<LOQ-0.14%
Volatiles organics	NS	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Unextracted	5.4%	8.2%	10.6%	4.5%	14.2%	8.3%	12.6%	30.6%	5-8%
Total	101.7%	101.2%	105.4%	91.6%	106.1%	94.8%	101.0%	98.6%	99-102%
[pyridine-^{14}C]-triflumezopyrim									
Triflumezopyrim	96.2%	90.8%	89.3%	89.1%	84.7%	76.8%	62.1%	43.3%	91-98%
IN-RPA19	0.29%	0.64%	0.91%	2.3%	2.6%	5.2%	9.7%	6.5%	-
Unidentified degradates[a]	0.68%	0.84%	2.1%	4.6%	4.2%	5.7%	8.9%	6.0%	<1.5%
CO_2	NS	<LOQ	<LOQ	<LOQ	<LOQ	0.27%	0.68%	1.2%	<LOQ
Volatiles organics	NS	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	0.26%	<LOQ
Unextracted	5.6%	10.0%	11.0%	6.5%	9.1%	8.8%	11.9%	33.4%	5-9%
Total	102.8%	102.3%	103.5%	102.6%	100.5%	96.7%	93.5%	92.1%	99-103%
[methylene-^{14}C]-triflumezopyrim									
Triflumezopyrim	94.5%	94.9%	88.4%	83.8%	71.8%	74.6%	54.4%	46.5%	90-98%
IN-RPA19	0.35%	0.98%	1.9%	3.3%	5.0%	7.4%	8.7%	10.6%	-
Unidentified degradates[a]	0.76%	1.4%	5.2%	4.4%	10.8%	9.8%	10.8%	13.6%	<1.6%
CO_2	NS	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	0.21%	1.6%	<LOQ
Volatiles organics	NS	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Unextracted	4.8%	7.3%	8.7%	11.0%	5.0%	9.1%	13.4%	23.4%	4-10%
Total	100.5%	104.6%	104.2%	102.6%	92.6%	100.9%	87.4%	96.0%	98-106%

NS: no sample

[a] No individual unidentified component accounts for >5% AR

Table 11 Phototransformation of triflumezopyrim, expressed as percentage of applied radioactivity, on dry irradiated soil samples

Degradate	Incubation period		
	0 hours	24 hours	5 days
[pyrimidine-^{14}C]-triflumezopyrim			
Triflumezopyrim	98.5%	97.0%	67.5%
IN-Y2186	<LOQ	<LOQ	14.7%
Unidentified degradates [a]	0.45%	1.4%	6.0%
CO_2	NS	0.14%	1.5%
Volatiles organics	NS	<LOQ	<LOQ
Unextracted	2.8%	6.7%	3.6%
Total	101.8%	105.4%	93.3%
[pyridine-^{14}C]-triflumezopyrim			
Triflumezopyrim	99.1%	85.9%	67.9%
IN-RPA19	<LOQ	5.0%	5.4%
Unidentified degradates [a]	0.00%	0.00%	9.6%
CO2	NS	0.15%	<LOQ
Volatiles organics	NS	<LOQ	0.19%
Unextracted	1.4%	8.6%	6.9%
Total	100.5%	99.6%	90.1%
[methylene-^{14}C]-triflumezopyrim			
Triflumezopyrim	97.4%	79.6%	74.2%
IN-RPA19	0.55%	7.1%	7.4%
Unidentified degradates [a]	0.00%	3.3%	1.5%
CO2	NS	<LOQ	<LOQ
Volatiles organics	NS	<LOQ	<LOQ

Degradate	Incubation period		
	0 hours	24 hours	5 days
Unextracted	1.2%	9.7%	7.7%
Total	99.1%	99.9%	90.8%

NS: no sample

[a] No individual unidentified component accounts for >5% AR

Based on the decline rate observed for triflumezopyrim, a half-life time of 12 days under intermittent irradiation was estimated (single 1st order kinetics) for soil.

Aerobic soil metabolism

The metabolism of triflumezopyrim was investigated in two aerobic soil systems by Lowrie (2015, TRIFLUMEZ_031) using [pyridine-^{14}C]-, [methylene-^{14}C]- and [pyrimidine-^{14}C]-radiolabelled triflumezopyrim.

Samples of field soil (Tama, USA, silty clay loam, pH 6.2, 3.4% organic matter, 22.25% moisture) and paddy soil (Kumagaya, Japan, loam, pH 5.5, 1.6% organic matter, 13.89% moisture) were dosed with radiolabelled triflumezopyrim at 1.0 µg/g total dry soil. Test systems were maintained in darkness at a nominal temperature of 25 ± 1°C for 178 days. Volatile organics and CO_2 were trapped with ethanediol and 1 M NaOH, respectively. Samples were taken at 0, 7, 14, 28, 60, 90, 120, 150 and 178 days after application.

The soil samples were extracted three times with acetonitrile. Extracts were analysed by HPLC to determine the metabolite pattern. Confirmation of the identity of triflumezopyrim and metabolites was performed by LC MS/MS analysis. The soil remaining after extraction was combusted followed by LSC.

The percentage recovery of the applied radioactivity in field and paddy soil is presented in Tables 12 and 13, respectively. In both soils, parent triflumezopyrim declined from 91–106% to 13–28% over the study time. At the same time CO_2 increased from < 1–5% to 10–37%, indicating significant mineralization. Identified metabolites were IN-RPD47 up to 3% in paddy soil at day 120; IN-SBY68 up to 8% in field soil at day 150; IN-SBV06 up to 3% in field soil at day 7 and IN-RPA16 (only in [methylene-^{14}C]-triflumezopyrim) around 1% in both soils.

Table 12 Metabolism of triflumezopyrim, expressed as percentage of applied radioactivity in field soil (Tama)

Degradate	Sampling time (days)								
	0	7	14	28	60	90	120	150	178
[pyrimidine-^{14}C]-triflumezopyrim									
Triflumezopyrim	92.6%	75.9%	61.4%	48.0%	29.3%	21.4%	19.0%	19.4%	18.1%
IN-RPD47	ND	0.34%	ND	0.34%	0.68%	0.56%	0.29%	0.36%	0.44%
IN-SBY68	ND	0.40%	2.8%	4.1%	6.0%	7.0%	6.4%	7.7%	7.1%
IN-SBV06	ND	2.3%	2.9%	2.2%	1.6%	1.3%	0.80%	0.85%	0.76%
Unidentified degradates	1.2%	4.4%	3.8%	5.6%	5.0%	2.0%	3.3%	2.2%	3.2%
Total extracted radioactivity	93.8%	83.3%	71.0%	42.5%	29.3%	32.2%	29.8%	30.6%	29.6%
CO_2	NS	4.6%	9.0%	16.0%	27.4%	31.6%	34.2%	35.9%	37.2%
Volatiles organics	NS	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Unextracted	4.8%	15.4%	23.3%	27.1%	28.9%	30.9%	34.3%	29.3%	30.4%
Total	98.6%	103.3%	103.3%	103.3%	98.9%	94.8%	98.3%	95.8%	97.2%
[pyridine-^{14}C]-triflumezopyrim									
Triflumezopyrim	96.5%	77.4%	60.7%	52.6%	39.4%	32.3%	33.4%	28.9%	24.8%
IN-RPD47	ND	0.24%	0.21%	0.22%	0.80%	0.24%	0.63%	0.66%	0.84%
IN-SBY68	ND	1.6%	2.6%	4.7%	5.4%	6.2%	6.0%	6.3%	6.8%
IN-SBV06	ND	2.6%	3.0%	2.6%	2.1%	1.4%	1.2%	0.52%	0.90%
Unidentified degradates	0.42%	5.4%	7.7%	6.3%	5.1%	4.2%	5.2%	4.8%	3.5%
Total extracted radioactivity	96.9%	87.3%	74.1%	66.4%	52.8%	44.4%	46.4%	41.2%	36.9%
CO_2	NS	1.2%	2.9%	5.9%	11.9%	15.8%	18.7%	21.0%	22.8%

Degradate	Sampling time (days)								
	0	7	14	28	60	90	120	150	178
Volatiles organics	NS	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Unextracted	5.2%	19.0%	28.8%	34.2%	36.6%	39.3%	40.3%	38.9%	42.4%
Total	102.1%	107.6%	106.0%	106.5%	101.3%	99.5%	105.4%	101.1%	102.0%
[methylene-^{14}C]-triflumezopyrim									
Triflumezopyrim	99.5%	77.3%	59.3%	41.2%	21.8%	18.6%	15.2%	14.9%	16.3%
IN-RPA16	0.56%	0.92%	1.2%	0.97%	0.77%	0.44%	0.4%	0.32%	0.43%
IN-SBY68	ND	1.1%	2.4%	4.9%	7.4%	6.2%	5.5%	6.7%	6.9%
IN-SBV06	0.09%	3.4%	3.1%	2.4%	1.7%	1.2%	0.68%	0.88%	0.93%
Unidentified degradates	0.12%	2.6%	5.2%	7.5%	4.2%	4.4%	5.3%	3.3%	3.1%
Total extracted radioactivity	100.2%	85.4%	71.2%	56.9%	36.0%	30.9%	27.2%	26.2%	27.7%
CO_2	NS	1.6%	4.6%	11.1%	21.8%	26.1%	28.8%	30.8%	32.3%
Volatiles organics	NS	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Unextracted	4.9%	17.2%	27.2%	34.9%	42.3%	40.7%	46.0%	38.4%	39.7%
Total	105.1%	104.2%	103.5%	102.8%	100.1%	97.8%	102.0%	95.4%	99.7%

NS: no sample

ND: not detected

Table 13 Metabolism of triflumezopyrim, expressed as percentage of applied radioactivity in paddy soil (Kumagaya)

Degradate	Sampling time (days)								
	0	7	14	28	60	90	120	150	178
[pyrimidine-^{14}C]-triflumezopyrim									
Triflumezopyrim	95.5%	76.6%	58.4%	52.0%	40.2%	37.6%	33.9%	28.4%	24.0%
IN-RPD47	ND	0.24%	0.55%	0.41%	1.2%	1.2%	2.7%	0.82%	0.90%
IN-SBY68	ND	ND	0.21%	0.81%	0.76%	1.4%	1.6%	1.1%	1.3%
IN-SBV06	ND	0.20%	0.30%	0.45%	0.62%	0.67%	0.89%	0.86%	0.97%
Unidentified degradates	1.3%	2.5%	2.7%	3.0%	1.6%	0.99%	0.34%	2.2%	2.2%
Total extracted radioactivity	96.8%	79.5%	62.2%	56.7%	44.4%	41.9%	39.4%	33.3%	29.4%
CO_2	NS	4.5%	8.8%	13.8%	21.2%	25.6%	28.3%	30.5%	32.2%
Volatiles organics	NS	<LOQ	0.10	0.10	0.10	0.10	0.10	0.10	0.10
Unextracted	7.3%	19.0%	30.9%	32.2%	37.3%	38.8%	39.7%	41.4%	39.2%
Total	104.2%	103.0%	101.9%	102.8%	103.0%	106.4%	107.4%	105.4%	100.9%
[pyridine-^{14}C]-triflumezopyrim									
Triflumezopyrim	106.2%	83.0%	69.8%	61.6%	47.6%	39.4%	35.1%	35.8%	27.7%
IN-RPD47	ND	0.22%	0.16%	0.52%	0.57%	1.2%	2.4%	1.4%	0.97%
IN-SBY68	ND	0.27%	0.35%	0.51%	1.2%	1.0%	1.6%	0.82%	0.88%
IN-SBV06	ND	0.30%	0.39%	0.31%	0.91%	0.68%	0.80%	0.67%	1.0%
Unidentified degradates	1.3%	2.3%	2.1%	2.4%	3.8%	1.8%	2.3%	3.9%	4.4%
Total extracted radioactivity	107.5%	86.1%	72.8%	65.4%	54.1%	44.2%	42.2%	42.6%	35.0%
CO_2	NS	0.35%	0.81%	1.7%	3.9%	5.8%	7.3%	8.5%	9.5%
Volatiles organics	NS	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Unextracted	8.0%	20.6%	31.3%	39.8%	48.0%	49.6%	52.2%	60.9%	58.2%
Total	115.4%	107.1%	105.0%	106.8%	106.1%	99.6%	101.7%	112.0%	102.6%
[methylene-^{14}C]-triflumezopyrim									
Triflumezopyrim	91.3%	78.3%	58.4%	60.4%	21.6%	18.9%	14.0%	30.6%	13. %
IN-RPA16	1.4%	0.88%	0.63%	0.91%	0.92%	1.0%	0.86%	0.72%	0.79%
IN-SBY68	ND	0.15%	0.28%	0.64%	0.62%	1.0%	1.1%	0.88%	1.2%
IN-SBV06	ND	0.31%	0.53%	0.59%	0.51%	0.60%	0.09%	0.66%	0.49%
Unidentified degradates	ND	1.2%	3.0%	2.2%	4.5%	2.4%	3.9%	3.5%	2.0%
Total extracted radioactivity	92.8%	80.9%	62.8%	64.7%	28.1%	23.9%	20.0%	36.3%	17.5%
CO_2	NS	0.47%	1.6%	4.3%	11.1%	15.0%	17.8%	20.1%	22.1%
Volatiles organics	NS	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Unextracted	7.2%	20.9%	38.3%	34.3%	58.7%	58.8%	56.0%	49.1%	56.5%
Total	100.0%	102.3%	102.7%	103.4%	97.9%	97.7%	93.8%	105.7%	96.1%

NS: no sample

ND: not detected

Based on the decline rate observed for triflumezopyrim, a half-life time of 53 days and 72 days was estimated (single 1st order kinetics) for field and paddy soil, respectively (Table 14)

Table 14 Calculated DT_{50} and DT_{90} values for triflumezopyrim in Tama and Kumagaya soil

Soil system	Phase	DT_{50} (days)	DT_{90} (days)
Silty clay loam field soil (Tama)	Soil	52.9	175.6
Loam paddy soil (Kumagaya)	Soil	71.9	239.0

In a second study by Bell (2014, TRIFLUMEZ_032), the metabolism of triflumezopyrim was investigated in flooded aerobic soil under viable and sterile conditions using [methylene-^{14}C]- and [pyrimidine-^{14}C]-radiolabelled triflumezopyrim.

Samples of rice paddy soil (Kumagaya, Japan, loam, pH 5.7, 1.6% organic matter, 5.4% moisture) were dosed with radiolabelled triflumezopyrim at 0.2 µg ai/g of soil (dry weight equivalent). The test item solution was applied to the surface water of test system followed by stirring to bring the soil in suspension. The soil:water ratio was 5:1 based on height, with a soil height of ca 5 cm and water column height of ca 1 cm. Viable and sterile incubations were maintained for up to 180 days under aerobic conditions in the dark at 25 °C. Volatile organics and CO_2 were trapped with ethanediol and 1 M NaOH, respectively. Samples were analysed after 0, 7 (viable samples only), 30, 60, 90 (viable samples only) 120, 150 (viable samples only) and 180 days of incubation.

The surface water samples were filtered and directly analysed by HPLC and LSC. The soil samples were extracted with acetonitrile followed by acetonitrile: 0.1 N acetic acid (9:1, v/v). Extracts were analysed by LSC for total radioactivity and by HPLC against reference standards to identify metabolites. Confirmation of the identity of triflumezopyrim and metabolites was performed by TLC analysis. The soil remaining after extraction was combusted followed by LSC.

In flooded aerobic soil incubated under viable condition, the amount of parent detected in the test system declined from 89–94% AR to 45–46% AR after 180 days. In comparison, dissipation was lower in flooded aerobic soil incubated under sterile conditions with the amount of parent detected in the test system declining from 92–95% AR at zero time to 77–79% AR after 180 days. No major metabolites were observed at > 10% AR at any sampling interval. Multiple minor components were observed including IN-RPD47 and IN-RPA16, none of which were considered major (see Tables 15 and 16).

Table 15 Biotransformation of triflumezopyrim, expressed as percentage of applied radioactivity in a viable flooded soil (Kumagaya)

Degradate	Matrix	Sampling time (days)							
		0	7	30	60	90	120	150	180
[pyrimidine-^{14}C]-triflumezopyrim									
Triflumezopyrim	Water	15.4%	7.0%	2.3%	3.3%	2.2%	2.6%	1.1%	1.2%
	Soil	73.2%	61.6%	51.0%	51.4%	51.9%	42.6%	42.8%	44.4%
	Total	88.5%	68.6%	53.3%	54.7%	54.1%	45.1%	43.9%	45.7%
IN-RPD47	Water	ND	ND	ND	ND	ND	ND	ND	ND
	Soil	ND	ND	ND	0.35%	ND	ND	ND	ND
	Total	ND	ND	ND	0.35%	ND	ND	ND	ND
Unidentified radioactivity	Water	0.6%	1.8%	1.5%	1.7%	0.59%	1.7%	0.81%	0.65%
	Soil	1.2%	2.8%	6.4%	5.5%	4.4%	6.4%	6.1%	4.6%
	Total	1.8%	4.6%	8.0%	6.8%	5.0%	8.2%	7.0%	5.2%
Total extracted radioactivity	Water	16.0%	8.7%	3.8%	5.0%	2.8%	4.3%	1.9%	1.9%
	Soil	74.3%	64.4%	57.5%	56.9%	56.3%	49.0%	48.9%	49.0%
	Total	90.3%	73.2%	61.3%	61.8%	59.1%	53.3%	50.4%	50.9%
CO_2		NS	0.21%	0.91%	1.5%	2.0%	2.5%	3.2%	3.8%
Unextracted		6.5%	26.7%	44.0%	43.2%	42.5%	45.5%	52.6%	51.9%
Total		96.9%	100.1%	106.2%	106.6%	103.6%	101.3%	106.6%	106.7%
[methylene-^{14}C]-triflumezopyrim									
Triflumezopyrim	Water	11.9%	7.2%	2.5%	2.3%	2.8%	1.8%	1.4%	1.6%
	Soil	82.5%	59.2%	48.8%	49.4%	45.4%	44.9%	41.2%	43.1%
	Total	94.4%	66.5%	51.2%	51.7%	48.2%	46.7%	42.6%	44.7%

Degradate	Matrix	Sampling time (days)							
		0	7	30	60	90	120	150	180
IN-RPA16	Water	0.10%	ND	0.08%	ND	ND	ND	ND	ND
	Soil	ND	ND	0.96%	0.82%	ND	ND	ND	1.1%
	Total	0.10%	ND	1.0%	0.82%	ND	ND	ND	1.1%
Unidentified radioactivity	Water	0.06%	1.4%	0.57%	0.53%	0.40%	0.57%	0.55%	0.23%
	Soil	1.1%	1.7%	4.0%	4.4%	4.9%	2.5%	3.5%	4.4%
	Total	1.1%	3.0%	4.6%	5.0%	5.3%	3.1%	4.0%	4.6%
Total extracted radioactivity	Water	12. %	8.8%	3.2%	2.8%	3.2%	2.4%	1.9%	1.8%
	Soil	83.610%	60.9%	53.8%	54.6%	50.3%	47.4%	44.7%	48.6%
	Total	95.7%	69.5%	56.9%	57.5%	53.6%	49.8%	46.6%	50.4%
CO_2		NS	0.19%	0.77%	1.5%	2.0%	2.4%	2.7%	3.4%
Unextracted		5.2%	28.2%	43.0%	41.8%	47.4%	43.4%	50.1%	45.9%
Total		100.9%	98.0%	100.6%	100.8%	103.0%	95.6%	99.4%	99.7%

NS: no sample

ND: not detected

Table 16 Biotransformation of triflumezopyrim, expressed as percentage of applied radioactivity in a sterile flooded soil (Kumagaya)

Degradate	Matrix	Sampling time (days)				
		0	30	60	120	180
[pyrimidine-^{14}C]-triflumezopyrim						
Triflumezopyrim	Water	11.9%	6.7%	4.2%	3.2%	2.7%
	Soil	79.7%	81.5%	80.4%	80.0%	74.4%
	Total	91.5%	88.2%	84.7%	83.2%	77.1%
IN-RPD47	Water	ND	ND	ND	ND	0.09%
	Soil	0.27%	ND	0.55%	0.67%	0.81%
	Total	0.27%	ND	0.55%	0.67%	0.90%
Unidentified radioactivity	Water	0.52%	0.38%	0.45%	0.41%	0.44%
	Soil	2.0%	3.0%	3.3%	ND	3.6%
	Total	2.5%	3.4%	3.8%	0.41%	4.0%
Total extracted radioactivity	Water	12.4%	7.2%	4.7%	3.6%	3.2%
	Soil	81.9%	84.4%	84.3%	80.7%	78.8%
	Total	94.3%	91.6%	89.0%	84.3%	82.0%
Unextracted		2.6%	10.5%	16.5%	18.0%	19.4%
Total		97.0%	102.1%	105.5%	102.3%	101.4%
[methylene-^{14}C]-triflumezopyrim						
Triflumezopyrim	Water	2.2%	3.6%	4.1%	3.8%	2.6%
	Soil	92.8%	83.5%	77.2%	75.6%	76.2%
	Total	95.0%	87.1%	81.4%	79.4%	78.8%
IN-RPA16	Water	ND	ND	ND	ND	0.04%
	Soil	ND	ND	0.32%	ND	ND
	Total	ND	ND	0.32%	ND	0.04%
Unidentified radioactivity	Water	ND	0.02%	0.08%	0.07%	0.08%
	Soil	1.3%	1.8%	4.6%	0.65%	1.4%
	Total	1.3%	1.9%	4.7%	0.72%	1.4%
Total extracted radioactivity	Water	2.2%	3.6%	4.2%	3.9%	2.7%
	Soil	94.1%	85.4%	81.8%	76.2%	77.6%
	Total	96.3%	89.0%	86.0%	80.1%	80.3%
Unextracted		2.9%	12.7%	17.2%	19.0%	24.8%
Total		99.2%	101.7%	103.2%	99.1%	105.1%

ND: not detected

Based on the overall decline rate observed for triflumezopyrim, a half-life time of 184 days and 740 days was estimated (single 1st order kinetics) for viable and sterile paddy soil, respectively (Table 17).

Table 17 Calculated DT_{50} and DT_{90} values for triflumezopyrim in viable and sterile paddy soil

Test System	Phase	DT_{50} (days)	DT_{90} (days)
Viable	Total system	183.7	610.2
Sterile	Total system	739.7	2457.0

Aerobic degradation in soil

The rate of degradation of triflumezopyrim was studied in three aerobic soil systems by Sannappa (2015, TRIFLUMEZ_033) using [pyridine-^{14}C]- and [pyrimidine-^{14}C]-radiolabelled triflumezopyrim at a nominal application rate of 5 µg/g oven dry soil. Soil characteristics are shown in Table 18.

Table 18 Characteristic of used soils

Soil Name	Texture	Soil Origin	pH		% Organic Matter
			Water	0.01 M CaCl2	
Lleida	Clay	Spain	7.7	7.5	3.5
Speyer	Loamy sand	Germany	5.6	5.3	3.0
Sassafras	Sandy loam	USA	6.3	5.7	2.0

Test systems were maintained in darkness at a nominal temperature of 25 ± 2 °C for 180 days. Volatile organics and CO_2 were trapped with ethanediol and 1 M KOH, respectively. Samples were taken at 0, 1, 14, 28, 60, 90, 120 and 178 days after application.

The soil samples were extracted three times with acetonitrile. Extracts were analysed by LSC for total radioactivity and by HPLC against reference standards to identify metabolites. Confirmation of the identity of triflumezopyrim and metabolites was performed by LC MS/MS analysis. The soil remaining after extraction was combusted followed by LSC.

In all soils, parent triflumezopyrim declined from 89–100% to 17–44% over the study time. Identified metabolites were IN-RPD47 and IN-SBY68 accounting for up to 9% and up to 8% at day 180, respectively (Tables 19 to 21).

Table 19 Biotransformation of triflumezopyrim, expressed as percentage of applied radioactivity in Lleida soil

Degradate	Sampling time (days)							
	0	1	14	28	60	90	120	180
[pyridine-^{14}C]-triflumezopyrim								
Triflumezopyrim	95.3%	92.1%	72.2%	60.9%	37.4%	28.3%	20.2%	16.6%
IN-RPD47	<LOQ	<LOQ	2.4%	4.6%	6.1%	5.9%	5.1%	4.0%
IN-SBY68	<LOQ	<LOQ	1.7%	2.5%	5.9%	6.9%	6.3%	4.8%
Others[1]	1.5%	<LOQ	<LOQ	<LOQ	4.4%	3.1%	3.4%	3.7%
Total extracted radioactivity	96.8%	92.1%	76.3%	68.0%	53.8%	44.2%	35.0%	29.1%
Non-extracted residue	1.8%	4.9%	16.7%	25.4%	38.8%	47.6%	55.8%	61.4%
Cumulative $^{14}CO_2$	ns	<LOQ	0.1%	0.2%	0.4%	0.6%	0.7%	0.8%
Volatile organics	ns	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Material Balance	98.6%	97.0%	93.1%	93.6%	93.0%	92.4%	91.5%	91.3%
[pyrimidine-^{14}C]-triflumezopyrim								
Triflumezopyrim	100.0%	95.2%	78.9%	64.7%	54.1%	38.6%	31.1%	19.9%
IN-RPD47	<LOQ	<LOQ	2.4%	4.5%	4.6%	6.3%	6.7%	4.7%
IN-SBY68	<LOQ	<LOQ	<LOQ	2.5%	4.0%	5.5%	5.9%	8.3%
Others [a]	<LOQ	<LOQ	<LOQ	3.0%	3.2%	4.1%	3.7%	6.0%
Total extracted radioactivity	100.0%	95.2%	81.3%	74.7%	65.9%	54.5%	47.4%	38.9%
Unextracted residue	2.0%	5.8%	12.5%	19.5%	26.6%	36.6%	43.2%	51.4%
Cumulative $^{14}CO_2$	ns	<LOQ	0.1%	0.2%	0.4%	0.5%	0.6%	0.7%
Volatile organics	ns	<LOQ	0.1%	0.1%	0.1%	0.1%	0.1%	0.1%
Material Balance	102.0%	101.0%	94.0%	94.5%	93.0%	91.7%	91.3%	91.1%

ns: no sample

[a] Consists of multiple components, none of which exceed 5% AR

Table 20 Biotransformation of triflumezopyrim, expressed as percentage of applied radioactivity in Speyer soil

Degradate	Sampling time (days)							
	0	1	14	28	60	90	120	180
[pyridine-^{14}C]-triflumezopyrim								
Triflumezopyrim	89.3%	86.6%	77.5%	69.4%	55.9%	50.0%	41.3%	39.3%
IN-RPD47	<LOQ	<LOQ	<LOQ	1.9%	2.9%	3.8%	2.7%	1.9%
IN-SBY68	<LOQ	<LOQ	<LOQ	1.5%	2.8%	2.7%	3.7%	3.7%
Others[1]	<LOQ	<LOQ	<LOQ	1.3%	1.9%	3.9%	5.9%	3.6%
Total extracted radioactivity	89.3%	86.6%	77.5%	74.1%	63.5%	60.4%	53.6%	48.5%
Unextracted residue	3.1%	5.1%	13.9%	17.6%	28.0%	30.8%	37.7%	42.4%
Cumulative $^{14}CO_2$	ns	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	0.1%	0.2%
Volatile organics	ns	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Material Balance	92.4%	91.7%	91.4%	91.7%	91.5%	91.2%	91.4%	91.1%
[pyrimidine-^{14}C]-triflumezopyrim								
Triflumezopyrim	94.3%	88.7%	78.7%	69.8%	59.4%	56.6%	49.9%	42.4%
IN-RPD47	<LOQ	<LOQ	1.7%	1.7%	2.1%	3.2%	1.7%	2.4%
IN-SBY68	<LOQ	<LOQ	<LOQ	2.4%	2.7%	2.3%	2.5%	3.0%
Others [a]	<LOQ	<LOQ	<LOQ	<LOQ	1.2%	1.5%	6.5%	4.9%
Total extracted radioactivity	94.3%	88.7%	80.4%	73.9%	65.4%	63.6%	60.6%	52.7%
Unextracted residue	3.5%	6.2%	12.8%	19.4%	27.2%	29.0%	31.6%	38.0%
Cumulative $^{14}CO_2$	ns	<LOQ	0.1%	0.2%	0.3%	0.4%	0.5%	0.7%
Volatile organics	ns	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Material Balance	97.8%	94.9%	93.3%	93.5%	92.9%	93.0%	92.7%	91.4%

ns: no sample

[a] Consists of multiple components, none of which exceed 5% AR

Table 21 Biotransformation of triflumezopyrim, expressed as percentage of applied radioactivity in Sassafras soil

Degradate	Sampling time (days)							
	0	1	14	28	60	90	120	180
[pyridine-^{14}C]-triflumezopyrim								
Triflumezopyrim	89.2%	90.2%	72.0%	61.9%	51.5%	49.0%	42.1%	39.9%
IN-RPD47	<LOQ	<LOQ	1.5%	3.2%	8.1%	8.6%	8.9%	9.1%
IN-SBY68	<LOQ	<LOQ	3.6%	3.9%	2.8%	2.9%	3.0%	1.8%
Others[1]	1.5%	<LOQ	3.1%	2.2%	2.2%	2.5%	3.0%	4.7%
Total extracted radioactivity	90.7%	90.2%	80.2%	71.2%	64.6%	63.0%	57.0%	55.5%
Unextracted residue	3.6%	6.0%	16.1%	21.2%	29.9%	30.4%	35.8%	36.7%
Cumulative $^{14}CO_2$	ns	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	0.1%
Volatile organics	ns	<LOQ	<LOQ	0.1%	0.1%	0.1%	0.1%	0.1%
Material Balance	94.3%	96.2%	96.3%	92.5%	94.6%	93.5%	92.9%	92.4%
[pyrimidine-^{14}C]-triflumezopyrim								
Triflumezopyrim	89.8%	86.6%	73.8%	66.1%	59.3%	53.3%	47.1%	44.1%
IN-RPD47	<LOQ	<LOQ	1.3%	3.0%	4.9%	7.9%	8.8%	8.6%
IN-SBY68	<LOQ	<LOQ	2.1%	4.0%	3.0%	2.8%	2.4%	1.7%
Others [a]	<LOQ	<LOQ	1.6%	<LOQ	<LOQ	<LOQ	<LOQ	1.4%
Total extracted radioactivity	89.8%	86.6%	78.8%	73.1%	67.2%	64.0%	58.3%	55.8%
Unextracted residue	3.0%	5.7%	13.2%	18.9%	24.2%	27.9%	32.9%	34.4%
Cumulative $^{14}CO_2$	ns	<LOQ	0.1%	0.2%	0.3%	0.3%	0.4%	0.5%
Volatile organics	ns	<LOQ	0.3%	0.3%	0.3%	0.3%	0.4%	0.7%
Material Balance	92.8%	92.3%	92.4%	92.5%	92.0%	92.5%	92.0%	91.4%

ns: no sample

[a] Consists of multiple components, none of which exceed 5% AR

Based on the decline rate observed for triflumezopyrim, a half-life time of 61, 132 and 133 days was estimated (single 1st order kinetics) for Lleida, Speyer and Sassafras soil, respectively (see Table 22).

Table 22 Calculated DT_{50} and DT_{90} values for triflumezopyrim

Soil name	DT_{50} (Days)	DT_{90} (Days)	r^2	χ^2
Lleida	60.5	201	0.959	6
Speyer	131.9	438.2	0.917	6
Sassafras	133.4	443.2	0.860	8

Confined rotational crops

A confined rotational crop study by Shankey, *et al*. (2015, TRIFLUMEZ_027) was conducted with [pyridine-^{14}C]-, [methylene-^{14}C]- and [pyrimidine-^{14}C]-radiolabelled triflumezopyrim applied at a rate of 0.1 kg ai/ha to a sandy loam soil under glasshouse conditions. After plant-back intervals (PBIs) of 30, 120 and 268 days lettuce, radish and wheat were cultivated as rotational crops.

Lettuce plants were sampled when immature (BBCH 45), and at normal maturity (BBCH 49). Spring wheat was sampled at forage (BBCH 30), hay (BBCH 61–85) and at maturity (BBCH 89). Radish plants were sampled when immature (BBCH 45, foliage only) and at maturity (BBCH 49)

The TRR in the samples was determined by combustion and LSC. Where initial combustion analysis revealed TRR concentrations greater than 0.010 mg/kg, subsamples of homogenized tissues were extracted two times with methanol followed by two times with methanol/water (7:3, v/v). Radioactivity in the post-extraction solids of wheat straw samples (30 d PBI for [pyridine-^{14}C]- and [pyrimidine-^{14}C]-triflumezopyrim; all PBIs for [methylene-^{14}C]-triflumezopyrim) were additionally extracted with water, acetonitrile, driselase in sodium acetate buffer, 1M hydrochloric acid and 0.1M sodium hydroxide. HPLC against reference compounds were applied for the characterisation and identification of the radioactivity.

TRR levels found in the model crops generally declined with longer PBIs. A summary of all TRRs found is presented in Table 23.

Table 23 Total radioactive residues in rotational crops after application of [^{14}C]-triflumezopyrim to bare soil at rates of 0.1 kg ai/ha

Crop matrix	30 d PBI		120 d PBI		268 d PBI	
	DAT	mg eq/kg	DAT	mg eq/kg	DAT	mg eq/kg
[pyridine-^{14}C]-triflumezopyrim						
Immature lettuce	73	0.003	162	0.005	303	0.006
Mature lettuce	87	0.003	176	0.003	326	<LOQ
Immature radish top	57	0.005	150	0.002	303	<LOQ
Mature radish root	73	0.005	169	0.001	316	<LOQ
Mature radish top	73	0.004	169	0.002	316	<LOQ
Spring wheat forage	57	0.008	176	0.001	316	<LOQ
Spring wheat hay	115	0.007	211	0.002	343	<LOQ
Spring wheat straw	195	0.021	291	0.011	378	0.010
Spring wheat grain	195	0.003	291	0.004	378	<LOQ
[methylene-^{14}C]-triflumezopyrim						
Immature lettuce	73	0.003	162	0.003	303	<LOQ
Mature lettuce	87	0.003	176	0.002	326	<LOQ
Immature radish top	57	0.005	150	0.001	303	<LOQ
Mature radish root	73	0.005	169	0.001	316	<LOQ
Mature radish top	73	0.008	169	0.003	316	<LOQ
Spring wheat forage	57	0.007	176	0.004	316	<LOQ
Spring wheat hay	115	0.018	211	0.005	343	<LOQ
Spring wheat straw	195	0.040	291	0.027	378	0.023
Spring wheat grain	195	0.004	291	0.004	378	<LOQ
[pyrimidine-^{14}C]-triflumezopyrim						
Immature lettuce	73	0.004	162	0.003	303	0.005
Mature lettuce	87	0.004	176	0.001	326	<LOQ
Immature radish top	57	0.006	150	0.002	303	<LOQ
Mature radish root	73	0.007	169	0.001	316	<LOQ
Mature radish top	73	0.009	169	0.004	316	<LOQ

Crop matrix	30 d PBI		120 d PBI		268 d PBI	
	DAT	mg eq/kg	DAT	mg eq/kg	DAT	mg eq/kg
Spring wheat forage	57	0.006	176	0.004	316	<LOQ
Spring wheat hay	115	0.008	211	0.005	343	<LOQ
Spring wheat straw	195	0.030	291	0.019	378	0.022
Spring wheat grain	195	0.003	291	0.002	378	<LOQ

Straw samples (from all radiolabels and soil ageing intervals) and the [methylene-^{14}C]-triflumezopyrim hay sample (30-day soil ageing interval) with residues >0.010 mg/kg were extracted. Other commodities were < 0.010 mg/kg and were not analysed further. The results of the identification of radioactive residues are presented in Tables 24 to 26.

In all samples the major identified compound was parent triflumezopyrim ranging from 0.001 mg eq/kg (7.5% TRR) in [pyridine-^{14}C]-triflumezopyrim straw at 268 d PBI to 0.008 mg eq/kg (30.2% TRR) in [methylene-^{14}C]-triflumezopyrim straw at 120 d PBI:

Other identified metabolites comprised of IN-R6U70, IN-RPA19, IN-R3Z91, IN-RPD47, IN-Y2186, IN-SBV06. Of these metabolites IN-RPD47 was highest in [pyridine-^{14}C]-triflumezopyrim straw at 30 d PBI with 0.002 mg eq/kg (7.2% TRR).

Multiple other unknown metabolites were characterized by HPLC, but none accounted for more than 0.003 mg eq/kg (14.6% TRR).

Table 24 Summary of identified/characterized residues in rotational crops following application of [pyridine-^{14}C]-triflumezopyrim

Fraction / Solubilizate	Radioactive residues in mg eq/kg (% TRR) Wheat straw		
	30 d PBI	120 d PBI	268 d PBI
TRR	0.026 (100%)	0.011 (100%)	0.008 (100%)
Triflumezopyrim	0.007 (25.5%)	0.004 (28.4%)	0.001 (7.5%)
IN-RPA19	0.001 (5.1%)	0.001 (4.9%)	< 0.001 (3.3%)
IN-R3Z91	-	< 0.001 (1.7%)	-
IN-RPD47	0.002 (7.2%)	< 0.001 (3.9%)	< 0.001 (4.6%)
IN-SBV06	0.001 (2.5%)	0.001 (5.2%)	-
Total identified	0.011 (40.3%)	0.006 (44.1%)	0.001 (15.4%)
Characterized by HPLC	0.004 (13.9%)	< 0.001 (11.8%)	0.002 (32.7%)
Further methanol:water extracts	<LOQ	-	0.001 (12.7%)
Acetonitrile soak	0.001 (2.6%)	-	-
Water soak	0.002 (4.8%)	-	-
Post extraction solids	0.010 (38.2%)	0.005 (44.2%)	0.003 (39.1%)
Enzyme extract	0.001 (2.3%)	-	-
1M HCl	0.001 (4.4%)	-	-
0.1M NaOH	0.002 (8.2%)	-	-
Total characterized	0.011 (36.2%)	< 0.001 (11.8%)	0.003 (45.4%)
Unextracted	0.006 (23.3%)	0.005 (44.2%)	0.003 (39.1%)
Total	0.028 (107.7%)	0.011 (100.0%)	0.007 (87.5%)

Table 25 Summary of identified/characterized residues in rotational crops following application of [methylene-^{14}C]-triflumezopyrim

Fraction / Solubilizate	Radioactive residues in mg eq/kg (% TRR) Wheat hay	Wheat straw		
	30 d PBI	30 d PBI	120 d PBI	268 d PBI
TRR	0.019 (100%)	0.040 (100%)	0.025 (100%)	0.029 (100%)
Triflumezopyrim	0.003 (15.3%)	0.009 (22.5%)	0.008 (30.2%)	0.004 (15.3%)
IN-RPA19	-	0.001 (2.6%)	0.001 (3.7%)	0.001 (2.2%)
IN-R3Z91	-	-	< 0.001 (1.6%)	< 0.001 (1.3%)
IN-SBV06	-	0.001 (1.6%)	0.001 (2.9%)	< 0.001 (1.8%)
Total identified	0.003 (15.3%)	0.011 (26.7%)	0.010 (38.4%)	0.005 (20.6%)
Characterized by HPLC	0.006 (25.0%)	0.007 (17.1%)	0.005 (16.5%)	0.009 (36.9%)
Further methanol:water	0.004 (20.5%)	0.003 (6.4%)	<LOQ	-

Fraction / Solubilizate	Radioactive residues in mg eq/kg (% TRR) Wheat hay 30 d PBI	Wheat straw 30 d PBI	Wheat straw 120 d PBI	Wheat straw 268 d PBI
extracts				
Acetonitrile soak	-	0.003 (6.4%)	0.001 (4.9%)	0.002 (7.8%)
Water soak	-	0.004 (9.5%)	0.002 (6.4%)	0.004 (13.6%)
Post extraction solids	0.008 (39.1)	0.013 (34.1)	0.009 (33.7)	0.006 (21.0)
Enzyme extract	-	0.001 (3.6%)	0.001 (2.7%)	0.001 (2.1%)
1M HCl	-	0.002 (5.2%)	0.001 (4.4%)	0.001 (3.6%)
0.1M NaOH	-	0.003 (8.0%)	0.001 (2.9%)	0.001 (3.6%)
Total characterized	0.010 (45.5%)	0.023 (56.2%)	0.011 (37.8%)	0.018 (67.6%)
Unextracted	0.008 (39.1%)	0.007 (17.3%)	0.006 (23.7%)	0.003 (11.7%)
Total	0.021 (110.5%)	0.041 (102.5%)	0.027 (108.0%)	0.026 (89.7%)

Table 26 Summary of identified/characterized residues in rotational crops following application of [pyrimidine-^{14}C]-triflumezopyrim

Fraction / Solubilizate	Radioactive residues in mg eq/kg (% TRR) Wheat straw 30 d PBI	Wheat straw 120 d PBI	Wheat straw 268 d PBI
TRR	0.033 (100%)	0.016 (100%)	0.029 (100%)
Triflumezopyrim	0.006 (18.7%)	0.005 (27.2%)	0.004 (14.1%)
IN-R6U70	0.001 (1.7%)	< 0.001 (2.5%)	0.001 (4.2%)
IN-R3Z91	< 0.001 (1.4%)	0.001 (3.6%)	0.001 (1.8%)
IN-RPD47	0.001 (3.1%)	0.001 (5.6%)	0.001 (4.9%)
IN-Y2186	0.001 (4.1%)	0.001 (3.1%)	0.001 (2.7%)
IN-SBV06	0.001 (1.7%)	< 0.001 (2.8%)	0.001 (2.3%)
Total identified	0.010 (30.7%)	0.008 (44.8%)	0.009 (30.0%)
Characterized by HPLC	0.008 (21.2%)	0.003 (17.3%)	0.011 (44.5%)[a]
Further methanol:water extracts	0.003 (9.8%)	<LOQ	-
Acetonitrile soak	0.003 (7.7%)	-	-
Water soak	0.004 (8.4%)	-	-
Post extraction solids	0.011 (30.7%)	0.006 (37.9%)	0.007 (25.5%)
Enzyme extract	0.001 (2.5%)	-	-
1M HCl	0.002 (6.2%)	-	-
0.1M NaOH	0.003 (8.7%)	-	-
Total characterized	0.023 (64.5%)	0.003 (17.3%)	0.011 (44.5%)
Unextracted	0.005 (13.3%)	0.006 (37.9%)	0.007 (25.5%)
Total	0.038 (115.2%)	0.017 (106.3%)	0.027 (93.1%)

[a] Contribution of individual peaks did not exceed 7% TRR (0.002 mg eg/kg)

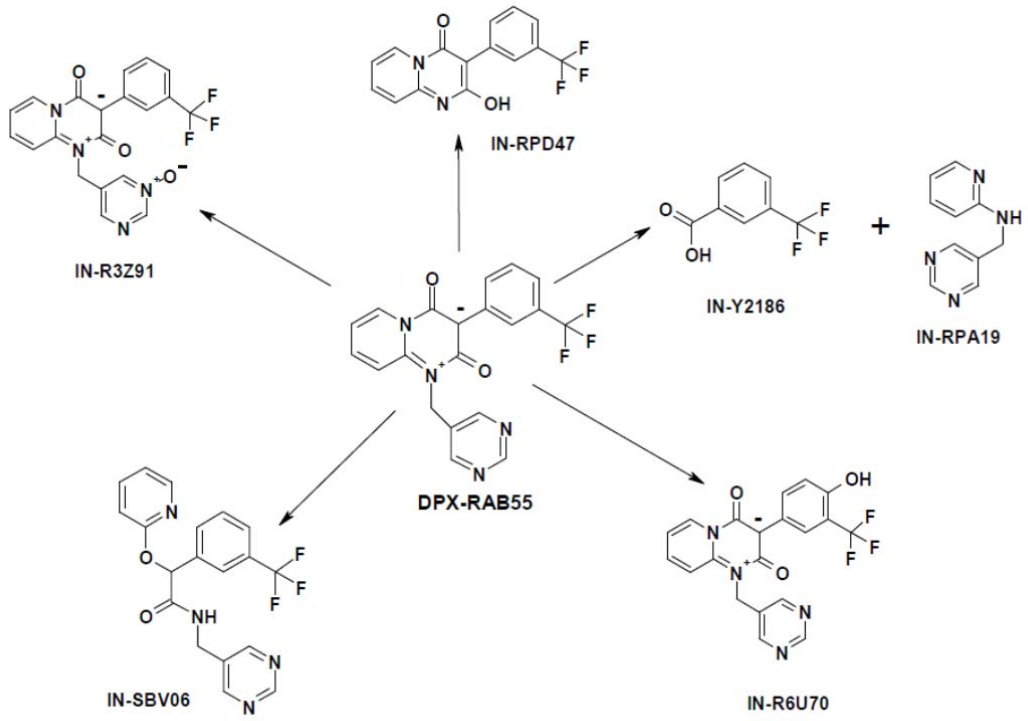


Figure 2 Proposed metabolic pathway of triflumezopyrim in rotational crops

Plant metabolism

The fate of triflumezopyrim in plants was investigated following soil and foliar application of ^{14}C-pyrimidine-, ^{14}C-methylene- and ^{14}C-pyridine-radiolabelled active substance to rice.

In all samples triflumezopyrim was strongly degraded into multiple metabolites or the radioactivity was incorporated into natural plant constituents. In all matrices parent triflumezopyrim was the major identified component. In the foliar application regime only, further metabolites quantified at amounts > 0.01 mg eq/kg: IN-RPA19 in straw and chaff at up to 0.039 mg eq/kg; IN-RPD47 in chaff and foliage up to 0.060 mg eq/kg; IN-SBV06 in chaff and straw up to 0.015 mg eq/kg; IN-Y2186 in chaff and foliage up to 0.034 mg eq/kg.

Chapleo S., Johnson J., 2015, TRIFLUMEZ_025.

The metabolic fate of [pyridine-^{14}C]-, [methylene-^{14}C]- and [pyrimidine-^{14}C]-radiolabelled triflumezopyrim in rice (*Oryza sativa*, cv. *Gleva*) was investigated by soil and foliar application. For the soil regime, one application to the soil around rice plants (BBCH 13, 3 leaves unfolded) was performed at a rate of 0.3 kg ai/ha, while for the foliar regime two spray application (BBCH 23, 3 tillers detectable; BBCH 69, end of flowering) were performed at a rate of 0.035 kg ai/ha each (total 0.07 kg ai/ha). The plant pots were flooded two days after the soil treatment (water level 3–4 cm) and kept under flooded conditions for the rest of the study. Plants receiving the soil treatment were sampled at 44 DAT (foliage, roots) and at grain maturity, 127/131 DAT (straw, chaff, grain and root). Plants receiving the foliar treatments were sampled at 0, 7 (all labels) and 14 (pyridine label only) days after the second treatment and at grain maturity, 64/68 days after second treatment (straw, chaff, grain and root).

Prior to sample processing, the foliage samples (0, 7, 14 DAT) were washed with methanol/water (1:1, v/v). The TRR in the samples was determined by combustion and LSC. In order to characterise and identify the radioactivity present, all samples were extracted with methanol,

followed by methanol/water (7:3, v/v) and additionally methanol: water (1:1,v/v) for immature foliage from the soil application. Radioactivity in the post-extraction solids was additionally extracted with water, acetonitrile, driselase in sodium acetate buffer, 1M hydrochloric acid and 0.1M sodium hydroxide. HPLC and TLC (for confirmation) against reference compounds were applied for the characterisation and identification of the radioactivity.

With the exception of roots, the TRR levels were always higher in crop fractions following foliar application, compared to soil application (foliage: 0.11–0.28 mg eq/kg in foliar vs. 0.063–0.12 mg eq/kg in soil; straw: 0.073–0.12 mg eq/kg in foliar vs. 0.068–0.073 mg eq/kg in soil; chaff: 0.31–0.55 mg eq/kg in foliar vs. 0.032–0.064 mg eq/kg in soil; grain: 0.067–0.12 mg eq/kg in foliar vs. 0.012–0.014 mg eq/kg in soil). A summary of the radioactive residues found in present in Table 27.

Table 27 Total radioactive residues in paddy rice matrices after one soil and two foliar application of [^{14}C]- triflumezopyrim

Sampling interval (DAT)	Matrix	[pyridine-^{14}C] triflumezopyrim [TRR in mg eq/kg[	[methylene-^{14}C] triflumezopyrim [TRR in mg eq/kg]	[pyrimidine-^{14}C] triflumezopyrim [TRR in mg eq/kg[
Single 0.3 kg ai/ha soil application				
44	Foliage	0.063	0.088	0.12
127-131	Straw	0.073	0.068	0.071
	Chaff	0.032	0.064	0.033
	Grain	0.014	0.014	0.012
	Roots	0.19	0.32	0.40
Two 0.035 kg ai/ha foliar applications				
0	Foliage	0.18	0.28	0.26
	Roots	0.021	0.024	0.024
7	Foliage	0.16	0.27	0.18
	Roots	0.031	0.023	0.022
14	Foliage	0.11	NA	NA
	Roots	0.043	NA	NA
64-68	Straw	0.10	0.12	0.073
	Chaff	0.55	0.46	0.31
	Grain	0.091	0.12	0.067
	Roots	0.022	0.028	0.022

NA = Not analysed, only the [pyridine-^{14}C] label was sampled for analysis

The radioactivity found in the fractions from the initial methanol/water extractions, in the additional extracts obtained from various treatments of the post-extraction solids and in the unextracted remainder is presented in Table 28. For roots, besides the determination of the TRR, no further analysis was performed.

Table 28 Extractability from paddy rice following a single 0.3 kg ai/ha soil application or two 0.035 kg ai/ha foliar applications of [^{14}C]-triflumezopyrim

Crop Fraction	Label	TRR [a]	Initial Extracts [b]		Further Extracts [c]		Unextracted	
		mg/kg	% TRR	mg/kg	% TRR	mg/kg	% TRR	mg/kg
Single 0.3 kg ai/ha soil application								
Foliage 44 DAT	[Pyridine-^{14}C]	0.063	47.0	0.030	NC	NC	52.9	0.033
	[Methylene-^{14}C]	0.088	36.5	0.033	NC	NC	63.5	0.056
	[Pyrimidine-^{14}C]	0.122	48.6	0.059	NC	NC	51.4	0.063
Straw	[Pyridine-^{14}C]	0.073	37.6	0.027	22.0	0.016	40.4	0.030
	[Methylene-^{14}C]	0.068	40.4	0.027	23.4	0.015	36.2	0.025
	[Pyrimidine-^{14}C]	0.071	43.0	0.030	26.8	0.019	30.3	0.021
Chaff	[Pyridine-^{14}C]	0.032	41.3	0.014	21.2	0.006	37.4	0.012
	[Methylene-^{14}C]	0.064	49.6	0.032	19.6	0.012	30.9	0.020
	[Pyrimidine-^{14}C]	0.033	54.4	0.018	17.3	0.005	28.3	0.009
Grain	[Pyridine-^{14}C]	0.014	36.9	0.005	40.8	0.006	22.3	0.003
	[Methylene-^{14}C]	0.014	27.8	0.004	54.7	0.008	17.6	0.002
	[Pyrimidine-^{14}C]	0.012	18.6	0.002	62.2	0.008	19.2	0.002

Crop Fraction	Label	TRR [a] mg/kg	Initial Extracts [b] % TRR	mg/kg	Further Extracts [c] % TRR	mg/kg	Unextracted % TRR	mg/kg
Two 0.035 kg ai/ha foliar applications								
Foliage 0 DAT	[Pyridine-^{14}C]	0.182	94.8	0.17	NC	NC	5.2	0.009
	[Methylene-^{14}C]	0.280	95.1	0.27	NC	NC	5.0	0.014
	[Pyrimidine-^{14}C]	0.264	95.0	0.25	NC	NC	4.9	0.013
Foliage 7 DAT	[Pyridine-^{14}C]	0.156	78.6	0.12	NC	NC	21.4	0.033
	[Methylene-^{14}C]	0.269	80.8	0.22	NC	NC	19.1	0.051
	[Pyrimidine-^{14}C]	0.175	86.2	0.15	NC	NC	13.8	0.024
Foliage 14 DAT	[Pyridine-^{14}C]	0.107	56.3	0.060	NC	NC	43.7	0.047
Straw	[Pyridine-^{14}C]	0.103	39.5	0.041	28.5	0.030	32.0	0.033
	[Methylene-^{14}C]	0.120	45.0	0.053	22.8	0.028	32.2	0.039
	[Pyrimidine-^{14}C]	0.073	54.3	0.040	22.8	0.015	22.9	0.017
Chaff	[Pyridine-^{14}C]	0.550	29.8	0.16	52.3	0.29	17.7	0.097
	[Methylene-^{14}C]	0.457	30.2	0.14	21.6	0.099	48.1	0.22
	[Pyrimidine-^{14}C]	0.308	42.9	0.13	50.7	0.11	19.8	0.061
Grain	[Pyridine-^{14}C]	0.091	21.0	0.019	47.0	0.043	31.8	0.029
	[Methylene-^{14}C]	0.118	20.5	0.024	50.0	0.059	29.5	0.035
	[Pyrimidine-^{14}C]	0.067	52.1	0.035	30.7	0.021	17.3	0.012

NC = Not conducted

[a] TRR values were determined as the sum of the radioactivity in the extracts and the PES measured by combustion after extraction; expressed as triflumezopyrim equivalents on a fresh weight basis. These values were determined from the dpm in each fraction, the specific activity and the weight extracted; there are slight rounding differences if calculated as the sum of the mg/kg in each fraction.

[b] Initial extraction with methanol (×2) followed by methanol:water (7:3, ×2).

[c] Further extractions were conducted only on samples from the final harvest; sequentially with water (1 hour or overnight, ambient ×2), acetonitrile (*ca*. 40°C, 2 × 1 hour), driselase (*ca.* 37 °C, 48 hours), 1M HCl (*ca*. 60 °C, 2 × 6 hours) and 0.1M NaOH (*ca*. 60 °C, 2 × 6 hours).

The distribution of radioactivity following a 0.3 kg ai/ha soil application and 2×0.035 kg ai/ha foliar applications for all three labels is presented in Tables 29 to 34. In soil application regime, triflumezopyrim was the major component in immature foliage, straw and chaff at 10.9–22.7% TRR (0.005–0.015 mg eq/kg) and 8.1-18.6% TRR (0.001-0.002 mg eq/kg) in grain. A similar result was obtained in the foliar application regime with triflumezopyrim accounting for 25.7–81.7% TRR (0.027–0.23 mg eq/kg) in immature foliage, 4.8–7.3% TRR (0.004-0.008 mg eq/kg) in straw, 13.9–29.6% TRR (0.063–0.16 mg eq/kg) in chaff, and 2.9–11.1% TRR (0.003-0.009 mg eq/kg) in grain. Identified metabolites for all labels and both applications included IN-RPA16, IN-RPA19, IN-RPD47, IN-R3Z91, IN-R6U70, IN-RUB93, IN-SBV06, and IN-Y2186. In the soil regime, metabolite IN-SBV06 was detected highest at 0.007 mg eq/kg in foilage, while in the foliar regime IN-R3Z91 was detected at 0.058 mg eq/kg in chaff.

Table 29 Summary of identified/characterized residues in paddy rice following a 0.3 kg ai/ha soil application of [pyridine-^{14}C]-triflumezopyrim

Fraction / Solubilizates	Radioactive residues in mg eq/kg (% TRR) Foliage (DAT 44)	Straw (DAT 127/133)	Chaff (DAT 127/133)	Grain (DAT 127/133)
TRR	0.063 (100%)	0.073 (100%)	0.032 (100%)	0.014 (100%)
Methanol/water extract	0.030 (47.0%)	0.025 (34.3%)	0.012 (36.1%)	0.005 (36.9%)
Triflumezopyrim	0.012 (18.9%)	0.009 (12.7%)	0.005 (15.7%)	0.001 (8.1%)
IN-RPA19	< 0.001 (0.7%)	0.001 (2.0%)	<LOD	<LOD
IN-R6U70	0.001 (1.8%)	0.001 (1.9%)	<LOD	<LOD
IN-SBV06	0.002 (3.7%)	0.001 (1.4%)	0.001 (3.7%)	<LOD
Characterized by HPLC	0.015 (22.0%)[a]	0.012 (16.4%)[b]	0.006 (16.8%)	0.004 (28.8%)
Further methanol/water extracts	-	0.002 (3.3%)	0.002 (5.2%)	<LOQ
Acetonitrile soak	-	<LOD	0.001 (4.6%)	0.001 (3.8%)
Water soak	-	0.001 (1.8%)	0.001 (3.5%)	< 0.001 (2.4%)
Post extraction solids	0.033 (52.9%)	0.045 (60.6%)	0.016 (50.5%)	0.008 (56.9%)
Enzyme extract	-	0.004 (5.7%)	<LOD	0.002 (13.0%)

Fraction / Solubilizates	Radioactive residues in mg eq/kg (% TRR)			
	Foliage (DAT 44)	Straw (DAT 127/133)	Chaff (DAT 127/133)	Grain (DAT 127/133)
1M HCl	-	0.008 (10.2%)	0.003 (9.3%)	0.002 (13.2%)
0.1M NaOH	-	0.003 (4.3%)	0.001 (3.8%)	0.001 (8.4%)
Total identified	0.015 (25.1%)	0.012 (18.0%)	0.006 (19.4%)	0.001 (8.1%)
Total characterized	0.015 (22.0%)	0.030 (41.7%)	0.014 (43.2%)	0.010 (69.6%)
Unextracted	0.033 (52.9%)	0.030 (40.4%)	0.012 (37.4%)	0.003 (22.3%)
Total	0.063 (100.0%)	0.073 (100.1%)	0.032 (100.0%)	0.014 (100.0%)

[a] Contribution of individual peaks did not exceed 7% TRR (0.004 mg eg/kg)

[b] Contribution of individual peaks did not exceed 4% TRR (0.003 mg eg/kg)

Table 30 Summary of identified/characterized residues in paddy rice following a 0.3 kg ai/ha soil application of [methylene-^{14}C]-triflumezopyrim

Fraction / Solubilizates	Radioactive residues in mg eq/kg (% TRR)			
	Foliage (DAT 44)	Straw (DAT 127/133)	Chaff (DAT 127/133)	Grain (DAT 127/133)
TRR	0.088 (100%)	0.068 (100%)	0.064 (100%)	0.014 (100%)
Methanol/water extract	0.033 (36.5%)	0.025 (37.2%)	0.029 (44.9%)	0.004 (27.8%)
Triflumezopyrim	0.012 (13.3%)	0.010 (14.3%)	0.007 (10.9%)	0.001 (9.0%)
IN-RPA19	0.001 (0.7%)	-	-	-
IN-RPA16	0.001 (0.9%)	0.001 (1.9%)	-	-
IN-R6U70	0.002 (1.9%)	< 0.001 (0.4%)	-	-
IN-R3Z91	-	< 0.001 (0.4%)	0.001 (1.9%)	-
IN-RUB93	0.001 (0.9%)	-	-	-
IN-SBV06	0.002 (2.5%)	0.001 (1.8%)	0.002 (2.9%)	-
Characterized by HPLC	0.015 (16.3%)[a]	0.010 (18.5%)[b]	0.019 (29.1%)[c]	0.003 (18.8%)
Further methanol/water extracts	<LOQ	0.002 (3.2%)	0.003 (4.7%)	<LOQ
Acetonitrile soak	-	0.001 (1.7%)	0.002 (3.4%)	<LOD
Water soak	-	0.001 (2.2%)	0.002 (4.0%)	0.001 (4.3%)
Post extraction solids	0.056 (63.5%)	0.039 (55.7%)	0.028 (43.1%)	0.009 (68.0%)
Enzyme extract	-	0.003 (4.1%)	0.002 (3.3%)	0.002 (15.4%)
1M HCl	-	0.007 (9.6%)	0.004 (5.6%)	0.003 (18.7%)
0.1M NaOH	-	0.004 (5.8%)	0.002 (3.3%)	0.002 (16.3%)
Total identified	0.019 (20.2%)	0.012 (18.8%)	0.010 (15.7%)	0.001 (9.0%)
Total characterized	0.015 (16.3%)	0.028 (45.1%)	0.034 (53.4%)	0.011 (73.5%)
Unextracted	0.056 (63.5%)	0.025 (36.2%)	0.020 (30.9%)	0.002 (17.6%)
Total	0.090 (102.3%)	0.065 (95.6%)	0.064 (100.0%)	0.014 (100.1%)

[a] Contribution of individual peaks did not exceed 5% TRR (0.005 mg eg/kg)

[b] Contribution of individual peaks did not exceed 10% TRR (0.006 mg eg/kg)

[c] One unknown peak accounting for 28% TRR (0.018 mg eg/kg)

Table 31 Summary of identified/characterized residues in paddy rice following a 0.3 kg ai/ha soil application of [pyrimidine-^{14}C]-triflumezopyrim

Fraction / Solubilizates	Radioactive residues in mg eq/kg (% TRR)			
	Foliage (DAT 44)	Straw (DAT 127/133)	Chaff (DAT 127/133)	Grain (DAT 127/133)
TRR	0.12 (100%)	0.071 (100%)	0.033 (100%)	0.012 (100%)
Methanol/water extract	0.052 (42.9%)	0.027 (38.9%)	0.016 (47.5%)	0.002 (18.6%)
Triflumezopyrim	0.015 (12.6%)	0.011 (15.5%)	0.008 (22.7%)	0.002 (18.6%)
IN-R3Z91	0.002 (2.0%)	0.002 (3.0%)	0.002 (5.3%)	-
IN-RPD47	0.002 (1.8%)	0.002 (3.0%)	0.001 (2.2%)	-
IN-Y2186	0.003 (2.4%)	0.002 (2.3%)	-	-
IN-R6U70	-	0.002 (2.6%)	0.002 (6.2%)	-
IN-SBV06	0.007 (5.5%)	0.001 (1.7%)	0.003 (7.8%)	-
Characterized by HPLC	0.023 (18.5%)[a]	0.008 (11.0%)	0.001 (3.3%)	-
Further methanol/water extracts	0.007 (5.7%)	0.003 (4.1%)	0.002 (6.9%)	<LOQ
Acetonitrile soak	-	0.002 (2.9%)	<LOD	<LOD

Fraction / Solubilizates	Radioactive residues in mg eq/kg (% TRR)			
	Foliage (DAT 44)	Straw (DAT 127/133)	Chaff (DAT 127/133)	Grain (DAT 127/133)
Water soak	-	0.003 (4.0%)	0.001 (2.3%)	0.001 (6.0%)
Post extraction solids	0.063 (51.4%)	0.035 (50.2%)	0.013 (43.3%)	0.009 (75.4%)
Enzyme extract	-	0.003 (4.6%)	0.001 (4.1%)	0.002 (20.1%)
1M HCl	-	0.008 (11.4%)	0.002 (7.4%)	0.003 (23.2%)
0.1M NaOH	-	0.003 (3.9%)	0.001 (3.5%)	0.002 (12.9%)
Total identified	0.029 (24.3%)	0.020 (28.1%)	0.016 (44.2%)	0.002 (18.6%)
Total characterized	0.030 (24.2%)	0.030 (41.9%)	0.008 (27.5%)	0.008 (62.2%)
Unextracted	0.063 (51.4%)	0.021 (30.3%)	0.009 (28.3%)	0.002 (19.2%)
Total	0.12 (100.0%)	0.071 (100.3%)	0.033 (100.0%)	0.012 (100.0%)

[a] Contribution of individual peaks did not exceed 3% TRR (0.003 mg eg/kg)

Table 32 Summary of identified/characterized residues in rice following a 2×0.035 kg ai/ha foliar applications of [pyridine-^{14}C]-triflumezopyrim

Fraction / Solubilizates	Radioactive residues in mg eq/kg (% TRR)					
	Foliage (DALT 0)	Foliage (DALT 7)	Foliage (DALT 14)	Straw (DALT 64/68)	Chaff (DALT 64/68)	Grain (DALT 64/68)
TRR	0.182 (100%)	0.156 (100%)	0.107 (100%)	0.103 (100%)	0.550 (100%)	0.091 (100%)
Surface wash and/or methanol/water extract	0.167 (91.5%)	0.115 (73.8%)	0.052 (49.2%)	0.036 (34.7%)	0.164 (29.8%)	0.016 (18.0%)
Triflumezopyrim	0.147 (80.4%)	0.050 (32.3%)	0.027 (25.7%)	0.008 (7.3%)	0.083 (15.1%)	0.005 (6.0%)
IN-RPA19	0.011 (5.9%)	0.030 (19.4%)	0.002 (2.1%)	0.002 (1.8%)	-	-
IN-R6U70	-	-	< 0.001 (0.4%)	-	0.004 (0.7%)	< 0.001 (0.5%)
IN-R3Z91	0.001 (0.3%)	-	-	-	-	0.001 (1.5%)
IN-RPD47	0.002 (0.9%)	0.003 (2.0%)	0.001 (0.6%)	0.002 (1.6%)	0.019 (3.5%)	< 0.001 (0.2%)
IN-SBV06	0.001 (0.5%)	0.004 (2.5%)	0.003 (3.2%)	0.002 (2.0%)	0.011 (2.1%)	0.001 (0.6%)
Characterized by HPLC	0.005 (3.5%)	0.028 (17.7%)[a]	0.019 (17.3%)[b]	0.037 (35.4%)[c]	0.045 (8.3%)	0.006 (9.1%)
Further solvent extracts	0.006 (3.3%)	0.007 (4.8%)	0.008 (7.1%)	0.005 (4.8%)	-	0.003 (3.0%)
Combined acetonitrile and water soaks	-	-	-	-	0.099 (17.9%)	0.009 (10.4%)
Triflumezopyrim	-	-	-	-	0.047 (8.5%)	0.003 (3.5%)
IN-RPA19	-	-	-	-	< 0.001 (0.1%)	0.001 (1.6%)
IN-RPD47	-	-	-	-	0.022 (4.0%)	0.001 (1.0%)
IN-SBV06	-	-	-	-	0.004 (0.7%)	-
Characterized by HPLC	-	-	-	-	0.025 (4.6%)	0.004 (4.4%)
Acetonitrile soak	-	-	-	0.002 (2.1%)	[d]	[d]
Water soak	-	-	-	0.004 (3.4%)	[d]	[d]
Post extraction solids	0.009 (5.2%)	0.033 (21.4%)	0.047 (43.7%)	0.057 (55.0%)	0.286 (52.1%)	0.063 (68.4%)
Enzyme extract	-	-	-	0.006 (5.6%)	0.012 (2.2%)	0.006 (6.2%)
Triflumezopyrim	-	-	-	-	0.002 (0.4%)	-
IN-R3Z91	-	-	-	-	0.002 (0.4%)	-

Fraction / Solubilizates	Radioactive residues in mg eq/kg (% TRR)					
	Foliage (DALT 0)	Foliage (DALT 7)	Foliage (DALT 14)	Straw (DALT 64/68)	Chaff (DALT 64/68)	Grain (DALT 64/68)
IN-RPD47	-	-	-	-	0.001 (0.2%)	-
Characterized by HPLC	-	-	-	-	0.005 (1.1%)	-
1M HCl	-	-	-	0.014 (13.3%)	0.036 (6.6%)	0.018 (19.6%)
Triflumezopyrim	-	-	-	-	-	0.001 (1.6%)
IN-RPA19	-	-	-	-	0.002 (0.3%)	-
Characterized by HPLC	-	-	-	0.013 (13.3%)	0.034 (6.2%)	0.017 (18.1%)
0.1M NaOH	-	-	-	0.004 (4.1%)	0.141 (25.6%)	0.010 (10.8%)
Triflumezopyrim	-	-	-	-	0.031 (5.6%)	-
IN-RPA19	-	-	-	-	0.025 (4.5%)	-
IN-RPD47	-	-	-	-	0.018 (3.2%)	-
Characterized by HPLC	-	-	-	-	0.068 (12.3%)	-
Total identified	0.162 (88.0%)	0.087 (56.1%)	0.033 (32.0%)	0.014 (12.7%)	0.271 (49.3%)	0.013 (16.5%)
Total characterized	0.011 (6.8%)	0.038 (22.5%)	0.027 (24.4%)	0.058 (55.4%)	0.177 (32.5%)	0.046 (51.6%)
Unextracted	0.009 (5.2%)	0.033 (21.4%)	0.047 (43.7%)	0.033 (32.0%)	0.097 (17.7%)	0.029 (31.8%)
Total	0.182 (100.0%)	0.158 (101.3%)	0.107 (100.0%)	0.105 (101.9%)	0.545 (99.1%)	0.088 (96.7%)

[a] Contribution of individual peaks did not exceed 5% TRR (0.008 mg eg/kg)

[b] One peak accounted for 12% TRR (0.013 mg eq/kg), while the contribution of all other peaks did not exceed 3% TRR (0.003 mg eg/kg)

[c] One peak accounted for 10% TRR (0.010 mg eq/kg), while the contribution of all other peaks did not exceed 3% TRR (0.003 mg eg/kg)

[d] For chaff and grain the acetonitrile and water soaks were combined and analysed by HPLC

Table 33 Summary of identified/characterized residues in rice following a 2×0.035 kg ai/ha foliar applications of [methylene-^{14}C]-triflumezopyrim

Fraction / Solubilizates	Radioactive residues in mg eq/kg (% TRR)				
	Foliage (DALT 0)	Foliage (DALT 7)	Straw (DALT 64/68)	Chaff (DALT 64/68)	Grain (DALT 64/68)
TRR	0.280 (100%)	0.269 (100%)	0.120 (100%)	0.457 (100%)	0.118 (100%)
Surface wash and/or methanol/water extract	0.262 (93.4%)	0.208 (77.4%)	0.049 (41.5%)	0.139 (30.2%)	0.021 (17.7%)
Triflumezopyrim	0.229 (81.7%)	0.073 (27.1%)	0.006 (4.8%)	0.054 (11.7%)	0.003 (2.9%)
IN-RPA19	0.009 (3.2%)	0.011 (4.1%)	0.005 (4.2%)	-	0.001 (0.5%)
IN-R6U70	0.002 (0.6%)	-	0.001 (0.7%)	0.007 (1.5%)	0.001 (0.7%)
IN-R3Z91	0.001 (0.2%)	-	0.001 (0.8%)	0.004 (0.8%)	0.001 (0.4%)
IN-SBV06	0.002 (0.6%)	0.007 (2.7%)	0.001 (1.0%)	0.008 (1.7%)	< 0.001 (0.3%)
Characterized by HPLC	0.019 (7.2%)	0.117 (43.7%)[b]	0.037 (30.0%)[b]	0.067 (14.7%)[d]	0.014 (13.0%)[e]
Further solvent extracts	0.005 (1.7%)	0.009 (3.4%)	0.004 (3.5%)	-	0.003 (2.8%)
Combined acetonitrile and water soaks	-	-	-	0.032 (7.0%)	-
Triflumezopyrim	-	-	-	0.010 (2.2%)	-
IN-RPA19	-	-	-	0.007 (1.5%)	-
Characterized by HPLC	-	-	-	0.015 (3.3%)	-
Acetonitrile soak	-	-	0.001 (0.5%)	[a]	0.003 (2.8%)
Water soak	-	-	0.002 (1.6%)	[a]	0.010 (8.3%)

Fraction / Solubilizates	Radioactive residues in mg eq/kg (% TRR)				
	Foliage (DALT 0)	Foliage (DALT 7)	Straw (DALT 64/68)	Chaff (DALT 64/68)	Grain (DALT 64/68)
Post extraction solids	0.014 (5.0%)	0.051 (19.1%)	0.064 (52.9%)	0.287 (62.7%)	0.081 (68.4%)
Enzyme extract	-	-	0.008 (6.6%)	0.008 (1.8%)	0.010 (8.5%)
1M HCl	-	-	0.012 (10.0%)	0.041 (8.9%)	0.021 (17.8%)
IN-RPA16	-	-	-	0.008 (1.7%)	-
Characterized by HPLC	-	-	-	0.034 (7.1%)	-
0.1M NaOH	-	-	0.005 (4.1%)	0.018 (3.9%)	0.015 (12.6%)
IN-RPA16	-	-	-	0.012 (2.6%)	-
Characterized by HPLC	-	-	-	0.006 (1.3%)	-
Total identified	0.243 (86.3%)	0.091 (33.9%)	0.014 (11.5%)	0.110 (23.7%)	0.006 (4.8%)
Total characterized	0.024 (8.9%)	0.126 (47.1%)	0.069 (56.3%)	0.130 (28.2%)	0.076 (65.8%)
Unextracted	0.014 (5.0%)	0.051 (19.1%)	0.039 (32.2%)	0.220 (48.1%)	0.035 (29.5%)
Total	0.281 (100.4%)	0.268 (99.6%)	0.122 (101.7%)	0.460 (100.7%)	0.117 (99.2%)

[a] For chaff the acetonitrile and water soaks were combined and analysed by HPLC

[b] One peak in the void volume accounted for 15% TRR (0.041 mg eq/kg) and was assumed to consist mainly of IN-RPA19, while the contribution of all other peaks did not exceed 4% TRR (0.011 mg eg/kg)

[c] One peak accounted for 16% TRR (0.018 mg eq/kg), while the contribution of all other peaks did not exceed 3% TRR (0.003 mg eg/kg)

[d] Contribution of individual peaks did not exceed 8% TRR (0.035 mg eg/kg)

[e] One peak accounted for 11% TRR (0.013 mg eq/kg), while the contribution of all other peaks did not exceed 1% TRR (0.001 mg eg/kg)

Table 34 Summary of identified/characterized residues in rice following a 2×0.035 kg ai/ha foliar applications of [pyrimidine-^{14}C]-triflumezopyrim

Fraction / Solubilizates	Radioactive residues in mg eq/kg (% TRR)				
	Foliage (DALT 0)	Foliage (DALT 7)	Straw (DALT 64/68)	Chaff (DALT 64/68)	Grain (DALT 64/68)
TRR	0.264 (100%)	0.175 (100%)	0.073 (100%)	0.308 (100%)	0.067 (100%)
Surface wash and/or methanol/water extract	0.234 (88.6%)	0.143 (82.2%)	0.037 (49.6%)	0.132 (42.9%)	0.033 (48.4%)
Triflumezopyrim	0.201 (75.9%)	0.063 (36.2%)	0.004 (5.7%)	0.043 (14.1%)	0.006 (9.1%)
IN-R6U70	0.005 (1.9%)	0.002 (1.2%)	0.001 (1.5%)	0.005 (1.5%)	-
IN-R3Z91	0.002 (0.8%)	0.004 (2.4%)	0.001 (1.2%)	0.015 (5.0%)	0.002 (3.1%)
IN-RPD47	0.003 (1.0%)	0.010 (5.8%)	0.002 (2.1%)	-	0.002 (2.4%)
IN-Y2186	0.007 (2.6%)	0.014 (7.7%)	0.004 (4.9%)	0.004 (1.4%)	0.004 (5.4%)
IN-SBV06	0.001 (0.4%)	0.004 (2.4%)	0.001 (1.4%)	0.004 (1.4%)	0.001 (1.4%)
Characterized by HPLC	0.017 (6.1%)	0.046 (26.5%)[b]	0.024 (32.9%)[c]	0.061 (19.7%)[d]	0.020 (27.0%)[e]
Further solvent extracts	0.017 (6.4%)	0.007 (4.0%)	0.003 (4.7%)	-	0.002 (3.7%)
Combined acetonitrile and water soaks	-	-	-	0.035 (11.2%)	-
Triflumezopyrim	-	-	-	0.018 (5.7%)	-
IN-RPD47	-	-	-	0.006 (1.8%)	-
IN-SBV06	-	-	-	0.001 (0.4%)	-
Characterized by HPLC	-	-	-	0.011 (3.3%)	-
Acetonitrile soak	-	-	0.001 (1.7%)	[a]	0.002 (2.8%)
Water soak	-	-	0.001 (1.8%)	[a]	0.001 (1.5%)
Post extraction solids	0.013 (4.9%)	0.024 (13.8%)	0.030 (42.2%)	0.141 (45.8%)	0.030 (43.7%)
Enzyme extract	-	-	0.003 (4.6%)	0.005 (1.5%)	0.003 (3.9%)
Triflumezopyrim	-	-	-	0.002 (0.5%)	-
IN-R3Z91	-	-	-	0.002 (0.7%)	-
Characterized by HPLC	-	-	-	0.002 (0.4%)	-
1M HCl	-	-	0.007 (10.2%)	0.012 (3.9%)	0.007 (10.7%)
0.1M NaOH	-	-	0.003 (4.5%)	0.063 (20.6%)	0.008 (11.8%)
IN-R6U70	-	-	-	0.008 (2.7%)	-
IN-R3Z91	-	-	-	0.041 (13.4%)	-
IN-Y2186	-	-	-	0.005 (1.6%)	-
Characterized by HPLC	-	-	-	0.009 (2.9%)	-
Total identified	0.219 (82.6%)	0.097 (55.7%)	0.013 (16.8%)	0.154 (50.5%)	0.015 (21.4%)
Total characterized	0.034 (12.5%)	0.053 (30.5%)	0.042 (60.4%)	0.095 (30.2%)	0.043 (61.4%)

Fraction / Solubilizates	Radioactive residues in mg eq/kg (% TRR)				
	Foliage (DALT 0)	Foliage (DALT 7)	Straw (DALT 64/68)	Chaff (DALT 64/68)	Grain (DALT 64/68)
Unextracted	0.013 (4.9%)	0.024 (13.8%)	0.017 (22.9%)	0.061 (19.8%)	0.012 (17.3%)
Total	0.266 (100.8%)	0.174 (99.4%)	0.072 (98.6%)	0.310 (100.7%)	0.070 (104.5%)

[a] For chaff the acetonitrile and water soaks were combined and analysed by HPLC

[b] Contribution of individual peaks did not exceed 8% TRR (0.014 mg eg/kg)

[c] Contribution of individual peaks did not exceed 7% TRR (0.005 mg eg/kg)

[d] Contribution of individual peaks did not exceed 5% TRR (0.015 mg eg/kg)

[e] Contribution of individual peaks did not exceed 7% TRR (0.005 mg eg/kg)

In order to investigate the presence of soluble conjugates, an aliquot of the solvent extract from foliage ([methylene-^{14}C]-triflumezopyrim; DAT 7) was digested with driselase. A comparison of the chromatographic profile revealed only little change indicating a minor contribution of conjugated metabolites.

It should be noted that a radioactive contaminant was detected in the grain and chaff samples. Analysis by LC-MS demonstrated that the contaminant was unrelated to triflumezopyrim and was assumed to result from cross contamination during threshing. Therefore, for the calculation of radioactive residues in chaff and grain samples, truncated HPLC chromatograms were used, omitting the retention time of the contaminant. Nevertheless, a second rice metabolism study without the contamination was provided.

Shankey M., McCallum C., 2015, TRIFLUMEZ_026.

The metabolic fate of [pyridine-^{14}C]-, [methylene-^{14}C]- and [pyrimidine-^{14}C]-radiolabelled triflumezopyrim in rice (*Oryza sativa*, cv. *Gleva*) was investigated by soil and foliar application. For the soil regime, one application to the soil around rice plants (BBCH 13/14, 3 leaves unfolded) was performed at a rate of about 0.3 kg ai/ha, while for the foliar regime two spray application (BBCH 23, 3 tillers detectable; BBCH 87, grain content solid) were performed at a rate of 0.035 kg ai/ha each (total 0.07 kg ai/ha). The plant pots were flooded two days after the soil treatment (water level 3–4 cm) and kept under flooded conditions for the rest of the study. Plants receiving the soil treatment were sampled at 51 DAT (foliage, roots) and at maturity, 119 DAT (straw, chaff, grain and root). Plants receiving the foliar treatments were sampled at 14 days after the first treatment and at maturity, 21 days after second treatment (straw, chaff, grain and root).

Prior to sample processing, the immature foliar-treated rice foliage samples were washed with methanol. The TRR in the samples was determined by combustion and LSC. In order to characterise and identify the radioactivity present, all samples were extracted with methanol, followed by methanol/water (7+3, v/v). Exhaustive extractions were conductedwith 50% methanol:50% (1N formic acid aqueous:0.1% sodium dodecyl sulphate (NaDS), 3:1, v/v) followed by a water pellet rinse, 0.1N NaOH, 1M HCl and for foliar treated [pyridine-2,6-^{14}C] and [methylene-^{14}C] straw samples 10N sodium hydroxide followed by acidification with hydrochloric acid (ca. pH1) to precipitate lignin bound residues. HPLC against reference compounds were applied for the characterisation and identification of the radioactivity. Selected samples were also analysed by TLC.

TRRs in samples receiving the soil application were 0.006–0.013 mg/kg in grain, 0.050–0.114 mg/kg in straw, 0.031-0.093 mg/kg in chaff and 0.049–0.066 mg/kg in immature foliage. TRRs in roots were 0.074-0.118 mg/kg. TRRs in samples receiving two foliar applications were 0.043–0.076 mg/kg in grain, 0.225-0.338 mg/kg in straw, 0.59–0.94 mg/kg in chaff and 0.096–0.129 mg/kg in immature foliage. TRRs in roots were 0.021-0.10 mg/kg. (Table 35).

Table 35 Total radioactive residues in paddy rice matrices after one soil and two foliar application of ^{14}C- triflumezopyrim

Sampling interval (DAT)	Matrix	[pyridine-^{14}C] triflumezopyrim [TRR in mg eq/kg[	[methylene-^{14}C] triflumezopyrim [TRR in mg eq/kg]	[pyrimidine-^{14}C] triflumezopyrim [TRR in mg eq/kg[
Single 0.3 kg ai/ha soil application				
51	Foliage	0.066	0.062	0.049
	Roots	0.118	0.114	0.091
119	Straw	0.114	0.093	0.050
	Chaff	0.093	0.045	0.031
	Grain	0.013	0.009	0.006
	Roots	0.087	0.079	0.074
Two 0.035 kg ai/ha foliar applications				
23[a]	Foliage	0.129	0.124	0.096
	Roots	0.024	0.032	0.021
21	Straw	0.338	0.331	0.225
	Chaff	0.940	0.763	0.594
	Grain	0.065	0.043	0.076
	Roots	0.100	0.060	0.061

[a] After first treatment

The radioactivity found in the fractions from the initial methanol/water extractions, in the additional extracts obtained from various treatments of the post-extraction solids and in the unextracted remainder is presented in Table 36. Extractions of grain from the soil application regime with methanol and aqueous methanol recovered less than limit of quantification. For roots, besides the determination of the TRR, no further analysis was performed.

Table 36 Extractability from paddy rice following a single 0.3 g ai/ha soil application or two 0.035 kg ai/ha foliar applications of [^{14}C]-triflumezopyrim

Crop Fraction	Label	TRR [a] mg/kg	Initial Extracts [b]		Further Extracts		Unextracted	
			% TRR	mg/kg	% TRR	mg/kg	% TRR	mg/kg
Single 0.3 kg ai/ha soil application								
Foliage	[Pyridine-^{14}C]	0.066	46.8	0.031	5.2[c]	0.003	48.0	0.032
	[Methylene-^{14}C]	0.062	47.0	0.030	6.5[c]	0.004	46.5	0.029
	[Pyrimidine-^{14}C]	0.049	48.7	0.024	4.9[c]	0.002	46.6	0.023
Straw	[Pyridine-^{14}C]	0.114	38.6	0.045	8.3[c]	0.009	53.0	0.061
	[Methylene-^{14}C]	0.093	37.6	0.035	14.5[c]	0.013	47.8	0.044
	[Pyrimidine-^{14}C]	0.050	46.1	0.024	9.9[c]	0.005	44.0	0.022
Chaff	[Pyridine-^{14}C]	0.093	31.3	0.029	NC	NC	68.7	0.064
	[Methylene-^{14}C]	0.045	26.0	0.011	NC	NC	74.0	0.033
	[Pyrimidine-^{14}C]	0.031	38.9	0.013	NC	NC	61.1	0.019
Grain	[Pyridine-^{14}C]	0.013	<LOQ		NC	NC	100.0	0.013
	[Methylene-^{14}C]	0.009	<LOQ		NC	NC	100.0	0.009
	[Pyrimidine-^{14}C]	0.006	<LOQ		NC	NC	100.0	0.006
Two 0.035 kg ai/ha foliar applications								
Foliage	[Pyridine-^{14}C]	0.129	63.7	0.083	5.4[c]	0.007	30.9	0.040
	[Methylene-^{14}C]	0.124	70.0	0.087	6.1[c]	0.007	23.9	0.029
	[Pyrimidine-^{14}C]	0.096	77.9	0.075	2.2[c]	0.002	20.6	0.020
Straw	[Pyridine-^{14}C]	0.338	54.6	0.185	35.5[d]	0.119	9.9	0.033
	[Methylene-^{14}C]	0.331	61.1	0.202	31.2[e]	0.104	7.6	0.025
	[Pyrimidine-^{14}C]	0.225	70.5	0.159	4.2[c]	0.010	25.2	0.056
Chaff	[Pyridine-^{14}C]	0.940	42.5	0.400	NC	NC	57.5	0.540
	[Methylene-^{14}C]	0.763	46.8	0.357	NC	NC	53.1	0.405
	[Pyrimidine-^{14}C]	0.594	53.0	0.315	NC	NC	47.0	0.279
Grain	[Pyridine-^{14}C]	0.065	46.8	0.031	17.0[f]	0.011	36.3	0.024
	[Methylene-^{14}C]	0.043	54.4	0.023	18.6[c]	0.008	27.1	0.012
	[Pyrimidine-^{14}C]	0.076	56.5	0.043	23.6[c]	0.018	19.9	0.015

NC = Further extractions were not conducted.

[a] TRR values were determined as the sum of the radioactivity in the extracts and the PES measured by combustion after extraction; expressed as triflumezopyrim equivalents on a fresh weight basis.

[b] Surface washing of foliage samples (foliar application only) with methanol, and initial extracts with methanol (×2) followed by methanol:water (7:3, ×2).

[c] Further extractions, 50% MeOH:50% (1N formic acid aq:0.1% NaDS, 3:1, v/v) (1x ca. 1hour, ambient with orbital shaking) followed by a water pellet rinse, 0.1N NaOH (ca. 60 °C, ca. 6 hours), 1M HCl (ca. 60 °C, ca. 6 hours).

[d] Further extractions, 50% MeOH:50% (1N formic acid aq:0.1% NaDS, 3:1, v/v) (1× *ca.* 1 hour, ambient with orbital shaking) followed by a water pellet rinse, 0.1N NaOH (*ca.* 60 °C, *ca.* 6 hours), 1M HCl (*ca.* 60 °C, *ca.*6 hours), 10N NaOH (*ca.* 130 °C, *ca.* 22 hours) followed by acidification with HCl (*ca.* pH 1) to precipitate lignin bound residue.

[e] Further extractions, 50% MeOH:50% (1N formic acid aq:0.1% NaDS, 3:1, v/v) (2× *ca.* 1hour, ambient with orbital shaking) followed by a water pellet rinse, 0.1N NaOH (*ca.* 60 °C, *ca.* 6h), 1M HCl (*ca.* 60 °C, ca.6 hours), 10N NaOH (*ca.* 130 °C, *ca.* 22 hours) followed by acidification with HCl (*ca.* pH 1) to precipitate lignin bound residue.

[f] Further extractions, 50% MeOH:50% (1N formic acid aq:0.1% NaDS, 3:1, v/v) (2× ca. 1 hour, ambient with orbital shaking) followed by a water pellet rinse, 0.1N NaOH (ca. 60 °C, ca. 6 hours), 1M HCl (ca. 60 °C, ca. 6 hours)

The distribution of radioactivity following a single 0.3 kg ai/ha soil application and 2×0.035 kg ai/ha foliar applications for all three labels is presented in Tables 37 to 42. In soil application regime, triflumezopyrim was the major component in immature foliage at 13.5–24.2% TRR (0.007–0.016 mg/kg), in the straw at 8.1-14.1% TRR (0.007–0.010 mg/kg) and in the chaff at 4.8–7.3% TRR (0.002–0.005 mg/kg). Extractions of grain samples produced results lower than the limit of quantification (LOQ). In the foliar application regime, triflumezopyrim accounted for 9.6–13.2% TRR (0.009–0.017 mg/kg) in immature foliage, 18.9–20.9% TRR (0.044-0.070 mg/kg) in straw, 17.2–24.6% TRR (0.146–0.162) in chaff and 21.8–27.7% TRR (0.009-0.018 mg/kg) in grain. Identified metabolites for all labels and both applications included IN-RPA16, IN-RPA19, IN-RPD47, IN-R3Z91, IN-R6U70, IN-R6U71, IN-R6U72, IN-R6U73, IN-SBV06 and IN-Y2186. In the soil regime, metabolite IN-RPA19 was detected highest at 0.004 mg eq/kg in straw, while in the foliar regime IN-RPA19 was detected at 0.039 mg eq/kg in chaff.

Table 37 Summary of identified/characterized residues in paddy rice following a 0.3 g ai/ha soil application of [pyridine-^{14}C]-triflumezopyrim

Fraction / Solubilizates	Radioactive residues in mg eq/kg (% TRR)		
	Foliage (DAT 51)	Straw (DAT 119)	Chaff (DAT 119)
TRR	0.066 (100%)	0.114 (100%)	0.093 (100%)
Methanol/water extract	0.027 (40.1%)	0.040 (35.2%)	0.021 (22.9%)
Triflumezopyrim	0.016 (24.2%)	0.010 (9.1%)	0.005 (6.0%)
IN-RPA19	0.002 (3.3%)	0.004 (3.1%)	0.001 (1.0%)
IN-R6U72	-	0.002 (1.4%)	< 0.001 (0.4%)
IN-R6U70	-	0.001 (1.0%)	< 0.001 (0.3%)
IN-R3Z91	-	0.001 (1.1%)	< 0.001 (0.3%)
IN-RPD47	-	0.002 (1.6%)	0.001 (1.4%)
IN-SBV06	0.001 (1.9%)	-	0.001 (1.1%)
Characterized by HPLC	0.007 (10.7%)	0.018 (17.7%)[a]	0.008 (12.3%)
Further methanol/water extracts	0.004 (6.7%)	0.004 (3.4%)	0.004 (4.6%)
Post extraction solids	0.035 (53.2%)	0.070 (61.3%)	0.064 (68.7%)
Surfactant	<LOQ	<LOQ	-
0.1M NaOH	0.001 (2.1%)	0.004 (3.5%)	-
1M HCl	0.002 (3.1%)	0.005 (4.8%)	-
Total identified	0.019 (29.4%)	0.020 (17.3%)	0.008 (10.5%)
Total characterized	0.014 (22.6%)	0.031 (29.4%)	0.020 (27.4%)
Unextracted	0.032 (48.0%)	0.061 (53.0%)	0.064 (68.7%)
Total	0.065 (98.5%)	0.112 (98.3%)	0.092 (98.9%)

[a] Contribution of individual peaks did not exceed 2% TRR (0.002 mg eg/kg)

Table 38 Summary of identified/characterized residues in paddy rice following a 0.3kg ai/ha soil application of [methylene-^{14}C]-triflumezopyrim

Fraction / Solubilizates	Radioactive residues in mg eq/kg (% TRR)		
	Foliage (DAT 51)	Straw (DAT 119)	Chaff (DAT 119)
TRR	0.062 (100%)	0.093 (100%)	0.045 (100%)
Methanol/water extract	0.021 (33.9%)	0.031 (32.9%)	0.005 (13.2%)
Triflumezopyrim	0.011 (18.1%)	0.008 (8.1%)	0.002 (4.8%)
IN-RPA19	0.002 (2.9%)	0.002 (2.4%)	-
IN-R6U72	-	-	< 0.001 (0.3%)
IN-R6U70	-	0.001 (0.8%)	-
IN-R3Z91	-	0.001 (1.0%)	-
IN-R6U71	0.001 (1.4%)	< 0.001 (0.3%)	-
IN-SBV06	0.001 (2.4%)	< 0.001 (0.5%)	< 0.001 (0.8%)
Characterized by HPLC	0.006 (9.1%)	0.017 (19.8%)[a]	0.001 (7.5%)
Further methanol/water extracts	0.005 (7.3%)	0.004 (4.7%)	0.005 (10.9%)
Post extraction solids	0.033 (53.0%)	0.057 (62.3%)	0.033 (74.0%)
Surfactant	0.001 (1.5%)	0.003 (3.3%)	-
0.1M NaOH	0.001 (2.4%)	0.006 (6.6%)	-
1M HCl	0.002 (2.6%)	0.004 (4.6%)	-
Total identified	0.015 (24.8%)	0.012 (13.1%)	0.002 (5.9%)
Total characterized	0.015 (22.9%)	0.034 (39.0%)	0.006 (18.4%)
Unextracted	0.029 (46.5%)	0.044 (47.8%)	0.033 (74.0%)
Total	0.059 (95.2%)	0.090 (96.8%)	0.041 (91.1%)

[a] Contribution of individual peaks did not exceed 6% TRR (0.005 mg eg/kg)

Table 39 Summary of identified/characterized residues in paddy rice following a 0.3kg ai/ha soil application of [pyrimidine-^{14}C]-triflumezopyrim

Fraction / Solubilizates	Radioactive residues in mg eq/kg (% TRR)		
	Foliage (DAT 51)	Straw (DAT 119)	Chaff (DAT 119)
TRR	0.049 (100%)	0.050 (100%)	0.031 (100%)
Methanol/water extract	0.021 (41.8%)	0.019 (38.4%)	0.009 (26.3%)
Triflumezopyrim	0.007 (13.5%)	0.007 (14.1%)	0.002 (7.3%)
IN-R6U72	0.001 (1.8%)	0.002 (4.6%)	0.001 (3.5%)
IN-R6U70	0.001 (1.3%)	-	-
IN-R3Z91	-	0.001 (1.5%)	-
IN-RPD47	0.003 (6.6%)	0.001 (2.1%)	0.001 (2.4%)
IN-Y2186	-	0.001 (2.2%)	-
IN-SBV06	0.001 (1.4%)	0.001 (1.1%)	< 0.001 (0.8%)
Characterized by HPLC	0.009 (17.2%)	0.006 (12.8%)	0.002 (12.1%)
Further methanol/water extracts	0.003 (6.9%)	0.004 (7.7%)	0.004 (12.6%)
Post extraction solids	0.025 (51.5%)	0.027 (53.9%)	0.019 (61.1%)
Surfactant	<LOQ	<LOQ	-
0.1M NaOH	0.001 (2.3%)	0.003 (5.8%)	-
1M HCl	0.001 (2.6%)	0.002 (4.1%)	-
Total identified	0.013 (24.6%)	0.013 (25.6%)	0.004 (14.0%)
Total characterized	0.014 (29.0%)	0.015 (30.4%)	0.006 (24.7%)
Unextracted	0.023 (46.6%)	0.022 (44.0%)	0.019 (61.1%)
Total	0.050 (102.0%)	0.050 (100.0%)	0.029 (93.6%)

Table 40 Summary of identified/characterized residues in paddy rice following 2×0.035 kg ai/ha foliar applications of [pyridine-^{14}C]-triflumezopyrim

Fraction / Solubilizates	Radioactive residues in mg eq/kg (% TRR)			
	Foliage (DAT 23[a])	Straw (DAT 21[b])	Chaff (DAT 21[b])	Grain (DAT 21[b])
TRR	0.129 (100%)	0.338 (100%)	0.940 (100%)	0.065 (100%)
Surface wash and/or methanol/water extract	0.080 (61.4%)	0.185 (54.6%)	0.328 (34.8%)	0.027 (41.4%)

Fraction / Solubilizates	Radioactive residues in mg eq/kg (% TRR)			
	Foliage (DAT 23[a])	Straw (DAT 21[b])	Chaff (DAT 21[b])	Grain (DAT 21[b])
Triflumezopyrim	0.028 (21.5%)	0.064 (18.9%)	0.162 (17.2%)	0.015 (22.3%)
IN-RPA19	0.012 (9.3%)	-	0.039 (4.1%)	-
IN-R6U73	< 0.001 (0.1%)	0.002 (0.7%)	0.003 (0.3%)	< 0.001 (0.2%)
IN-R6U72	< 0.001 (0.1%)	-	-	-
IN-R6U71	0.003 (1.9%)			
IN-R6U70	0.001 (0.9%)	0.004 (1.1%)	0.003 (0.4%)	-
IN-R3Z91	< 0.001 (0.3%)	0.002 (0.4%)	0.002 (0.2%)	< 0.001 (0.2%)
IN-RPD47	-	0.006 (1.7%)	0.012 (1.3%)	0.001 (1.3%)
IN-SBV06	0.005 (3.7%)	0.010 (2.9%)	0.015 (1.6%)	0.001 (1.8%)
Characterized by HPLC	0.031 (23.5%)[c]	0.101 (28.8%)[d]	0.094 (9.8%)	0.008 (18.7%)
Further methanol/water extracts	-	-	-	0.004 (5.4%)
Post extraction solids	0.047 (36.3%)	0.152 (45.4%)	0.540 (57.5%)	0.034 (51.7%)
Surfactant	0.001 (0.9%)	0.010 (3.1%)	-	0.006 (9.3%)
Triflumezopyrim	-	-	-	0.003 (5.4%)
IN-RPD47	-	-	-	< 0.001 (0.5%)
IN-SBV06	-	-	-	< 0.001 (0.6%)
Characterized by HPLC	-	-	-	0.001 (3.0%)
0.1M NaOH	0.002 (1.6%)	0.024 (7.1%)	-	0.004 (6.1%)
1M HCl	0.004 (2.9%)	0.026 (7.8%)	-	<LOQ
10N Base Reflux	-	0.038 (11.3%)	-	-
Lignin Fraction	-	0.021 (6.2%)	-	-
Total identified	0.049 (37.8%)	0.088 (25.7%)	0.236 (25.1%)	0.020 (32.3%)
Total characterized	0.038 (28.9%)	0.220 (64.3%)	0.094 (9.8%)	0.016 (30.2%)
Unextracted	0.040 (30.9%)	0.033 (9.9%)	0.540 (57.5%)	0.024 (36.3%)
Total	0.127 (98.5%)	0.341 (100.9%)	0.870 (92.6%)	0.060 (92.3%)

[a] After first treatment;

[b] After second treatment

[c] Contribution of individual peaks did not exceed 9% TRR (0.011 mg eg/kg)

[d] Contribution of individual peaks did not exceed 6% TRR (0.019 mg eg/kg)

Table 41 Summary of identified/characterized residues in paddy rice following 2×0.035 kg ai/ha foliar applications of [methylene-^{14}C]-triflumezopyrim

Fraction / Solubilizates	Radioactive residues in mg eq/kg (% TRR)			
	Foliage (DAT 23[a])	Straw (DAT 21[b])	Chaff (DAT 21[b])	Grain (DAT 21[b])
TRR	0.124 (100%)	0.331 (100%)	0.763 (100%)	0.043 (100%)
Surface wash and/or methanol/water extract	0.087 (70.0%)	0.202 (61.1%)	0.315 (41.3%)	0.016 (37.8%)
Triflumezopyrim	0.022 (17.6%)	0.063 (18.9%)	0.151 (19.9%)	0.009 (22.2%)
IN-RPA19	0.010 (7.7%)	0.022 (6.7%)	0.030 (3.9%)	0.001 (2.8%)
IN-RPA16	< 0.001 (0.3%)	-	-	-
IN-R6U73	-	0.003 (0.9%)	0.004 (0.5%)	-
IN-R6U72	0.003 (3.0%)	-	-	-
IN-R6U71	0.003 (2.3%)	0.003 (0.9%)	0.002 (0.3%)	< 0.001 (0.6%)
IN-R6U70	< 0.001 (0.4%)	0.003 (1.0%)	-	< 0.001 (0.3%)
IN-R3Z91	-	0.003 (0.9%)	0.003 (0.4%)	-
IN-SBV06	0.004 (3.6%)	0.006 (1.8%)	0.015 (2.0%)	0.001 (2.3%)
Characterized by HPLC	0.043 (35.2%)[c]	0.102 (30.9%)[d]	0.109 (14.2%)[e]	0.002 (9.6%)
Further methanol:water extracts	-	-	-	0.007 (16.6%)
Post extraction solids	0.036 (30.0%)	0.126 (37.7%)	0.405 (53.1%)	0.020 (45.7%)
Surfactant	0.001 (1.1%)	0.016 (4.6%)	-	<LOQ
Triflumezopyrim	-	0.007 (2.0%)	-	-
IN-RPA19	-	0.005 (1.4%)	-	-
IN-SBV06	-	0.001 (0.2%)	-	-
Characterized by HPLC	-	0.004 (1.0%)	-	-
0.1M NaOH	0.002 (1.9%)	0.008 (2.5%)	-	0.008 (18.6%)
1M HCl	0.004 (3.1%)	0.017 (5.1%)	-	<LOQ

Fraction / Solubilizates	Radioactive residues in mg eq/kg (% TRR)			
	Foliage (DAT 23[a])	Straw (DAT 21[b])	Chaff (DAT 21[b])	Grain (DAT 21[b])
10N Base Reflux	-	0.027 (8.2%)	-	-
Lignin Fraction	-	0.033 (9.8%)	-	-
Total identified	0.042 (34.9%)	0.116 (34.7%)	0.205 (27.0%)	0.011 (28.2%)
Total characterized	0.050 (41.3%)	0.187 (56.5%)	0.109 (14.2%)	0.017 (44.8%)
Unextracted	0.029 (23.9%)	0.025 (7.5%)	0.405 (53.1%)	0.012 (27.1%)
Total	0.121 (97.6%)	0.328 (99.1%)	0.719 (94.2%)	0.040 (93.0%)

[a] After first treatment;

[b] After second treatment;

[c] Contribution of individual peaks did not exceed 11% TRR (0.014 mg eg/kg)

[d] Contribution of individual peaks did not exceed 8% TRR (0.026 mg eg/kg)

[e] Contribution of individual peaks did not exceed 4% TRR (0.028 mg eg/kg)

Table 42 Summary of identified/characterized residues in paddy rice following 2×0.035 kg ai/ha foliar applications of [pyrimidine-^{14}C]-triflumezopyrim

Fraction / Solubilizates	Radioactive residues in mg eq/kg (% TRR)			
	Foliage (DAT 23[a])	Straw (DAT 21[b])	Chaff (DAT 21[b])	Grain (DAT 21[b])
TRR	0.096 (100%)	0.225 (100%)	0.594 (100%)	0.076 (100%)
Surface wash and/or methanol/water extract	0.075 (77.9%)	0.159 (70.5%)	0.315 (53.0%)	0.043 (56.5%)
Triflumezopyrim	0.017 (18.2%)	0.044 (19.5%)	0.146 (24.6%)	0.017 (21.8%)
IN-R6U73	-	< 0.001 (0.1%)	-	-
IN-R6U72	0.015 (16.4%)	0.032 (14.0%)	0.022 (3.8%)	0.002 (3.3%)
IN-R6U71	0.005 (5.6%)	0.004 (1.7%)	0.004 (0.8%)	0.001 (0.9%)
IN-R6U70	0.002 (2.2%)	-	0.001 (0.2%)	< 0.001 (0.5%)
IN-R3Z91	0.002 (2.2%)	0.003 (1.5%)	0.004 (0.6%)	0.001 (0.9%)
IN-RPD47	-	0.003 (1.5%)	0.013 (2.1%)	0.001 (0.8%)
IN-Y2186	-	0.008 (3.6%)	0.034 (5.7%)	0.009 (12.3%)
IN-SBV06	0.003 (3.3%)	0.007 (3.1%)	0.012 (2.1%)	0.001 (1.9%)
Characterized by HPLC	0.028 (29.8%)[c]	0.058 (25.3%)[d]	0.076 (13.1%)[e]	0.011 (14.3%)[f]
Further methanol:water extracts	-	-	-	-
Post extraction solids	0.022 (22.8%)	0.066 (29.4%)	0.279 (47.0%)	0.033 (43.5%)
Surfactant	<LOQ	<LOQ	-	0.008 (11.0%)
0.1M NaOH	0.001 (0.7%)	0.003 (1.3%)	-	0.010 (12.6%)
1M HCl	0.001 (1.5%)	0.007 (2.9%)	-	<LOQ
10N Base Reflux	-	-	-	-
Lignin Fraction	-	-	-	-
Total identified	0.044 (47.9%)	0.101 (45.0%)	0.236 (39.9%)	0.032 (42.4%)
Total characterized	0.030 (32.0%)	0.068 (29.5%)	0.076 (13.1%)	0.029 (37.9%)
Unextracted	0.020 (20.6%)	0.056 (25.2%)	0.279 (47.0%)	0.015 (19.9%)
Total	0.094 (97.8%)	0.225 (100.0%)	0.591 (99.5%)	0.076 (100.0%)

[a] After first treatment ; [b] After second treatment

[c] Contribution of individual peaks did not exceed 5% TRR (0.005 mg eg/kg)

[d] Contribution of individual peaks did not exceed 7% TRR (0.015 mg eg/kg)

[e] Contribution of individual peaks did not exceed 5% TRR (0.031 mg eg/kg)

[f] Contribution of individual peaks did not exceed 6% TRR (0.004 mg eg/kg)

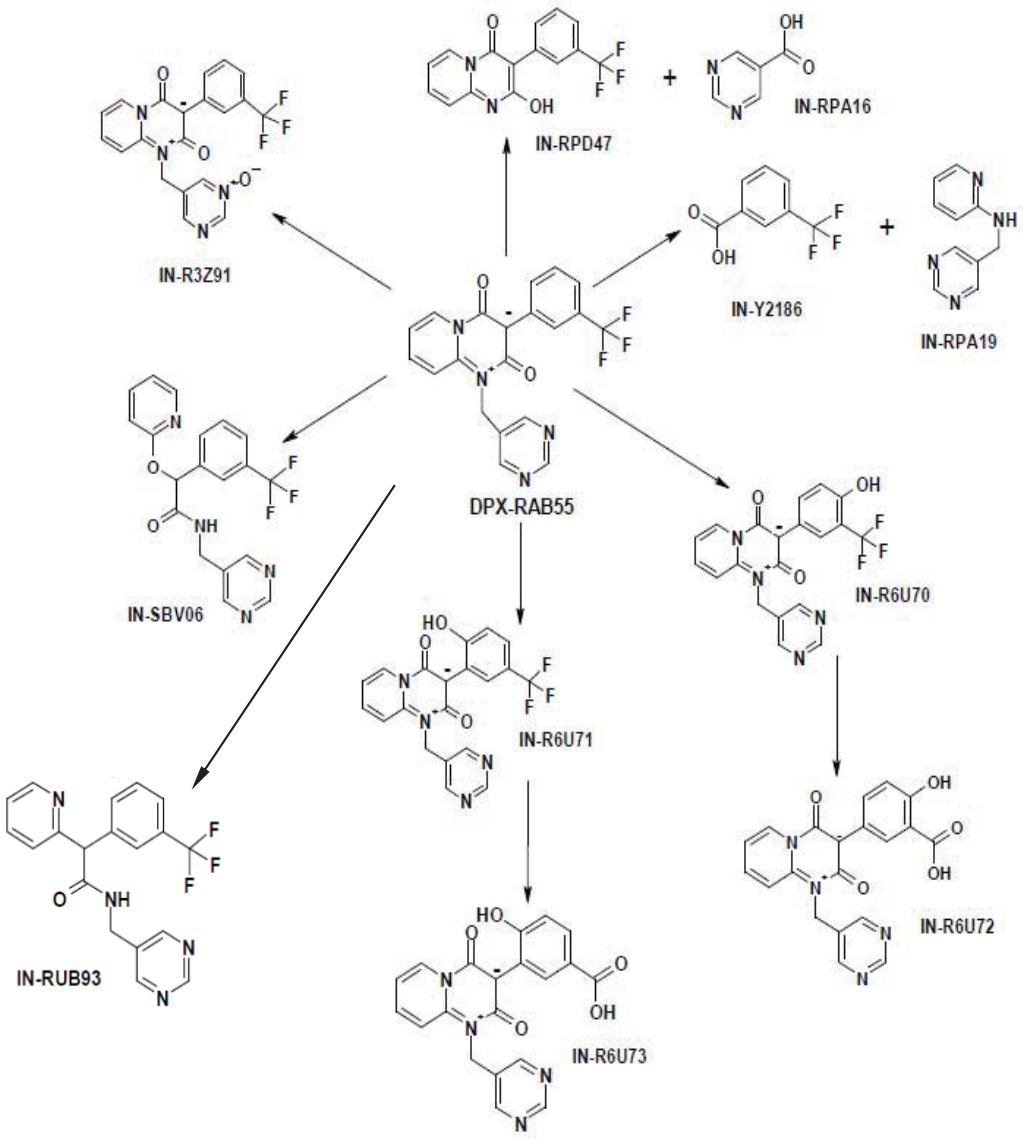


Figure 3 Proposed metabolic pathway of triflumezopyrim in rice

Animal metabolism

Metabolism studies on lactating goats and hens were provided using [pyridine-^{14}C]-, [methylene-^{14}C]- and [pyrimidine-^{14}C]-radiolabelled triflumezopyrim.

In lactating goats the transfer of radioactivity into tissues and milk was low, showing highest TRR levels in kidney, followed by liver and milk. Parent triflumezopyrim was the principal component identified in all samples. The predominant metabolite was the glucuronic acid and sulphate conjugates of IN-R6U70 and/or unconjugated IN-R6U70.

In laying hens transfer of radioactivity into tissues and eggs was even lower, showing highest TRR levels in liver. Parent triflumezopyrim was the principal component identified in egg and liver,

but was not detected in muscle and fat. Several metabolites were identified, but were never > 0.01 mg eq/kg, with the exception of IN-R3Z91 and IN-R6U70 in liver.

Lactating goats

Green M., Strathdee A., 2016a, TRIFLUMEZ_028.

The metabolic fate of triflumezopyrim in lactating goats was investigated using [pyrimidine-^{14}C], [methylene-^{14}C]- and [pyridine-^{14}C]-radiolabelled triflumezopyrim. The compound was administered for seven consecutive days to three lactating goats (one per label) in gelatine capsules at 21.960 mg ai/kg feed (0.674 mg/kg bw) for [pyrimidine-^{14}C]-, 24.760 mg ai/kg feed (0.598 mg/kg bw) for [methylene-^{14}C]- or 20.376 mg ai/kg feed (0.575 mg/kg bw) for [pyridine-^{14}C]-triflumezopyrim. Excreta and milk were collected daily. The animals were sacrificed approximately 6 hours after the last dose. Liver, kidney, muscle, omental fat, renal fat, subcutaneous fat, bile and gastrointestinal tract contents were collected.

Total radioactivity in liquid samples such as urine, cage wash, milk and various extracts was directly measured by LSC. All other samples were subjected to combustion prior to the determination of total radioactivity by LSC. All samples were analysed within 180 days except for bile (891 days).

Samples of milk, liver, kidney, muscle and faeces were extracted with acetonitrile, followed by acetonitrile:water (9:1, v/v) and acetonitrile:water (1:1, v/v). Extracts of muscle and milk were partitioned against hexane to remove fatty material. Fat samples were extracted with dichloromethane first, followed by the extraction scheme described above. The dichloromethane extract was evaporated to dryness, reconstituted in hexane and partitioned against acetonitrile. Bile samples, as well as acetonitrile/water extracts from liver and kidney were partitioned twice with ethyl acetate to separate conjugated and non-conjugated metabolites. After evaporation of the ethyl acetate and reconstitution in water, samples were deconjugated with β-Glucuronidase. Post extraction solids from liver were further characterized by treatment with protease from *Streptomyces griseus*. For identification/characterization sample extracts were analysed by HPLC against reference standards. Confirmation of metabolite identities was accomplished by LC-MS and/or TLC.

The total recovery of the administered radioactivity was between 81–94%. The majority of the radioactivity was found in the faeces (36–53%), followed by urine (19–29%) and the G.I. track content (11–12%). Radioactive residues in the edible matrices were highest in milk (~2%), while for all other matrices radioactive residues were between < 0.1% and 0.35%. A summary of the recovered radioactivity is presented in Table 43.

Table 43 Recovered radioactive residues after oral administration of ^{14}C-labelled triflumezopyrim for 7 consecutive days to goats

Radiolabel	[pyrimidine-3-^{14}C] (0.674 mg/kg bw)		[methylene-^{14}C] (0.598 mg/kg bw)		[pyridine-2,6-^{14}C] (0.575 mg/kg bw)	
Matrix	% AR	TRR in mg eq/kg	% AR	TRR in mg eq/kg	% AR	TRR in mg eq/kg
Faeces	52.56	N/A	50.20	N/A	35.91	N/A
Urine	19.44	N/A	29.42	N/A	28.63	N/A
Cage wash	2.53	N/A	0.96	N/A	3.03	N/A
Milk	1.94	0.281	2.32	0.604	1.15	0.360
Cream (day 4-6)	NC	0.282	NC	0.547	NC	0.367
Skim milk (day 4-6)	NC	0.324	NC	0.662	NC	0.401
Liver	0.23	0.538	0.35	0.813	0.24	0.484
Kidney	0.03	0.581	0.06	0.932	0.07	0.889
Muscle [a]	0.12	0.024	0.23	0.039	0.25	0.041
Omental fat[a]	<0.1	0.007	<0.1	0.011	<0.1	0.013
Renal fat[a]	<0.1	0.009	<0.1	0.016	<0.1	0.044
Subcutaneous fat[a]	<0.1	0.015	<0.1	0.015	<0.1	0.020
G.I. tract Contents	12.14	N/A	11.09	N/A	11.42	N/A
Total	88.87		94.40		80.45	

[a] Total muscle mass was assumed to be approximately 25% of body weight and total fat mass approximately 15% of body weight. Each fat type accounted for the following percentages, renal fat ca. 0.9%, omental fat ca. 4.1% and subcutaneous fat ca. 9.4% (Meat and Offal Yields of Goats)

NC: not calculated, no mass balance provided

In milk the total radioactivity increased over the whole dosing period of 7 days for all labels administered, starting from 0.266–0.473 mg eq/kg at day 1 to a terminal concentration of 0.442–1.035 mg eq/kg at day 7. The results are summarised in the following table:

Table 44 Recovered radioactive residues in milk after oral administration of ^{14}C-labelled triflumezopyrim for 7 consecutive days to goats

TRR in milk Days	[pyrimidine-3-^{14}C] (0.674 mg/kg bw) TRR in mg eq/kg	[methylene-^{14}C] (0.598 mg/kg bw) TRR in mg eq/kg	[pyridine-2,6-^{14}C] (0.575 mg/kg bw) TRR in mg eq/kg
1	0.266	0.473	0.332
2	0.264	0.585	0.430
3	0.292	0.615	0.423
4	0.323	0.598	0.451
5	0.296	0.257	0.263
6	0.344	0.691	0.463
7	0.442	1.035	0.617

The initial acetonitrile/water (dichloromethane for fat) extractions released 78.1–99.4% TRR from tissues and milk. Protease digestion of the liver residues remaining after aqueous acetonitrile extraction liberated 11.3–11.6% TRR (0.056–0.093 mg eq/kg) leaving 0.6–16.0% TRR, (0.001–0.084 mg/kg) in the unextracted solids in all matrices. A summary of the results is presented in Table 45.

Table 45 Characterization of radioactivity in milk and tissues from [^{14}C]-triflumezopyrim dosed lactating goats

Sample Fraction	Radioactive residues in mg eq/kg (% TRR) Milk (Day 4-6 Composite)	Liver	Kidney	Muscle	Omental Fat	Renal Fat	Subcutaneous Fat
[pyrimidine-3-^{14}C]-triflumezopyrim							
Combined acetonitrile/ water extracts	0.279 (99.4%)	0.44 (82.8%)	0.57 (97.4%)	0.022 (91.4%)	<LOQ	<LOQ	<LOQ
Dichloromethane soluble extract	NC	NC	NC	NC	0.006 (88.1%)	0.008 (88.2%)	0.013 (84.0%)
Solvent/water extracts not analysed	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ	<LOQ
Protease treatment	NA	0.061 (11.3%)	NA	NA	NA	NA	NA
Unextracted residues	0.002 (0.6%)	0.032 (6.0%)	0.015 (2.5%)	0.002 (8.6%)	0.001 (11.9%)	0.001 (11.8%)	0.002 (16.0%)
Total recovered radioactivity	0.28 (100.0%)	0.54 (100.0%)	0.58 (99.9%)	0.024 (100.0%)	0.007 (100.0%)	0.009 (100.0%)	0.015 (100.0%)
[methylene-^{14}C]-triflumezopyrim							
Combined acetonitrile/ water extracts	0.60 (98.9%)	0.64 (78.1%)	0.89 (95.9%)	0.036 (92.6%)	<LOQ	<LOQ	<LOQ
Dichloromethane soluble extract	NC	NC	NC	NC	0.010 (94.8%)	0.015 (92.5%)	0.013 (88.9%)
Solvent/water extracts not analysed	<LOQ	NA	NA	<LOQ	<LOQ	<LOQ	<LOQ
Protease treatment	NA	0.093 (11.5%)	NA	NA	NA	NA	NA
Unextracted residues	0.007 (1.1%)	0.084 (10.3%)	0.038 (4.1%)	0.003 (7.4%)	0.001 (5.2%)	0.001 (7.5%)	0.002 (11.1%)
Total recovered	0.60	0.81	0.93	0.039	0.011	0.016	0.015

Sample / Fraction	Radioactive residues in mg eq/kg (% TRR)						
	Milk (Day 4-6 Composite)	Liver	Kidney	Muscle	Omental Fat	Renal Fat	Subcutaneous Fat
radioactivity	(100.0%)	(100.0%)	(100.0%)	(100.0%)	(100.0%)	(100.0%)	(100.0%)
[pyridine-^{14}C]-triflumezopyrim							
Combined acetonitrile/ water extracts	0.36 (98.8%)	0.40 (83.1%)	0.87 (97.9%)	0.039 (95.2%)	<LOQ	<LOQ	<LOQ
Dichloromethane soluble extract	NC	NC	NC	NC	0.012 (95.2%)	0.037 (84.5%)	0.018 (90.4%)
Solvent/water extracts not analysed	<LOQ	NA	NA	<LOQ	0.001 (10.7%)(A)	0.008 (17.1%)(B)	<LOQ
Protease treatment	NA	0.056 (11.6%)	NA	NA	NA	NA	NA
Unextracted residues	0.004 (1.2%)	0.026 (5.3%)	0.020 (2.2%)	0.002 (4.8%)	0.001 (4.8%)	0.001 (2.1%)	0.002 (9.6%)
Total recovered radioactivity	0.36 (100.0%)	0.48 (100.0%)	0.89 (100.1%)	0.041 (100.0%)	0.013 (100.0%)	0.044 (100.0%)	0.020 (100.0%)

NA = Not applicable

NC = Not conducted

<LOQ = Less than limit of quantification

(A) Hexane fraction obtained following partitioning of the concentrated acetonitrile-miscible sample derived from the dichloromethane extract

(B) Includes the acetonitrile extract of the dichloromethane extracted solids and the hexane fraction obtained following partitioning of the concentrated acetonitrile-miscible sample derived from the dichloromethane extract

Triflumezopyrim was the principal extracted component in day 4–6 composite milk (81.1–82.8% TRR; 0.232–0.490 mg/kg), liver (36.8–54.1% TRR; 0.198–0.374 mg/kg), kidney (69.5–82.6% TRR; 0.417–0.734 mg/kg), muscle (63.7–88.7% TRR; 0.015–0.035 mg/kg), and fat (69.6–92.6% TRR; 0.006–0.031 mg/kg) from all radiolabels. The predominant metabolite in liver and kidney was unconjugated IN-R6U70 and its glucuronic acid and sulphate conjugates. Additionally, metabolites IN-RPA16, IN-R6U73, IN-R3Z91 and IN-RPD47 were identified.

Table 46 Summary of identified/characterized residues in milk and tissues from [pyrimidine-3-^{14}C]-triflumezopyrim dosed lactating goats

Sample	Radioactive residues in mg eq/kg (% TRR)						
	Milk (Day 4-6 Composite)	Liver	Kidney	Muscle	Omental Fat	Renal Fat	Subcutaneous Fat
TRR	0.28 (100%)	0.54 (100%)	0.58 (100%)	0.024 (100%)	0.007 (100%)	0.009 (100%)	0.015 (100%)
Concentrated extracts	0.28 (99.4%)	0.45 (82.8%)	0.57 (97.4%)	0.022 (91.4%)	0.006 (88.1%)	0.008 (88.2%)	0.013 (84.0%)
Triflumezopyrim	0.23 (82.4%)	0.20 (36.4%)	0.42 (71.7%)	0.015 (63.7%)	0.006 (88.1%)	0.007 (82.0%)	0.012 (76.8%)
IN-R6U73	-	0.015 (2.7%)	-	-	-	-	-
Glucuronic acid	-	0.15 (27.0%)	0.084 (14.5%)	-	-	-	-
Sulphate conjugate of IN-R6U70	-	0.045 (8.3%)	0.012 (2.0%)	-	-	-	-
IN-R6U70	0.048 (17.0%)	0.027 (5.0%)	0.038 (6.6%)	0.002 (7.3%)	-	< 0.001 (6.2%)	0.001 (7.2%)
IN-R3Z91	-	0.018 (3.4%)	0.016 (2.7%)	-	-	-	-
Characterized by HPLC	-	-	-	0.005 (20.4%)	-	-	-
Post extraction solids	0.002 (0.6%)	0.093 (17.3%)	0.015 (2.5%)	0.002 (8.6%)	0.001 (11.9%)	0.001 (11.8%)	0.002 (16.0%)

Sample	Radioactive residues in mg eq/kg (% TRR) Milk (Day 4-6 Composite)	Liver	Kidney	Muscle	Omental Fat	Renal Fat	Subcutaneous Fat
Protease digest	-	0.061 (11.3%)	-	-	-	-	-
Triflumezopyrim	-	0.002 (0.4%)	-	-	-	-	-
IN-R6U73	-	0.008 (1.4%)	-	-	-	-	-
Characterized by HPLC	-	0.052 (9.4%)	-	-	-	-	-
Total identified	0.28 (99.4%)	0.46 (84.6%)	0.57 (97.5%)	0.017 (71.0%)	0.006 (88.1%)	0.007 (88.2%)	0.013 (84.0%)
Unextracted	0.002 (0.6%)	0.032 (6.0%)	0.015 (2.5%)	0.002 (8.6%)	0.001 (11.9%)	0.001 (11.8%)	0.002 (16.0%)
Total	0.28 (100.4%)	0.54 (100.4%)	0.58 (100.2%)	0.024 (100.0%)	0.007 (100.0%)	0.008 (88.9%)	0.015 (100.0%)

Table 47 Summary of identified/characterized residues in milk and tissues from [methylene-^{14}C]-triflumezopyrim dosed lactating goats

Sample	Radioactive residues in mg eq/kg (% TRR) Milk (Day 4-6 Composite)	Liver	Kidney	Muscle	Omental Fat	Renal Fat	Subcutaneous Fat
TRR	0.60 (100%)	0.81 (100%)	0.93 (100%)	0.039 (100%)	0.011 (100%)	0.016 (100%)	0.015 (100%)
Concentrated extracts	0.58 (96.6%)	0.64 (78.1%)	0.89 (95.9%)	0.036 (92.6%)	0.010 (94.8%)	0.015 (92.5%)	0.013 (88.9%)
Triflumezopyrim	0.49 (81.1%)	0.37 (45.7%)	0.65 (69.5%)	0.035 (88.7%)	0.010 (92.6%)	0.013 (84.2%)	0.012 (82.3%)
IN-RPA16	-	-	0.009 (1.0%)	-	-	-	-
IN-R6U73	-	0.011 (1.3%)	-	-	-	-	-
Glucuronic acid conjugate of IN-R6U70	-	0.11 (13.0%)	0.052 (5.6%)	-	-	-	-
Sulphate conjugate of IN-R6U70	-	0.033 (4.1%)	0.007 (0.8%)	-	-	-	-
IN-R6U70	0.070 (11.6%)	0.038 (4.7%)	0.091 (9.8%)	0.002 (3.9%)	< 0.001 (2.2%)	0.001 (8.3%)	0.001 (4.8%)
IN-R3Z91	0.024 (3.9%)	0.029 (3.6%)	0.021 (2.2%)	-	-	-	< 0.001 (1.8%)
Characterized by HPLC	-	0.047 (5.8%)	0.063 (6.9%)	-	-	-	-
Post extraction solids	0.007 (1.1%)	0.177 (21.8%)	0.038 (4.1%)	0.003 (7.4%)	0.001 (5.2%)	0.001 (7.5%)	0.002 (11.1%)
Protease digest	-	0.093 (11.5%)	-	-	-	-	-
Triflumezopyrim	-	0.002 (0.2%)	-	-	-	-	-
IN-R6U73	-	0.007 (0.9%)	-	-	-	-	-
IN-R3Z91	-	0.003 (0.4%)	-	-	-	-	-
Characterized by HPLC	-	0.084 (10.2%)	-	-	-	-	-
Total identified	0.58 (96.6%)	0.60 (73.9%)	0.83 (88.9%)	0.037 (92.6%)	0.010 (94.8%)	0.014 (92.5%)	0.013 (88.9%)
Unextracted	0.007 (1.1%)	0.084 (10.3%)	0.038 (4.1%)	0.003 (7.4%)	0.001 (5.2%)	0.001 (7.5%)	0.002 (11.1%)
Total	0.59 (97.9%)	0.82 (100.4%)	0.93 (99.7%)	0.040 (102.6%)	0.011 (100.0%)	0.015 (93.8%)	0.015 (100.0%)

Table 48 Summary of identified/characterized residues in milk and tissues from [pyridine-2,6-^{14}C]-triflumezopyrim dosed lactating goats

Sample	Radioactive residues in mg eq/kg (% TRR)						
	Milk (Day 4-6 Composite)	Liver	Kidney	Muscle	Omental Fat	Renal Fat	Subcutaneous Fat
TRR	0.36 (100%)	0.48 (100%)	0.89 (100%)	0.041 (100%)	0.013 (100%)	0.044 (100%)	0.020 (100%)
Concentrated extracts	0.36 (98.8%)	0.40 (83.1%)	0.87 (97.9%)	0.034 (83.2%)	0.011 (84.5%)	0.036 (80.8%)	0.018 (90.4%)
Triflumezopyrim	0.30 (82.8%)	0.26 (54.1%)	0.73 (82.6%)	0.032 (78.3%)	0.011 (82.8%)	0.031 (69.6%)	0.016 (82.2%)
IN-R6U73	-	-	-	-	-	-	-
Glucuronic acid	-	0.050 (10.3%)	0.040 (4.5%)	-	-	-	-
Sulphate conjugate of IN-R6U70	-	0.039 (8.0%)	0.012 (1.3%)	-	-	-	-
IN-R6U70	0.058 (16.0%)	0.025 (5.2%)	0.054 (6.1%)	0.002 (4.9%)	< 0.001 (1.7%)	0.003 (7.8%)	0.001 (5.7%)
IN-R3Z91	-	0.027 (5.5%)	0.013 (1.5%)	-	-	0.001 (2.5%)	0.001 (2.5%)
IN-RPD47	-	-	-	-	-	< 0.001 (0.9%)	-
Characterized by HPLC	-	-	0.016 (1.8%)	-	-	-	-
Post extraction solids	0.004 (1.2%)	0.082 (16.9%)	0.020 (2.2%)	0.002 (4.8%)	0.001 (4.8%)	0.001 (2.1%)	0.002 (9.6%)
Protease digest	-	0.056 (11.6%)	-	-	-	-	-
IN-R6U73	-	0.007 (1.5%)	-	-	-	-	-
IN-R6U70	-	0.021 (4.3%)	-	-	-	-	-
Characterized by HPLC	-	0.028 (5.8%)	-	-	-	-	-
Extracts not analysed	-	-	-	-	-	0.006 (13.4%)	-
Total identified	0.36 (98.8%)	0.43 (88.9%)	0.85 (96.0%)	0.034 (83.2%)	0.011 (84.5%)	0.035 (80.8%)	0.018 (90.4%)
Unextracted	0.004 (1.2%)	0.026 (5.3%)	0.020 (2.2%)	0.002 (4.8%)	0.001 (4.8%)	0.001 (2.1%)	0.002 (9.6%)
Total	0.36 (100.0%)	0.48 (100.2%)	0.89 (100.0%)	0.036 (88.0%)	0.012 (92.3%)	0.042 (95.5%)	0.020 (100.0%)

Laying hens

Green M., Strathdee A., 2016b, TRIFLUMEZ_029.

The metabolic fate of triflumezopyrim in laying hens was investigated using [pyrimidine-^{14}C], [methylene-^{14}C]- or [pyridine-^{14}C]-radiolabelled triflumezopyrim. Each of the compounds was administered for 14 consecutive days to 3 groups of laying hens (5 hens per group) in gelatine capsules at 13.777 mg ai/kg feed (7.599 mg/kg bw) for [pyrimidine-^{14}C]-, 14.289 mg ai/kg feed (7.625 mg/kg bw) for [methylene-^{14}C]- and 14.886 mg ai/kg feed (7.757 mg/kg bw) for [pyridine-^{14}C]- triflumezopyrim. Excreta and cage wash were collected once daily from each group of hens and eggs were collected twice daily. The hens were sacrificed approximately 6 hours after the last dose. Liver, muscle, abdominal fat, and gastrointestinal tract contents were collected.

Total radioactivity in liquid samples such as cage wash, egg and various extracts was directly measured by LSC. All other samples were subjected to combustion prior to the determination of total radioactivity by LSC.

Pooled samples of egg, liver, muscle and excreta were extracted with acetonitrile, followed by acetonitrile:water (9:1, v/v) and acetonitrile:water (1:1, v/v). Extracts of liver, egg, muscle and excreta were partitioned against hexane to remove fatty material. Fat samples were extracted with dichloromethane first, followed by the extraction scheme described above. The dichloromethane extract was evaporated to dryness, reconstituted in hexane and partitioned against acetonitrile. Post extraction solids from egg and liver were further characterized by treatment with protease from *Streptomyces griseus*. For identification/characterization sample extracts of egg, liver and excreta were analysed by HPLC against reference standards, while muscle and fat were analysed by TLC. Confirmation of metabolite identities in excreta and liver was accomplished by LC-MS and TLC.

The total recovery of the administered radioactivity was between 89–97%. The majority of the radioactivity was found in excreta (83–90%), followed by cage wash (4–6%) and the G.I. track content (1–2%). Radioactive residues in the edible matrices were highest in whole egg (0.07–0.09%). TRR levels in eggs reached a plateau after approximated one week. A summary of the recovered radioactivity is presented in Table 49.

Table 49 Recovered radioactive residues in eggs after oral administration of ^{14}C-labelled triflumezopyrim for 14 consecutive days to laying hens

TRR in eggs Days	[pyrimidine-3-^{14}C] TRR in mg eq/kg	[methylene-^{14}C] TRR in mg eq/kg	[pyridine-2,6-^{14}C] TRR in mg eq/kg
1	< 0.001	0.014	0.004
2	0.014	0.019	0.014
3	0.014	0.018	0.014
4	0.022	0.029	0.023
5	0.020	0.029	0.021
6	0.027	0.036	0.031
7	0.029	0.038	0.031
8	0.031	0.039	0.026
9	0.032	0.030	0.032
10	0.028	0.027	0.026
11	0.018	0.028	0.021
12	0.025	0.029	0.028
13	0.032	0.031	0.032
14	0.025	NS	0.031

NS: no sample

Table 49 Recovered radioactive residues after oral administration of ^{14}C-labelled triflumezopyrim for 14 consecutive days to laying hens

Radiolabel	[pyrimidine-3-^{14}C] (7.599 mg/kg bw)		[methylene-^{14}C] (7.625 mg/kg bw)		[pyridine-2,6-^{14}C] (7.757 mg/kg bw)	
Matrix	% AR	TRR in mg eq/kg	% AR	TRR in mg eq/kg	% AR	TRR in mg eq/kg
Excreta	89.5	N/A	83.7	N/A	83.3	N/A
Cage wash	5.9	N/A	4.7	N/A	4.2	N/A
Whole egg	0.07	N/A	0.09	N/A	0.07	N/A
Liver	0.05	0.30	0.06	0.38	0.05	0.28
Muscle	< 0.01	0.006	< 0.01	0.012	< 0.01	0.005
Abdominal fat	< 0.01	0.004	< 0.01	0.008	< 0.01	0.014
G.I. tract Contents	1.81	N/A	1.67	N/A	1.2	N/A
Total	97.3		90.2		88.9	

The combined solvent extracts contained 55.6–94.3% TRR. Protease digestion of the egg and liver residues remaining after solvent extraction liberated 12.2–12.6% TRR (0.003 mg eq/kg) and

14.0–20.1% TRR (0.043–0.059 mg eq/kg), respectively. Unextracted solids in all matrices accounted for 5.7–44.4% TRR. A summary of the results is presented in Table 50.

Table 50 Characterization of radioactivity in eggs and tissues from [^{14}C]-triflumezopyrim dosed laying hens

Sample Fraction	Radioactive residues in mg eq/kg (% TRR)			
	Whole Egg (Day 9-13 Composite)	Liver	Muscle	Abdominal Fat
[pyrimidine-3-^{14}C]-triflumezopyrim				
Combined solvent extracts [a]	0.023 (91.9%)	0.240 (78.8%)	0.005 (84.5%)	0.004 (94.3%)
Protease treatment	NA	0.043 (14.0%)	NA	NA
Unextracted residues	0.002 (8.1%)	0.022 (7.2%)	0.001 (15.5%)	< 0.001 (5.7%)
Total recovered radioactivity	0.025 (100.0%)	0.304 (100.0%)	0.006 (100.0%)	0.004 (100.0%)
[methylene-^{14}C]-triflumezopyrim				
Combined solvent extracts [a]	0.020 (79.8%)	0.297 (78.2%)	0.010 (81.2%)	0.007 (93.3%)
Protease treatment	0.003 (12.6%)	0.059 (15.5%)	NA	NA
Unextracted residues	0.002 (7.6%)	0.024 (6.2%)	0.002 (18.8%)	0.001 (6.7%)
Total recovered radioactivity	0.025 (100.0%)	0.380 (100.0%)	0.012 (100.0%)	0.008 (100.0%)
[pyridine-^{14}C]-triflumezopyrim				
Combined solvent extracts [a]	0.020 (79.1%)	0.207 (72.8%)	0.003 (55.6%)	0.013 (92.8%)
Protease treatment	0.003 (12.2%)	0.057 (20.1%)	NA	NA
Unextracted residues	0.002 (8.7%)	0.020 (7.1%)	0.002 (44.4%)	0.001 (7.2%)
Total recovered radioactivity	0.025 (100.0%)	0.284 (100.0%)	0.005 (100.0%)	0.014 (100.0%)

[a] Acetonitrile/water extracts for egg, liver and muscle; dichloromethane (DCM) extract for fat, prior to solvent partitioning and concentration

Triflumezopyrim was the principal extracted component in Day 9–13 composite eggs (47.6–65.2% TRR; 0.012–0.016 mg/kg) and liver (50.1–52.0% TRR; 0.143–0.198 mg/kg) from all radiolabels. Among the identified metabolites only IN-R3Z91 in liver occurred in significant amounts (9.5–14.0% TRR; 0.027–0.053 mg/kg). Other metabolites identified at lower levels were IN-R6U70, IN-RPD47, IN-R3Z91 and IN-SBV06. A summary of the results is presented in Tables 51 to 53.

Table 51 Summary of identified/characterized residues in eggs and tissues from [pyrimidine-3-^{14}C]-triflumezopyrim dosed laying hens

Sample	Radioactive residues in mg eq/kg (% TRR)			
	Whole Egg	Liver	Muscle	Abdominal fat
TRR	0.025 (100%)	0.30 (100%)	0.006 (100%)	0.004 (100%)
Concentrated extracts	0.023 (91.9%)	0.23 (75.4%)	0.002 (30.4%)	0.003 (71.1%)
Triflumezopyrim	0.016 (65.2%)	0.16 (51.0%)	< 0.001 (2.4%)	-
IN-R6U70	0.001 (3.5%)	0.009 (2.9%)	< 0.001 (1.7%)	0.001 (25.1%)
IN-RPD47	0.001 (2.4%)	-	-	-
IN-R3Z91	-	0.040 (13.3%)	-	-
IN-SBV06	< 0.001 (1.9%)	-	-	-
Characterized by HPLC or TLC	0.005 (19.0%)	0.024 (8.3%)	0.002 (26.3%)	0.002 (46.0%)
Extracts not further analysed	-	0.010 (3.4%)	-	< 0.001 (9.6%)
Post extraction solids	0.002 (8.1%)	0.065 (21.2%)	0.001 (15.5%)	< 0.001 (5.7%)
Protease digest	-	0.043 (14.0%)	-	-
Characterized by HPLC or TLC	-	0.042 (14.0%)	-	-
Total identified	0.018 (73.0%)	0.20 (67.2%)	< 0.001 (4.1%)	0.001 (25.1%)
Unextracted	0.002 (8.1%)	0.022 (7.2%)	0.001 (15.5%)	< 0.001 (5.7%)
Total	0.025 (100.0%)	0.30 (99.3%)	0.003 (50.0%)	0.003 (75.0%)

Table 52 Summary of identified/characterized residues in eggs and tissues from [methylene-^{14}C]-triflumezopyrim dosed laying hens

Sample	Radioactive residues in mg eq/kg (% TRR)			
	Whole Egg	Liver	Muscle	Abdominal fat
TRR	0.025 (100%)	0.38(100%)	0.012 (100%)	0.008 (100%)
Concentrated extracts	0.020 (79.8%)	0.28 (74.6%)	0.005 (45.3%)	0.003 (39.0%)
Triflumezopyrim	0.014 (54.8%)	0.20 (52.0%)	-	-
IN-R6U70	0.001 (3.0%)	0.011 (2.9%)	0.003 (21.8%)	0.001 (17.2%)
IN-R3Z91	< 0.001 (0.8%)	0.053 (14.0%)	-	-
IN-SBV06	0.001 (2.0%)	-	-	-
Characterized by HPLC or TLC	0.004 (19.2%)	0.081 (21.2%)	0.003 (23.5%)	0.002 (21.8%)
Extracts not further analysed	-	0.014 (3.6%)	-	0.004 (54.3%)
Post extraction solids	0.002 (7.6%)	0.083 (21.7%)	0.002 (18.8%)	0.001 (6.7%)
Protease digest	0.003 (12.6%)	0.059 (15.5%)	-	-
Characterized by HPLC or TLC	-	0.059 (15.4%)	-	-
Total identified	0.016 (60.6%)	0.26 (68.9%)	0.003 (21.8%)	0.001 (17.2%)
Unextracted	0.002 (7.6%)	0.024 (6.2%)	0.002 (18.8%)	0.001 (6.7%)
Total	0.025 (100.0%)	0.38 (102.6%)	0.008 (66.7%)	0.008 (100.0%)

Table 53 Summary of identified/characterized residues in eggs and tissues from [pyridine-^{14}C]-triflumezopyrim dosed laying hens

Sample	Radioactive residues in mg eq/kg (% TRR)			
	Whole Egg	Liver	Muscle	Abdominal fat
TRR	0.025 (100%)	0.28(100%)	0.005 (100%)	0.014 (100%)
Concentrated extracts	0.020 (79.1%)	0.20 (68.9%)	0.002 (30.6%)	0.005 (35.2%)
Triflumezopyrim	0.012 (47.6%)	0.14 (50.1%)	-	-
IN-R6U70	0.001 (4.0%)	0.008 (2.9%)	-	0.002 (11.8%)
IN-RPD47	0.001 (3.2%)	0.004 (1.4%)	-	-
IN-R3Z91	0.001 (4.0%)	0.027 (9.5%)	-	-
IN-SBV06	0.001 (2.6%)	-	-	-
Characterized by HPLC or TLC	0.004 (17.8%)	0.014 (4.9%)	0.001 (30.6%)	0.003 (23.4%)
Extracts not further analysed	-	0.011 (3.9%)	-	0.009 (57.6%)
Post extraction solids	0.005 (20.9%)	0.077 (27.2%)	0.002 (44.4%)	0.001 (7.2%)
Protease digest	0.003 (12.2%)	0.057 (20.1%)	-	NA
Triflumezopyrim	-	0.001 (0.2%)		
IN-R3Z91	-	0.002 (0.7%)		
Characterized by HPLC or TLC	-	0.053 (19.2%)		
Total identified	0.016 (61.4%)	0.184 (64.8%)	-	0.002 (11.8%)
Unextracted	0.002 (8.7%)	0.020 (7.1%)	0.002 (44.4%)	0.001 (7.2%)
Total	0.025 (100.0%)	0.282 (99.3%)	0.003 (75.0%)	0.015 (107.1%)

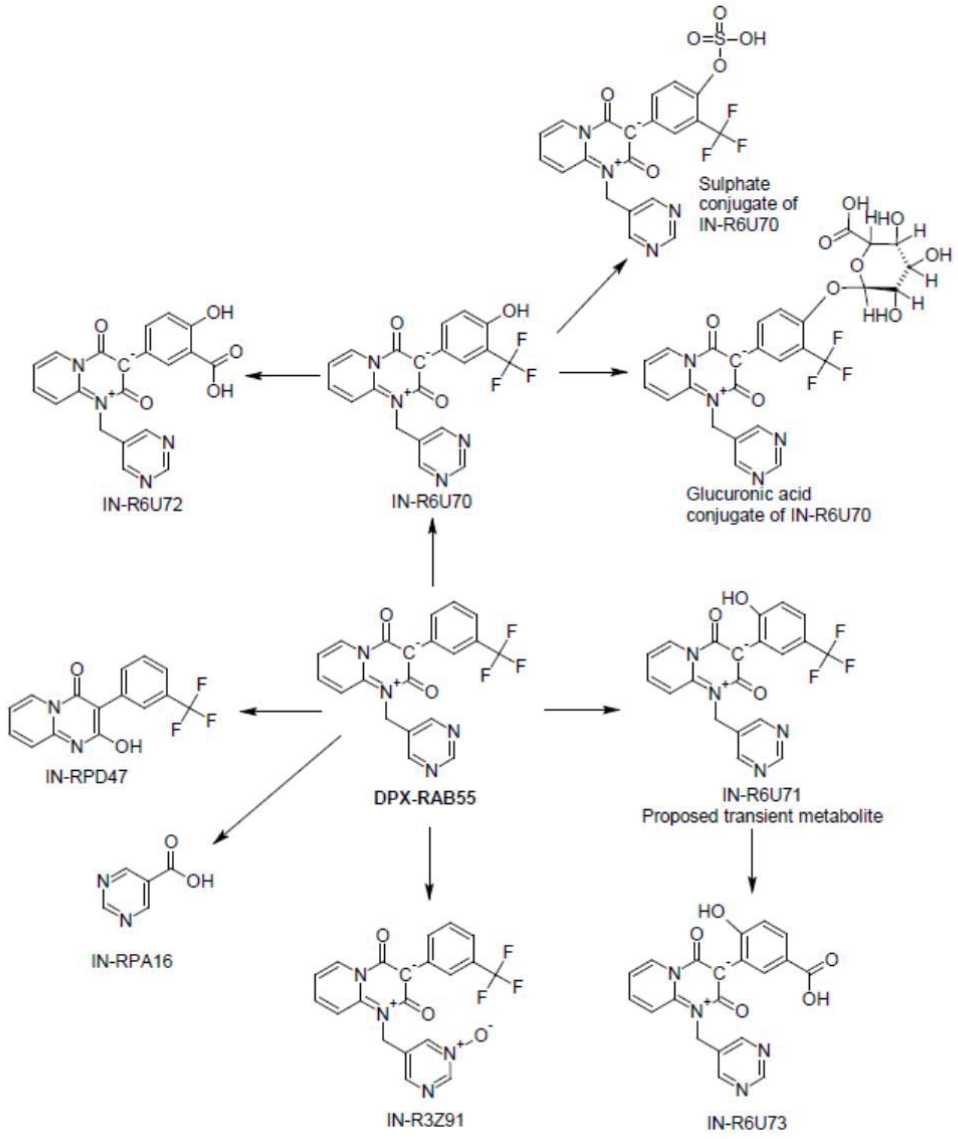


Figure 4 Proposed metabolic pathway of triflumezopyrim in animals

RESIDUE ANALYSIS

Analytical methods

For the analysis of triflumezopyrim and metabolites in various plant and animal matrices analytical methods suitable for enforcement and data generation purposes were submitted. In the following table an overview of these methods is presented.

Table 54 Overview of analytical methods for triflumezopyrim and metabolites

Method	Matrix	Extraction	Clean-Up	Detection, LOQ
DuPont-36348	Rice grain Rice straw Rice plant	Methanol/water (70/30, v/v)	SPE Oasis HLB	HPLC-MS/MS Triflumezopyrim: m/z 399→78, 399→306 or m/z 399→278, 399→121, and 399→306 IN-RPA16: m/z 123→79,

				125→52 LOQ: 0.01 mg/kg
DuPont-36133 QuEChERS method	Cucumber Lemon Wheat grain Oilseed rape seed	Acetonitrile/water (1/1, v/v)	Dispersive SPE with PSA, C18	HPLC-MS/MS Triflumezopyrim: m/z 399→278, 399→121 IN-RPA16: m/z 125→52, 125→70 LOQ: 0.01 mg/kg
DuPont-45170, Revision No. 1	Rice grain Rice straw Rice plant Grape Soybean seed	Methanol/water (70/30, v/v)	SPE Oasis HLB	HPLC-MS/MS Triflumezopyrim: m/z 399→306, 399→278 IN-RPD47: m/z 307→78, 307→157) IN-R3Z91: m/z 415→395, 415→398 IN-RPA19: m/z 187→160, 187→66, 187→93 IN-Y2186: m/z 189→145, 189→85 IN-R6U72: m/z 389→251, 389→208 LOQ: 0.01 mg/kg
DuPont-38927	Brown rice Rice hulls Rice straw	Methanol/water (70/30, v/v)	SPE Oasis HLB	HPLC-MS/MS Triflumezopyrim: m/z 399→121 IN-RPA16: m/z 123→79 LOQ: 0.01 mg/kg (brown rice); 0.02 mg/kg (rice hulls and straw)
DuPont-36347	Milk Cream Egg Liver Kidney Muscle Fat	Acetonitrile/water (90/10, v/v)	None	HPLC-MS/MS Triflumezopyrim: m/z 399→121, 399→278 LOQ: 0.01 mg/kg
DuPont-36133 QuEChERS method	Eggs Milk Muscle Fat	Acetonitrile/water (1/1, v/v)	Dispersive SPE with PSA, C18	HPLC-MS/MS Triflumezopyrim: m/z 399→306, 399→278 LOQ: 0.01 mg/kg

Plant materials

Enforcement methods

DuPont-36348 (Pentz, Swaim and Cabusas, 2014, TRIFLUMEZ_034; Swaim, 2015, TRIFLUMEZ_035)

Method 1 (for triflumezopyrim): Samples (5 g grain, whole plant; 2.5 g straw) were homogenised with methanol/water (70/30, v/v) followed by centrifugation. An aliquot of the supernatant was cleaned-up on an Oasis HLB SPE column and analytes eluted with methanol and acetonitrile. The eluates were diluted with 0.01 M formic acid and evaporated to the aqueous remainder. After addition of 0.5 mL acetonitrile the extracts were brought to final volume with 0.01 M formic acid. Samples were analysed with LC-MS/MS in postive electrospray ionization using an Ace® Excel 2 C18 PFP column and monitoring the ion transitions m/z 399→78, 399→306

Method 2 (for triflumezopyrim and IN-RPA16): Extraction and clean-up identically to Method 1. However, elution from the SPE column was performed with acetonitrile/0.5 M ammonium hydroxide (90/10, v/v) and after evaporation of the extract to the aqueous remainder, the pH was adjusted to 3 using 1M formic acid.

Samples were analysed with LC-MS/MS using an Agilent Zorbax XDB C18 column. Triflumezopyrim was measured in positive electrospray ionization and monitoring the ion transitions m/z 399→278, 399→121, and 399→306, while IN-RPA16 was measured in negative electrospray ionization and monitoring the ion transitions m/z 123→79. As for IN-RPA16 no stable second ion transition could be identified, confirmation was done by a sample preparation without SPE clean-up.

Quantitation was accomplished by using external standards in solvent.

Table 55 Recovery data for method DuPont-36348 measuring triflumezopyrim and IN-RPA16 in plant matrices

Matrix	Fortification level (mg/kg)	n	Recovery, mean (%)	RSD (%)	Analyte, MRM transition
Method 1: Triflumezopyrim only; SPE Elution: Methanol and acetonitrile					
Rice grain	0.01	5	86	6.6	Triflumezopyrim, m/z: 399→78 Quantitation
	0.1	5	86	3.7	
Rice straw	0.01	5	78	4.3	
	0.1	5	80	4.7	
Rice, whole plants	0.01	5	83	3.8	
	0.1	5	85	3.0	
Rice grain	0.01	5	85	3.3	Triflumezopyrim, m/z: 399→306 Confirmation
	0.1	5	85	3.2	
Rice straw	0.01	5	78	2.6	
	0.1	5	81	3.3	
Rice, whole plants	0.01	5	83	3.4	
	0.1	5	84	3.9	
Method 2: Triflumezopyrim and IN-RPA16; SPE Elution: 90:10 Acetonitrile:0.5M ammonium hydroxide					
Rice grain	0.01	5	107	5.9	Triflumezopyrim, m/z: 399→278 Quantitation
	0.1	5	98	5.6	
Rice straw	0.01	5	104	3.8	
	0.1	5	104	2.8	
Rice, whole plants	0.01	5	104	3.4	
	0.1	5	104	4.4	
Rice grain	0.01	5	107	3.8	Triflumezopyrim, m/z: 399→306 Confirmation
	0.1	5	98	6.3	
Rice straw	0.01	5	111	6.2	
	0.1	5	106	2.2	
Rice, whole plants	0.01	5	94	7.3	
	0.1	5	104	4.2	
Rice grain	0.01	5	104	10	Triflumezopyrim, m/z: 399→121 Confirmation
	0.1	5	96	6.1	
Rice straw	0.01	5	114	9.2	
	0.1	5	104	1.9	
Rice, whole plants	0.01	5	104	8.2	
	0.1	5	101	3.3	
Rice grain	0.01	5	89	1.0	IN-RPA16, m/z: 123→79 Quantitation
	0.1	5	86	3.6	
Rice straw	0.01	5	97	4.9	
	0.1	5	96	1.7	
Rice, whole plants	0.01	5	84	2.9	
	0.1	5	95	2.7	
Rice grain	0.01	5	86	3.0	IN-RPA16, m/z: 123→79 Confirmation (no SPE clean-up)
	0.1	5	91	1.5	
Rice straw	0.01	5	94	6.1	
	0.1	5	91	16	
Rice, whole plants	0.01	5	89	7.2	
	0.1	5	91	6.2	

DuPont-36348, Supplement No. 1 (Cabusas, Manikandan, 2016, TRIFLUMEZ_036)

The sample preparation was identical to Method 2 of DuPont-36348, with the exception that 10 g of rice and 5 g of straw was used.

Table 56 Recovery data for method DuPont-36348, Supplement No. 1 measuring triflumezopyrim and IN-RPA16 in plant matrices

Matrix	Fortification level (mg/kg)	n	Recovery, mean (%)	RSD (%)	Analyte, MRM transition
Rice grain	0.01	5	96	3.1	Triflumezopyrim, m/z: 399→121 Quantitation
	0.1	5	102	1.1	
Rice straw	0.01	5	98	1.9	
	0.1	5	99	2.5	
Rice grain	0.01	5	104	3.0	Triflumezopyrim, m/z: 399→278 Confirmation
	0.1	5	102	1.1	
Rice straw	0.01	5	100	2.9	
	0.1	5	98	2.2	
Rice grain	0.01	5	101	3.4	Triflumezopyrim, m/z: 399→66 Confirmation
	0.1	5	101	2.3	
Rice straw	0.01	5	99	4.1	
	0.1	5	100	2.4	
Rice grain	0.01	5	93	10.1	IN-RPA16, m/z: 123→79 Quantitation
	0.1	5	101	1.8	
Rice straw	0.01	5	96	4.4	
	0.1	5	103	0.9	
Rice grain	0.01	5	96	8.8	IN-RPA16, m/z: 123→79 Confirmation (no SPE clean-up)
	0.1	5	104	13.1	
Rice straw	0.01	5	96	6.2	
	0.1	5	103	1.6	

Independent laboratory validation of DuPont 36348 (Schernikau, 2015, TRIFLUMEZ_037

The sample preparation was identical to DuPont-36348, Supplement No. 1. However, a modified HPLC gradient was used to achieve a better sensitivity for monitoring two ion transitions of IN-RPA16 (m/z 125→52 and m/z 123→79). As matrix effects >20% were detected in whole plant samples using the modified method, quantitation was done with external standards in blank matrix for all analytes and matrices.

Table 57 Recovery data for the ILV of method DuPont-36348 measuring triflumezopyrim in plant matrices

Matrix	Fortification level (mg/kg)	n	Recovery, mean (%)	RSD (%)	Analyte, MRM transition
Modified gradient					
Rice, whole plants	0.01	5	79	13	Triflumezopyrim, m/z: 399→278 Quantitation
	0.1	5	81	5.5	
Rice, grain	0.01	5	83	5.8	
	0.1	5	79	11	
Rice, straw	0.01	5	83	3.5	
	0.1	5	85	11	
Rice, whole plants	0.01	5	74	20	Triflumezopyrim, m/z: 399→306 Confirmation
	0.1	5	81	5.9	
Rice, grain	0.01	5	81	6.7	
	0.1	5	78	10	
Rice, straw	0.01	5	80	5.0	
	0.1	5	83	10	
Rice, whole plants	0.01	5	83	9.5	IN-RPA16, m/z: 125→52 Quantitation
	0.1	5	96	5.5	
Rice, grain	0.01	5	75	7.2	
	0.1	5	88	3.4	
Rice, straw	0.01	5	88	9.3	
	0.1	5	97	2.1	
Rice, whole plants	0.01	5	95	14	IN-RPA16, m/z: 123→79 Confirmation
	0.1	5	98	4.7	

Matrix	Fortification level (mg/kg)	n	Recovery, mean (%)	RSD (%)	Analyte, MRM transition
Modified gradient					
Rice, grain	0.01	5	78	7.0	
	0.1	5	95	3.8	
Rice, straw	0.01	5	85	11	
	0.1	5	93	2.2	
Original gradient					
Rice, whole plants	0.01	3	85	6.2	Triflumezopyrim, m/z: 399→278 Quantitation
	0.1	3	85	5.1	
Rice, grain	0.01	3	85	9.8	
	0.1	3	83	5.5	
Rice, whole plants	0.01	3	87	7.1	Triflumezopyrim, m/z: 399→306 Confirmation
	0.1	3	85	7.5	
Rice, grain	0.01	3	91	11	
	0.1	3	83	3.7	
Rice, whole plants	0.01	3	79	1.5	IN-RPA16, m/z: 123→79 Quantitation
	0.1	3	89	4.9	
Rice, grain	0.01	3	88	0.0	
	0.1	3	95	4.0	
Rice, whole plants	0.01	3	83	4.5	IN-RPA16, m/z: 123→79 Confirmation
	0.1	3	98	2.6	
Rice, grain	0.01	3	93	5.4	
	0.1	3	107	0.5	

DuPont-36133 QuEChERS method (Birnschein, 2015, TRIFLUMEZ_038

Samples were shaken with acetonitrile/water (1/1, v/v). Separation of water and acetonitrile phase was obtained by addition of sodium citrate, sodium hydrogencitrate sesquihydrate, magnesium sulfate and sodium chloride. For lemon 5M NaOH was added additionally. After centrifugation (an freeze out for oilseed rape seeds) the acetonitrile layer was purified by shaking with PSA, C18 and dried with magnesium sulfate. Samples were analysed with LC-MS/MS in positive electrospray ionization using an Agilent Zorbax SB-C3 column and monitoring the ion transitions m/z 399→306, 399→278 (triflumezopyrim) and m/z 125→52, 125→70 (IN-RPA16). As matrix effects >20% were detected in wheat grain and oilseed rape seed samples, quantitation was done with external standards in blank matrix.

Table 58 Recovery data for DuPont-36133 (QuEChERS method) measuring triflumezopyrim in plant matrices

Matrix	Fortification level (mg/kg)	n	Recovery, mean (%)	RSD (%)	Analyte, MRM transition
Cucumber	0.01	5	95	7	Triflumezopyrim, m/z: 399→306 Quantitation
	0.1	5	96	1	
Lemon	0.01	5	92	2	
	0.1	5	89	2	
Wheat grain	0.01	5	105	3	
	0.1	5	99	5	
Oilseed rape seed	0.01	5	101	4	
	0.1	5	100	3	
Cucumber	0.01	5	100	2	Triflumezopyrim, m/z: 399→278 Confirmation
	0.1	5	95	1	
Lemon	0.01	5	93	2	
	0.1	5	90	2	
Wheat grain	0.01	5	106	4	
	0.1	5	102	5	
Oilseed rape seed	0.01	5	104	4	
	0.1	5	101	5	

The method was unsuccessfully validated in all matrices for IN-RPA16

Data generation methods

DuPont-45170, Revision No. 1 (Pentz and Cabusas, 2016,TRIFLUMEZ_039)

Samples were homogenised with methanol/water (70/30, v/v) followed by centrifugation. An aliquot of the supernatant was cleaned-up on an Oasis HLB SPE column and analytes eluted with methanol and acetonitrile. The eluates were diluted with 0.01 M formic acid and evaporated to the aqueous remainder. After addition of acetonitrile the extracts were brought to final volume with 0.01 M formic acid. Samples were analysed with LC-MS/MS using an Agilent Zorbax XDB C18 column. Positive electrospray ionization was used for triflumezopyrim (m/z 399→278, 399→121), IN-RPD47 (m/z 307→78, 307→157), IN-R3Z91 (m/z 415→395, 415→398), IN-RPA19 (m/z 187→160, 187→66, 187→93). Negative electrospay ionization was used for IN-Y2186 (m/z 189→145, 189→85) and IN-R6U72 (m/z 389→251, 389→208). Quantitation was accomplished by using external standards in solvent.

Table 59 Recovery data for method DuPont-45170, Revision No. 1 measuring triflumezopyrim, IN-RPD47, IN-R3Z91, IN-RPA19, IN-R6U72 and IN-Y2186 in plant matrices

Matrix	Fortification level (mg/kg)	n	Recovery, mean (%)	RSD (%)	Analyte, MRM transition
Rice plants	0.01	5	88	13.6	Triflumezopyrim, m/z: 399→278 Quantitation
	0.1	5	90	7.2	
Rice grain	0.01	5	81	3.2	
	0.1	5	82	5.7	
Rice straw	0.01	5	81	11.9	
	0.1	5	79	9.9	
Grape	0.01	5	102	9.1	
	0.1	5	99	2.3	
Soybean seed	0.01	5	84	3.4	
	0.1	5	83	10.5	
Rice plants	0.01	5	86	13.8	Triflumezopyrim, m/z: 399→121 Confirmation
	0.1	5	90	4.7	
Rice grain	0.01	5	79	11.0	
	0.1	5	88	14.1	
Rice straw	0.01	5	86	12.3	
	0.1	5	82	8.6	
Grape	0.01	5	106	7.8	
	0.1	5	105	4.1	
Soybean seed	0.01	5	81	10.8	
	0.1	5	84	11.2	
Rice plants	0.01	5	81	12.9	IN-RPD47, m/z: 307→78 Quantitation
	0.1	5	85	10.7	
Rice grain	0.01	5	85	5.2	
	0.1	5	84	6.4	
Rice, straw	0.01	5	90	15.0	
	0.1	5	85	4.9	
Grape	0.01	5	97	5.5	
	0.1	5	95	6.9	
Soybean seed	0.01	5	76	8.8	
	0.1	5	77	13.6	
Rice plants	0.01	5	86	13.4	IN-RPD47, m/z: 307→157 Confirmation
	0.1	5	85	11.2	
Rice grain	0.01	5	78	8.2	
	0.1	5	82	6.6	
Rice straw	0.01	5	87	11.2	
	0.1	5	85	6.1	
Grape	0.01	5	97	9.9	
	0.1	5	100	7.7	
Soybean seed	0.01	5	81	12.2	
	0.1	5	81	9.8	
Rice plants	0.01	5	82	19.8	IN-R3Z91, m/z: 415→395 Quantitation
	0.1	5	90	11.4	
Rice grain	0.01	5	92	18.9	
	0.1	5	90	2.6	

Matrix	Fortification level (mg/kg)	n	Recovery, mean (%)	RSD (%)	Analyte, MRM transition
Rice straw	0.01	5	89	10.3	
	0.1	5	79	3.6	
Grape	0.01	5	97	9.9	
	0.1	5	99	7.7	
Soybean seed	0.01	5	84	9.1	
	0.1	5	86	8.3	
Rice plants	0.01	5	83	11.4	IN-R3Z91, m/z: 415→398
	0.1	5	88	11.5	Confirmation
Rice grain	0.01	5	81	13.6	
	0.1	5	90	6.8	
Rice straw	0.01	5	77	13.7	
	0.1	5	76	6.7	
Grape	0.01	5	97	13.1	
	0.1	5	95	4.0	
Soybean seed	0.01	5	88	4.4	
	0.1	5	85	6.3	
Rice plants	0.01	5	81	6.9	IN-Y2186, m/z: 189→145
	0.1	5	81	10.8	Quantitation
Rice grain	0.01	5	92	3.0	
	0.1	5	93	2.7	
Rice straw	0.01	5	92	12.6	
	0.1	5	84	3.9	
Grape	0.01	5	78	4.5	
	0.1	5	79	3.8	
Soybean seed	0.01	5	83	4.5	
	0.1	5	80	10.7	
Rice plants	0.01	5	88	8.1	IN-Y2186, m/z: 189→85
	0.1	5	85	9.1	Confirmation
Rice grain	0.01	5	91	16.4	
	0.1	5	89	3.8	
Rice straw	0.01	5	89	15.1	
	0.1	5	83	12.3	
Grape	0.01	5	79	7.5	
	0.1	5	83	6.6	
Soybean seed	0.01	5	81	5.4	
	0.1	5	82	6.5	
Rice straw	0.01	5	88	12	IN-RPA19, m/z: 187→160
	0.1	5	98	14	Quantitation
Rice straw	0.01	5	75	13	IN-RPA19, m/z: 187→93
	0.1	5	91	13	Confirmation
Rice straw	0.01	5	76	14	IN-RPA19, m/z: 187→66
	0.1	5	86	12	Confirmation
Rice straw	0.01	5	89	11	IN-R6U72, m/z: 307→252
	0.1	5	117	6	Quantitation
Rice straw	0.01	5	103	4	IN-R6U72, m/z: 307→208
	0.1	5	117	4	Confirmation

Independent laboratory validation of DuPont-45170 (Schernikau and Colorado, 2016, TRIFLUMEZ_040)

The sample preparation was identical to DuPont-45170. Despite matrix effects were < 20%, quantitation was done with external standards in blank matrix and solvent.

Table 60 Recovery data for the ILV of method DuPont-45170, measuring triflumezopyrim, IN-RPD47, IN-R3Z91, IN-RPA19, IN-R6U72 and IN-Y2186 in plant matrices (quantified with solvent standards)

Matrix	Fortification level (mg/kg)	n	Recovery, mean (%)	RSD (%)	Analyte, MRM transition
Solvent standards					
Rice, plants	0.01	5	74	8.8	Triflumezopyrim, m/z: 399→278
	0.1	5	71	9.8	Quantitation
Rice, grain	0.01	5	74	4.1	

Matrix	Fortification level (mg/kg)	n	Recovery, mean (%)	RSD (%)	Analyte, MRM transition
Solvent standards					
	0.1	5	73	4.5	
Rice, straw	0.01	5	70	7.3	
	0.1	5	73	3.8	
Rice, plants	0.01	5	73	9.3	Triflumezopyrim, m/z: 399→121
	0.1	5	70	6.6	Confirmation
Rice, grain	0.01	5	86	7.5	
	0.1	5	72	4.5	
Rice, straw	0.01	5	73	11	
	0.1	5	71	4.3	
Rice, plants	0.01	5	70	4.2	IN-R3Z91, m/z: 415→395
	0.1	5	71	4.0	Quantitation
Rice, grain	0.01	5	74	8.1	
	0.1	5	74	1.7	
Rice, straw	0.01	5	70	10	
	0.1	5	70	13	
Rice, plants	0.01	5	77	4.4	IN-R3Z91, m/z: 415→398
	0.1	5	70	2.0	Confirmation
Rice, grain	0.01	5	86	7.0	
	0.1	5	77	2.1	
Rice, straw	0.01	5	72	6.6	
	0.1	5	70	13	
Rice, plants	0.01	5	71	3.5	IN-RPD47, m/z: 307→78
	0.1	5	71	1.6	Quantitation
Rice, grain	0.01	5	73	8.7	
	0.1	5	73	1.2	
Rice, straw	0.01	5	72	7.7	
	0.1	5	72	6.5	
Rice, plants	0.01	5	71	6.3	IN-RPD47, m/z: 307→157
	0.1	5	70	2.2	Confirmation
Rice, grain	0.01	5	78	14	
	0.1	5	74	3.2	
Rice, straw	0.01	5	74	8.4	
	0.1	5	71	4.7	
Rice, plants	0.01	5	90	9.1	IN-Y2186, m/z: 189→145
	0.1	5	93	2.9	Quantitation
Rice, grain	0.01	5	89	7.1	
	0.1	5	83	1.8	
Rice, straw	0.01	5	93	8.0	
	0.1	5	103	4.7	
Rice, plants	0.01	5	92	9.2	IN-Y2186, m/z: 189→85
	0.1	5	88	6.1	Confirmation
Rice, grain	0.01	5	84	8.3	
	0.1	5	80	3.6	
Rice, straw	0.01	5	97	13	
	0.1	5	104	2.9	

Table 61 Recovery data for the ILV of method DuPont-45170, measuring triflumezopyrim, IN-RPD47, IN-R3Z91, IN-RPA19, IN-R6U72 and IN-Y2186 in plant matrices (quantified with matrix-matched standards)

Matrix	Fortification level (mg/kg)	n	Recovery, mean (%)	RSD (%)	Analyte, MRM transition
Rice, plants	0.01	5	90	8.5	Triflumezopyrim, m/z: 399→278
	0.1	5	86	9.5	Quantitation
Rice, grain	0.01	5	78	3.9	
	0.1	5	77	4.6	
Rice, straw	0.01	5	84	7.7	
	0.1	5	88	3.5	
Rice, plants	0.01	5	92	9.3	Triflumezopyrim, m/z: 399→121
	0.1	5	89	6.5	Confirmation
Rice, grain	0.01	5	90	7.4	
	0.1	5	75	4.3	

Matrix	Fortification level (mg/kg)	n	Recovery, mean (%)	RSD (%)	Analyte, MRM transition
Rice, straw	0.01	5	85	12	
	0.1	5	83	4.2	
Rice, plants	0.01	5	86	3.6	IN-R3Z91, m/z: 415→395
	0.1	5	87	4.1	Quantitation
Rice, grain	0.01	5	79	8.4	
	0.1	5	79	1.6	
Rice, straw	0.01	5	87	10	
	0.1	5	88	13	
Rice, plants	0.01	5	97	4.3	IN-R3Z91, m/z: 415→398
	0.1	5	88	2.1	Confirmation
Rice, grain	0.01	5	89	7.1	
	0.1	5	80	2.0	
Rice, straw	0.01	5	85	6.4	
	0.1	5	84	13	
Rice, plants	0.01	5	88	4.1	IN-RPD47, m/z: 307→78
	0.1	5	87	1.5	Quantitation
Rice, grain	0.01	5	81	8.5	
	0.1	5	82	1.0	
Rice, straw	0.01	5	89	7.8	
	0.1	5	90	6.8	
Rice, plants	0.01	5	85	6.6	IN-RPD47, m/z: 307→157
	0.1	5	84	2.2	Confirmation
Rice, grain	0.01	5	81	14	
	0.1	5	77	3.2	
Rice, straw	0.01	5	89	8.3	
	0.1	5	87	4.4	
Rice, plants	0.01	5	79	9.0	IN-Y2186, m/z: 189→145
	0.1	5	82	2.6	Quantitation
Rice, grain	0.01	5	80	7.0	
	0.1	5	75	1.8	
Rice, straw	0.01	5	86	8.1	
	0.1	5	96	4.3	
Rice, plants	0.01	5	85	9.4	IN-Y2186, m/z: 189→85
	0.1	5	82	6.0	Confirmation
Rice, grain	0.01	5	87	8.0	
	0.1	5	83	3.8	
Rice, straw	0.01	5	93	12	
	0.1	5	100	2.7	

DuPont-38927 (Zhu Y., 2015 TRIFLUMEZ_041)

Homogenised samples were extracted twice with 48 mL methanol/water (70/30, v/v) + 2 mL 0.5 M aqueous ammonia solution followed by fitration. An aliquot of the extract was concentrated to a smaller volume and the pH adjusted to 3 with 0.01 M formic acid. Cleaned-up was performed on an Oasis HLB SPE column. Analytes were eluted with acetonitrile/0.5 M ammonium hydroxide (90/10, v/v). The eluates were diluted with 0.01 M formic acid and evaporated to the aqueous remainder. After addition of acetonitrile the extracts were brought to final volume with 0.01 M formic acid. Samples were analysed with LC-MS/MS using a Waters Acquity UPLCTM BEH C18. Triflumezopyrim was measured in positive electrospray ionization and monitoring the ion transition m/z 399→121, while IN-RPA16 was measured in negative electrospray ionization and monitoring the ion transition m/z 123→79. Quantitation was accomplished by using external standards in solvent.

Table 62 Recovery data for method DuPont-45170 measuring triflumezopyrim and IN-RPA16 in rice matrices

Matrix	Fortification level (mg/kg)	n	Recovery, mean (%)	RSD (%)	Analyte, MRM transition
Brown rice	0.01	5	98	4.1	Triflumezopyrim, m/z: 399→121
	0.1	5	98	4.1	Quantitation
	1.0	5	93	3.5	
Rice hulls	0.02	5	96	5.5	
	0.2	5	89	1.2	

Matrix	Fortification level (mg/kg)	n	Recovery, mean (%)	RSD (%)	Analyte, MRM transition
	2.0	5	95	0.4	
Rice straw	0.02	5	96	4.2	
	0.2	5	84	3.7	
	2.0	5	84	2.3	
Brown rice	0.01	5	87	5.1	IN-RPA16, m/z: 123→79 Quantitation
	0.1	5	78	1.7	
	1.0	5	94	5.3	
Rice hulls	0.02	5	88	3.3	
	0.2	5	79	10.5	
	2.0	5	102	1.0	
Rice straw	0.02	5	82	3.5	
	0.2	5	77	2.2	
	2.0	5	88	8.3	

Extraction efficiency (Cochrane, 2015, TRIFLUMEZ_042)

To compare the extraction efficiency of four different extraction protocols for plant matrices, a radiovalidation with ^{14}C-radiolabelled triflumezopyrim was performed. Samples from the rice metabolism studies performed with [methylene-^{14}C]- and [pyrimidine-3-^{14}C]-triflumezopyrim were used and extracted differently. The quantification of the radioactivity was done by LSC and HPLC-RD. In the following table, the basic extraction protocols are summarized:

Table 63 Overview of extraction protocols used for the estimation of the extraction efficiency for triflumezopyrim and metabolites IN-RPA16 and INY2186 in rice grain and straw

Extraction method	Description
1 (according to metabolism studies)	• Portions of homogenized rice matrices were extracted two times with methanol and two times with methanol:water (70:30, v/v) in a homogenizer. • After centrifugation, the supernatants were decanted and pooled. • The pooled extracts were evaporated to dryness and reconstituted in acetonitrile/water (1:1, v/v) prior to HPLC analysis.
2 (according to DuPont-36133; QuEChERS method)	• Portions of homogenized rice matrices were extracted with acetonitrile by means of shaking by hand. Rice grain was supplemented with 10 mL water prior to extraction. • Subsequently, a blend of buffer salts was added (MgSO4, NaCl, disodium citrate and trisodium citrate). Samples were shaken again and the phases separated by centrifugation, • Aliquots of the extracts were evaporated to dryness and reconstituted in acetonitrile/water (1:1, v/v) prior to HPLC analysis.
3 (according to DuPont-36348)	• Portions of homogenized rice matrices were extracted two times with methanol:water (70:30, v/v) in a homogenizer. • After centrifugation, the supernatants were decanted, pooled and made up to volume. • Aliquots of the pooled extracts were evaporated to dryness and reconstituted in acetonitrile/water (1:1, v/v) prior to HPLC analysis.
4 (according to DuPont-38927, China Modified Residue Method)	• Portions of homogenized rice matrices were extracted two times with methanol:water (70:30, v/v) and 0.5M aqueous ammonia on a flask shaker. • After centrifugation, the supernatants were decanted, pooled and made up to volume. • Aliquots of the pooled extracts were evaporated to dryness and reconstituted in acetonitrile/water (1:1, v/v) prior to HPLC analysis.

The extraction efficiency of the different protocols was compared to the extraction protocol 1 used in the plant metabolism studies. Both, the extractions of total TRR as well as the specific concentrations for triflumezopyrim and metabolites IN-RPA16 and INY2186 were considered. In the following tables the performance of each of the extraction protocols is summarized:

Table 64 Extraction efficiency for triflumezopyrim and metabolite IN-RPA16 in rice plants treated with [Methylene-^{14}C]-triflumezopyrim

Extraction method	TRR extracted		Triflumezopyrim extracted		IN-RPA16 extracted	
	mg eq/kg	% extracted	mg eq/kg	% extracted	mg eq/kg	% extracted
Rice grain						
1 (metabolism study)	0.028	100.0	0.017	100.0	0.001	100.0

Extraction method	TRR extracted		Triflumezopyrim extracted		IN-RPA16 extracted	
	mg eq/kg	% extracted	mg eq/kg	% extracted	mg eq/kg	% extracted
2	0.018	64.3	0.017	100.0	ND	NA
3	0.024	85.7	0.011	64.7	ND	NA
4	0.027	96.4	0.013	76.5	ND	NA
Rice straw						
1 (metabolism study)	0.208	100.0	0.090	100.0	0.016	100.0
2	0.075	36.1	0.056	62.2	ND	NA
3	0.198	95.2	0.092	102.2	ND	NA
4	0.222	106.7	0.096	106.7	ND	NA

NA not applicable

ND not detected

Table 65 Extraction efficiency for triflumezopyrim and metabolite IN-Y2186 in rice plants treated with [pyrimidine-3-^{14}C]-triflumezopyrim

Extraction method	TRR extracted		Triflumezopyrim extracted		IN-Y2186 extracted	
	mg eq/kg	% extracted	mg eq/kg	% extracted	mg eq/kg	% extracted
Rice grain						
1 (metabolism study)	0.059	100.0	0.036	100.0	0.018	100.0
2	0.039	66.1	0.009	25.0	0.014	77.8
3	0.051	86.5	0.030	83.3	0.013	72.2
4	0.056	94.9	0.027	75.0	0.013	72.2
Rice straw						
1 (metabolism study)	0.176	100.0	0.070	100.0	0.015	100.0
2	0.054	30.7	0.022	31.4	0.004	26.7
3	0.167	94.9	0.064	91.4	0.008	53.3
4	0.170	96.6	0.065	92.9	0.025	166.7

NA not applicable

ND not detected

Animal materials

DuPont-36347 (Pentz & Cabusas, 2014, TRIFLUMEZ_043)

Samples were homogenised with acetonitrile followed by acetonitrile/water (90/10, v/v). After centrifugation, the extract was made up to volume with acetonitrile/water (90/10, v/v). Prior to analysis the extract was further diluted 1:10 with 0.01 M formic acid. Samples were analysed with LC-MS/MS in positive electrospray ionization using an Agilent Zorbax XDB C18 column and monitoring the ion transitions m/z 399→121, 399→278. Quantitation was accomplished by using external standards in solvent.

Table 66 Recovery data for DuPont-36347 measuring triflumezopyrim in animal matrices

Matrix	Fortification level (mg/kg)	n	Recovery, mean (%)	RSD (%)	Analyte, MRM transition
Milk	0.01	5	93	10	Triflumezopyrim, m/z: 399→121
	0.1	5	93	8	Quantitation
Cream	0.01	5	97	13	
	0.1	5	107	2	
Egg	0.01	5	72	5	
	0.1	5	91	5	
Fat	0.01	5	96	10	
	0.1	5	95	2	
Kidney	0.01	5	99	10	
	0.1	5	105	7	
Liver	0.01	5	97	8	
	0.1	5	101	11	
Muscle	0.01	5	81	4	
	0.1	5	97	3	

Matrix	Fortification level (mg/kg)	n	Recovery, mean (%)	RSD (%)	Analyte, MRM transition
Milk	0.01	5	96	7	Triflumezopyrim, m/z: 399→278 Confirmation
	0.1	5	92	7	
Cream	0.01	5	95	10	
	0.1	5	106	2	
Egg	0.01	5	75	2	
	0.1	5	91	3	
Fat	0.01	5	96	7	
	0.1	5	91	8	
Kidney	0.01	5	88	5	
	0.1	5	110	4	
Liver	0.01	5	82	10	
	0.1	5	96	16	
Muscle	0.01	5	81	4	
	0.1	5	99	2	

Independent laboratory validation of DuPont-36347 (Gu, 2014, TRIFLUMEZ_044)

The sample preparation was identical to DuPont-36347.

Table 67 Recovery data for the ILV of method DuPont-36347, measuring triflumezopyrim in animal matrices

Matrix	Fortification level (mg/kg)	n	Recovery, mean (%)	RSD (%)	Analyte, MRM transition
Egg	0.01	5	93	6	Triflumezopyrim, m/z: 399→121 Quantitation
	0.1	5	96	3	
Liver	0.01	5	98	10	
	0.1	5	101	3	
Milk	0.01	5	80	4	
	0.1	5	109	4	
Egg	0.01	5	95	5	Triflumezopyrim, m/z: 399→278 Confirmation
	0.1	5	97	4	
Liver	0.01	5	100	5	
	0.1	5	100	4	
Milk	0.01	5	79	6	
	0.1	5	105	3	

DuPont-36133 QuEChERS method (Birnschein, 2015, TRIFLUMEZ_038

Samples were shaken with acetonitrile/water (1/1, v/v). Separation of water and acetonitrile phase was obtained by addition of sodium citrate, sodium hydrogencitrate sesquihydrate, magnesium sulfate and sodium chloride. After centrifugation (and freeze out over night for eggs and fat) the acetonitrile layer was purified by shaking with PSA, C18 and dried with magnesium sulfate. Prior to analysis, samples were diluted with acetonitrile/water (1/1, v/v) + 0.1% formic acid. Samples were analysed with LC-MS/MS in positive electrospray ionization using an Agilent Zorbax SB-C3 column and monitoring the ion transitions m/z 399→306, 399→278 for triflumezopyrim. As matrix effects were <20% in all samples, quantitation was done with external standards in solvent.

Table 68 Recovery data for DuPont-36133 (QuEChERS method) measuring triflumezopyrim in animal matrices

Matrix	Fortification level (mg/kg)	n	Recovery, mean (%)	RSD (%)	Analyte, MRM transition
Milk	0.01	5	93	3	Triflumezopyrim, m/z: 399→306 Quantitation
	0.1	5	95	3	
Meat	0.01	5	85	1	
	0.1	5	89	2	
Egg	0.01	5	101	6	

Matrix	Fortification level (mg/kg)	n	Recovery, mean (%)	RSD (%)	Analyte, MRM transition
	0.1	5	101	1	
Fat	0.01	5	102	6	
	0.1	5	106	2	
Milk	0.01	5	93	2	Triflumezopyrim, m/z: 399→278
	0.1	5	94	2	Confirmation
Meat	0.01	5	85	3	
	0.1	5	90	2	
Egg	0.01	5	103	4	
	0.1	5	101	1	
Fat	0.01	5	97	5	
	0.1	5	106	2	

Extraction efficiency for animal matrices (Cochrane, 2015, TRIFLUMEZ_042)

To compare the extraction efficiency of three different extraction protocols for animal matrices, a radiovalidation with ^{14}C-radiolabelled triflumezopyrim was performed. Samples of milk, liver and muscle were taken from the lactating goat metabolism study performed with [methylene-^{14}C]- or [pyridine-^{14}C]-triflumezopyrim, while samples of eggs were taken from the laying hen metabolism study performed with [pyrimidine-3-^{14}C]-triflumezopyrim. All samples were extracted according to the protocols in Table 69. The quantification of the radioactivity was done by LSC and HPLC-RD.

Table 69 Overview of extraction protocols used for the estimation of the extraction efficiency for triflumezopyrim in animal matrices

Extraction method	Description
1 (according to lactating goat and laying hen metabolism studies)	Tissues (liver, muscle milk, egg) were homogenized two times with acetonitrile, two times with acetonitrile:water (9+1, v/v) and two times with acetonitrile:water (1+1, v/v). Aliquots of extracts with significant radioactivity were pooled, concentrated and reconstituted in acetonitrile/water (1:1, v/v) prior to HPLC analysis.
2 (according to DuPont-36347)	Samples of homogenized tissues were extracted with acetonitrile followed by acetonitrile/water (9+1, v/v). After centrifugation, the extract was made to volume with acetonitrile/water (9+1, v/v). Aliquots of the extracts concentrated and reconstituted in acetonitrile/water (1:1, v/v) prior to HPLC analysis.
3 (according to DuPont-36133; QuEChERS method)	Portions of homogenized tissues were extracted with acetonitrile by means of shaking by hand (addition of water to egg samples). Subsequently, a blend of buffer salts was added (MgSO4, NaCl, disodium citrate and trisodium citrate). Samples were shaken again and the phases separated by centrifugation, Aliquots of the extracts were evaporated to dryness and reconstituted in acetonitrile/water (1:1, v/v) prior to HPLC analysis.

The extraction efficiency of the different protocols was compared to the extraction protocol 1 used in the animal metabolism studies. Both, the extractions of total TRR as well as the specific concentrations for triflumezopyrim were considered. In the following tables the performance of each of the extraction protocols is summarized:

Table 70 Extraction efficiency for triflumezopyrim in milk and liver from lactating goat treated with [methylene-^{14}C]-triflumezopyrim

Extraction method	TRR extracted		Triflumezopyrim extracted	
	mg eq/kg	% extracted	mg eq/kg	% extracted
Milk				
1 (metabolism study)	0.601	100.0	0.467	100.0
2	0.597	99.3	0.469	100.4
3	0.533	88.7	0.432	92.5
Liver				
1 (metabolism study)	0.637	100.0	0.386	100.0
2	0.493	77.4	0.329	85.2
3	0.386	60.6	NA	NA

NA not applicable

Table 14 Extraction efficiency for triflumezopyrim in muscle from lactating goat treated with [pyridine-^{14}C]-triflumezopyrim

Extraction method	TRR extracted		Triflumezopyrim extracted	
	mg eq/kg	% extracted	mg eq/kg	% extracted
Muscle				
1 (metabolism study)	0.037	100.0	0.027	100.0
2	0.040	108.1	0.026	96.3

Table 15 Extraction efficiency for triflumezopyrim in egg from laying hen treated with [pyrimidine-3-^{14}C]-triflumezopyrim

Extraction method	TRR extracted		Triflumezopyrim extracted	
	mg eq/kg	% extracted	mg eq/kg	% extracted
Muscle				
1 (metabolism study)	0.025	100.0	0.017	100.0
2	0.023	92.0	0.011	64.7
3	0.025	100.0	0.019	111.8

Stability of pesticides in stored analytical samples

Plant matrices

Swaim L., 2015, TRIFLUMEZ_046

The storage stability of triflumezopyrim and IN-RPA16 in different frozen rice commodities was demonstrated over a period of 16 month and 6 month, respectively.

Homogenized samples of rice commodities were fortified with either triflumezopyrim or IN-RPA16 at a rate of 0.1 mg/kg. The fortified commodity samples were stored frozen (-25.0 to -10.0 °C) and analysed for triflumezopyrim after 0, 1, 3, 6, 12 and 16 month, while for IN-RPA16 samples were analysed only up to 6 month. For each fortification level two samples were measured. All samples were analysed according to method DuPont-36348.

Table 73 Storage stability of triflumezopyrim and IN-RPA16 in rice commodities fortified at 0.1 mg/kg

Matrix	Storage period (month)	Triflumezopyrim		IN-RPA16	
		Mean remaining (%)	Mean concurrent recovery (%)	Mean remaining (%)	Mean concurrent recovery (%)
Rice whole plant	0	88	-	95	-
	1	77	79	95	99
	3	89	97	89	93
	6	105	119	93	102
	12	85	86	NA	NA
	16	105	107	NA	NA
Rice grain	0	91	-	86	-
	1	93	92	90	92
	3	90	99	84	89
	6	100	107	94	103
	12	84	87	NA	NA
	16	93	94	NA	NA
Rice straw	0	80	-	100	-
	1	84	86	98	101
	3	72	76	90	96
	6	99	116	100	103
	12	69	80	NA	NA
	16	94	97	NA	NA

Schemikau N. and Colorado C.S., 2016, TRIFLUMEZ_045

In this preliminary report, the storage stability of triflumezopyrim metabolites IN-RPD47, IN-R3Z91 and IN-Y2186 in different frozen rice commodities was demonstrated over a period of 6 months.

Homogenized samples of rice commodities were fortified with either IN-RPD47, IN-R3Z91 or IN-Y2186 at a rate of 0.1 mg/kg. These fortified commodities were stored deep frozen (≤ -18 °C) and were analysed after 0, 1, 3 and 6 month. For each fortification level two samples were measured. All samples were analysed according to method DuPont-45170.

Table 74 Storage stability of triflumezopyrim metabolites IN-RPD47, IN-R3Z91 and IN-Y2186 in rice commodities fortified at 0.1 mg/kg

Matrix	Storage period (month)	IN-RPD47		IN-R3Z91		IN-Y2186	
		Mean remaining (%)	Mean concurrent recovery (%)	Mean remaining (%)	Mean concurrent recovery (%)	Mean remaining (%)	Mean concurrent recovery (%)
Rice whole plant	0	72	-	71	-	74	-
	1	78	84	78	89	83	86
	3	74	74	82	88	67	79
	6	75	73	72	72	71	73
Rice grain	0	77	-	78	-	83	-
	1	76	108	75	86	92	89
	3	71	72	77	81	88	89
	6	78	73	76	82	87	93
Rice straw	0	82	-	88	-	75	-
	1	103	84	75	72	79	80
	3	81	74	68	74	72	73
	6	90	90	75	81	89	100

Animal matrices

No data submitted. All samples from the feeding study were analysed within 30 days after collection.

USE PATTERN

Registered uses for triflumezopyrim were submitted for rice only (Table 75). The original registered labels for use in China were submitted in the original language as well as in its English translation. Also labels for Singapore and Cambodia were submitted. As the applicant has not received registration approval to date for the other countries, no labels are currently available.

Table 75 List of uses of triflumezopyrim

Country	Crops or crop groups	Formulation	Application details					Pre harvest interval (PHI) in days
			Method	Growth stage at last treatment	g ai/ha	No	Interval (day)	
Cereals								
China	Rice	106 g/L SC	Foliar	N/A[b]	25	1-2[a]	21	21
Cambodia	Rice	106 g/L SC	Foliar	N/A[b]	25	1	-	25
Singapore	Rice	106 g/L SC	Foliar	N/A[b]	25	1	-	21

[a] Only one application per year will be promoted to prevent the development of insect resistance.

[b] Treatment depends on pest occurrence, not on plant development stage.

RESULTS OF SUPERVISED RESIDUE TRIALS ON CROPS

The Meeting received information on supervised residue trials of triflumezopyrim for rice only. Residue levels were reported as measured. Application rates were always reported as triflumezopyrim equivalents. Application rates, spray concentrations and mean residue results have generally been rounded to the even with two significant figures. HR and STMR values from the trials conducted according to maximum GAP have been used for the estimation of maximum residue levels. These results are underlined.

Preparation for grain with hull, brown rice and hull was done as follows: rice ears were threshed using a threshing machine to obtain grain with hull. After drying in the shade (20–30 ℃, ＜7days), the grain was shelled by a rough machine to get brown rice and hulls.

Laboratory reports included method validation including batch recoveries with spiking at residue levels similar to those occurring in samples from the supervised trials. Dates of analyses or duration of residue sample storage were also provided. Field reports provided data on the sprayers used and their calibration, plot size, residue sample size and sampling date. Although trials included control plots, no control data are recorded in the tables except where residues in control samples exceeded the LOQ. Residue data are recorded unadjusted for % recovery.

Rice

Table 76 Residues of triflumezopyrim and IN-RPA16 in brown rice following foliar application

Location, Year (variety)	Application Form.	No	g ai/ha	g ai/hL	Growth stage	Residues, mg/kg (mean) Sample	DALT	Triflumezo-pyrim	IN-RPA16	Report/Trial No., Reference, analytical method, validation data, storage period
China Qianjin town Xiaoshan District Hangzhou, Zhejiang 2013 (Xiushui 09)	SC	2	25	3.3	BBCH 59-61	Brown rice	14 21 28	3× < 0.01 3× < 0.01 3× < 0.01	3× < 0.01 3× < 0.01 3× < 0.01	DuPont-38927, Zhu (2015, TRIFLUMEZ_041) analytical method: DuPont-36348, storage period: <12 month (not validated for IN-RPA16) Samples from 3 replicate plots
	SC	3	25	3.3	BBCH 59-71	Brown rice	14 21 28	3× < 0.01 3× < 0.01 3× < 0.01	3× < 0.01 3× < 0.01 3× < 0.01	
	SC	2	37.5	5.0	BBCH 59-61	Brown rice	14 21 28	3× < 0.01 3× < 0.01 3× < 0.01	3× < 0.01 3× < 0.01 3× < 0.01	
	SC	3	37.5	5.0	BBCH 59-71	Brown rice	14 21 28	3× < 0.01 3× < 0.01 3× < 0.01	3× < 0.01 3× < 0.01 3× < 0.01	
China Qianjin town Xiaoshan District Hangzhou, Zhejiang 2014 (Zhe 108)	SC	2	25	3.3	BBCH 59-61	Brown rice	14 21 28	3× < 0.01 3× < 0.01 3× < 0.01	3× < 0.01 3× < 0.01 3× < 0.01	DuPont-38927, Zhu (2015, TRIFLUMEZ_041) analytical method: DuPont-36348, storage period: <12 month (not validated for IN-RPA16) Samples from 3 replicate plots
	SC	3	25	3.3	BBCH 59-71	Brown rice	14 21 28	3× < 0.01 3× < 0.01 3× < 0.01	3× < 0.01 3× < 0.01 3× < 0.01	
	SC	2	37.5	5.0	BBCH 59-71	Brown rice	14 21 28	3× < 0.01 3× < 0.01 3× < 0.01	3× < 0.01 3× < 0.01 3× < 0.01	
	SC	3	37.5	5.0	BBCH 59-71	Brown rice	14 21 28	3× < 0.01 3× < 0.01 3× < 0.01	3× < 0.01 3× < 0.01 3× < 0.01	
China Dalu village Zhaodian town Gaoqing county Zibo Shandong 2013 (Yanfeng 47)	SC	2	25	3.3	BBCH 59-61	Brown rice	14 21 28	3× < 0.01 3× < 0.01 3× < 0.01	3× < 0.01 3× < 0.01 3× < 0.01	DuPont-38927, Zhu (2015, TRIFLUMEZ_041) analytical method: DuPont-36348, storage period: <12 month (not validated for IN-RPA16) Samples from 3 replicate plots
	SC	3	25	3.3	BBCH 59-71	Brown rice	14 21 28	3× < 0.01 3× < 0.01 3× < 0.01	3× < 0.01 3× < 0.01 3× < 0.01	
	SC	2	37.5	5.0	BBCH 59-61	Brown rice	14 21 28	3× < 0.01 3× < 0.01 3× < 0.01	3× < 0.01 3× < 0.01 3× < 0.01	
	SC	3	37.5	5.0	BBCH 59-71	Brown rice	14 21 28	0.011, 0.012, 0.012 (0.012) 3× < 0.01 3× < 0.01	3× < 0.01 3× < 0.01 3× < 0.01	

Location, Year (variety)	Application Form.	No	g ai/ha	g ai/hL	Growth stage	Residues, mg/kg (mean) Sample	DALT	Triflumezo-pyrim	IN-RPA16	Report/Trial No., Reference, analytical method, validation data, storage period
China Dalu village Zhaodian town Gaoqing county Zibo Shandong 2014 (Yanfeng 47)	SC	2	25	3.3	BBCH 59-61	Brown rice	14 21 28	3× < 0.01 3× < 0.01 3× < 0.01	3× < 0.01 3× < 0.01 3× < 0.01	Samples from 3 DuPont-38927, Zhu (2015, TRIFLUMEZ_041) analytical method: DuPont-36348, storage period: <12 month (not validated for IN-RPA16) Samples from 3 replicate plots
	SC	3	25	3.3	BBCH 59-71	Brown rice	14 21 28	3× < 0.01 3× < 0.01 3× < 0.01	3× < 0.01 3× < 0.01 3× < 0.01	
	SC	2	37.5	5.0	BBCH 59-71	Brown rice	14 21 28	3× < 0.01 3× < 0.01 3× < 0.01	3× < 0.01 3× < 0.01 3× < 0.01	
	SC	3	37.5	5.0	BBCH 59-71	Brown rice	14 21 28	3× < 0.01 3× < 0.01 3× < 0.01	3× < 0.01 3× < 0.01 3× < 0.01	
China Education and Research Experimental Base Hunan Agricultural University Changsha Hunan 2013 (Xiannong 1)	SC	2	25	3.3	BBCH 59-61	Brown rice	14 21 28	3× < 0.01 3× < 0.01 3× < 0.01	3× < 0.01 3× < 0.01 3× < 0.01	DuPont-38927, Zhu (2015, TRIFLUMEZ_041) analytical method: DuPont-36348, storage period: <12 month (not validated for IN-RPA16) Samples from 3 replicate plots
	SC	3	25	3.3	BBCH 59-71	Brown rice	14 21 28	3× < 0.01 3× < 0.01 3× < 0.01	3× < 0.01 3× < 0.01 3× < 0.01	
	SC	2	37.5	5.0	BBCH 59-61	Brown rice	14 21 28	0.010, 0.010, 0.011 (0.010) 3× < 0.01 3× < 0.01	3× < 0.01 3× < 0.01 3× < 0.01	
	SC	3	37.5	5.0	BBCH 59-71	Brown rice	14 21 28	0.013, 0.014, 0.015 (0.014) < 0.01, 0.011, 0.011 (0.011) 3× < 0.01	3× < 0.01 3× < 0.01 3× < 0.01	
China Education and Research Experimental Base Hunan Agricultural University Changsha Hunan 2014 (Huanghuajing)	SC	2	25	3.3	BBCH 59-61	Brown rice	14 21 28	3× < 0.01 3× < 0.01 3× < 0.01	3× < 0.01 3× < 0.01 3× < 0.01	DuPont-38927, Zhu (2015, TRIFLUMEZ_041) analytical method: DuPont-36348, storage period: <12 month (not validated for IN-RPA16) Samples from 3 replicate plots
	SC	3	25	3.3	BBCH 59-71	Brown rice	14 21 28	3× < 0.01 3× < 0.01 3× < 0.01	3× < 0.01 3× < 0.01 3× < 0.01	
	SC	2	37.5	5.0	BBCH 59-71	Brown rice	14 21 28	3× < 0.01 3× < 0.01 3× < 0.01	3× < 0.01 3× < 0.01 3× < 0.01	
	SC	3	37.5	5.0	BBCH 59-71	Brown rice	14 21 28	3× < 0.01 3× < 0.01 3× < 0.01	3× < 0.01 3× < 0.01 3× < 0.01	

DALT: days after last treatment

Table 77 Residues of triflumezopyrim and IN-RPA16 in rice grain following foliar application

Location, Year (variety)	Application Form.	No	g ai/ha	g ai/hL	Growth stage	Residues, mg/kg Sample	DALT	Triflumezo-pyrim	IN-RPA16	Report/Trial No., Reference, analytical method, validation data, storage period
China Qianjin town Xiaoshan District Hangzhou, Zhejiang 2013 (Xiushui 09)	SC	2	25	3.3	BBCH 59-61	Rice grain	14 21 28	0.067, 0.068, 0.068 (0.068) 0.053, 0.050, 0.050 (<u>0.051</u>) 0.043, 0.044, 0.045 (0.044)	3× < 0.02 3× < 0.02 3× < 0.02	DuPont-38927, Zhu (2015, TRIFLUMEZ_041) analytical method: DuPont-36348, storage period: <12 month (not validated for IN-RPA16) Samples from 3 replicate plots
	SC	3	25	3.3	BBCH 59-71	Rice grain	14 21 28	0.062, 0.068, 0.064 (0.065) 0.052, 0.050, 0.053 (0.052) 0.023, 0.056, 0.041 (0.040)	3× < 0.02 3× < 0.02 3× < 0.02	
	SC	2	37.5	5.0	BBCH 59-61	Rice grain	14 21 28	0.084, 0.078, 0.080 (0.081) 0.064, 0.074, 0.072 (0.070) 0.051, 0.052, 0.052 (0.052)	3× < 0.02 3× < 0.02 3× < 0.02	
	SC	3	37.5	5.0	BBCH 59-71	Rice grain	14 21 28	0.085, 0.083, 0.090 (0.086) 0.075, 0.072, 0.072 (0.073) 0.090, 0.079, 0.086 (0.085)	3× < 0.02 3× < 0.02 3× < 0.02	
China Qianjin town Xiaoshan District Hangzhou, Zhejiang 2014 (Zhe 108)	SC	2	25	3.3	BBCH 59-61	Rice grain	14 21 28	0.027, 0.046, 0.037 (0.037) 0.026, 0.027, 0.025 (0.026) 0.036, 0.032, 0.033 (<u>0.034</u>)	3× < 0.02 3× < 0.02 3× < 0.02	DuPont-38927, Zhu (2015, TRIFLUMEZ_041) analytical method: DuPont-36348, storage period: <12 month (not validated for IN-RPA16) Samples from 3 replicate plots
	SC	3	25	3.3	BBCH 59-71	Rice grain	14 21 28	0.062, 0.067, 0.065 (0.065) 0.039, 0.043, 0.043 (0.042) 0.050, 0.052, 0.052 (0.051)	3× < 0.02 3× < 0.02 3× < 0.02	
	SC	2	37.5	5.0	BBCH 59-71	Rice grain	14 21 28	0.054, 0.056, 0.055 (0.055) 0.037, 0.038, 0.041 (0.039) 0.023, < 0.02, 0.021 (0.022)	3× < 0.02 3× < 0.02 3× < 0.02	
	SC	3	37.5	5.0	BBCH 59-71	Rice grain	14 21 28	0.050, 0.054, 0.051 (0.052) 0.051, 0.049, 0.049 (0.050) 0.076, 0.079, 0.077 (0.077)	3× < 0.02 3× < 0.02 3× < 0.02	

Location, Year (variety)	Application Form.	No	g ai/ha	g ai/hL	Growth stage	Residues, mg/kg Sample	DALT	Triflumezo-pyrim	IN-RPA16	Report/Trial No., Reference, analytical method, validation data, storage period
China Dalu village Zhaodian town Gaoqing county Zibo Shandong 2013 (Yanfeng 47)	SC	2	25	3.3	BBCH 59-61	Rice grain	14 21 28	0.048, 0.043, 0.046 (0.046) 0.032, 0.033, 0.031 (0.032) 0.023, 0.021, 0.020 (0.021)	3× < 0.02 3× < 0.02 3× < 0.02	DuPont-38927, Zhu (2015, TRIFLUMEZ_041) analytical method: DuPont-36348, storage period: <12 month (not validated for IN-RPA16) Samples from 3 replicate plots
	SC	3	25	3.3	BBCH 59-71	Rice grain	14 21 28	0.088, 0.087, 0.088 (0.088) 0.036, 0.035, 0.033 (0.035) 0.043, 0.039, 0.041 (0.041)	3× < 0.02 3× < 0.02 3× < 0.02	
	SC	2	37.5	5.0	BBCH 59-61	Rice grain	14 21 28	0.085, 0.090, 0.090 (0.088) 0.067, 0.075, 0.075 (0.072) 0.064, 0.054, 0.060 (0.059)	3× < 0.02 3× < 0.02 3× < 0.02	
	SC	3	37.5	5.0	BBCH 59-71	Rice grain	14 21 28	0.14, 0.13, 0.13 (0.13) 0.083, 0.085, 0.092 (0.087) 0.097, 0.091, 0.099 (0.096)	3× < 0.02 3× < 0.02 3× < 0.02	
China Dalu village Zhaodian town Gaoqing county Zibo Shandong 2014 (Yanfeng 47)	SC	2	25	3.3	BBCH 59-61	Rice grain	14 21 28	3× < 0.02 3× < 0.02 3× < 0.02	3× < 0.02 3× < 0.02 3× < 0.02	DuPont-38927, Zhu (2015, TRIFLUMEZ_041) analytical method: DuPont-36348, storage period: <12 month (not validated for IN-RPA16) Samples from 3 replicate plots
	SC	3	25	3.3	BBCH 59-71	Rice grain	14 21 28	3× < 0.02 3× < 0.02 3× < 0.02	3× < 0.02 3× < 0.02 3× < 0.02	
	SC	2	37.5	5.0	BBCH 59-71	Rice grain	14 21 28	0.024, 0.023, 0.024 (0.024) 3× < 0.02 0.028, 0.021, 0.026 (0.025)	3× < 0.02 3× < 0.02 3× < 0.02	
	SC	3	37.5	5.0	BBCH 59-71	Rice grain	14 21 28	0.031, 0.028, 0.032 (0.030) 0.022, 0.022, 0.024 (0.023) 3× < 0.02	3× < 0.02 3× < 0.02 3× < 0.02	
China Education and Research Experimental Base Hunan	SC	2	25	3.3	BBCH 59-61	Rice grain	14 21 28	0.12, 0.12, 0.12 (0.12) 0.081, 0.082, 0.085 (0.083) 0.035, 0.038, 0.038 (0.037)	3× < 0.02 3× < 0.02 3× < 0.02	DuPont-38927, Zhu (2015, TRIFLUMEZ_041) analytical method: DuPont-36348, storage period: <12

Location, Year (variety)	Application Form.	No	g ai/ha	g ai/hL	Growth stage	Residues, mg/kg Sample	DALT	Triflumezo-pyrim	IN-RPA16	Report/Trial No., Reference, analytical method, validation data, storage period
Agricultural University Changsha Hunan 2013 (Xiannong 1)	SC	3	25	3.3	BBCH 59-71	Rice grain	14 21 28	0.12, 0.12, 0.12 (0.12) 0.083, 0.073, 0.082 (0.079) 0.049, 0.052, 0.052 (0.051)	3× < 0.02 3× < 0.02 3× < 0.02	month (not validated for IN-RPA16) Samples from 3 replicate plots
	SC	2	37.5	5.0	BBCH 59-61	Rice grain	14 21 28	0.21, 0.22, 0.21 (0.21) 0.17, 0.16, 0.17 (0.17) 0.066, 0.060, 0.067 (0.064)	3× < 0.02 3× < 0.02 3× < 0.02	
	SC	3	37.5	5.0	BBCH 59-71	Rice grain	14 21 28	0.25, 0.23, 0.25 (0.024) 0.17, 0.19, 0.18 (0.18) 0.090, 0.083, 0.092 (0.088)	3× < 0.02 3× < 0.02 3× < 0.02	
China Education and Research Experimental Base Hunan Agricultural University Changsha Hunan 2014 (Huanghuajing)	SC	2	25	3.3	BBCH 59-61	Rice grain	14 21 28	0.042, 0.040, 0.042 (0.041) 0.028, 0.037, 0.031 (<u>0.032</u>) 3× < 0.020	3× < 0.02 3× < 0.02 3× < 0.02	DuPont-38927, Zhu (2015, TRIFLUMEZ_041) analytical method: DuPont-36348, storage period: <12 month (not validated for IN-RPA16) Samples from 3 replicate plots
	SC	3	25	3.3	BBCH 59-71	Rice grain	14 21 28	0.098, 0.12, 0.11 (0.11) 0.047, 0.058, 0.052 (0.052) 3× < 0.020	3× < 0.02 3× < 0.02 3× < 0.02	
	SC	2	37.5	5.0	BBCH 59-71	Rice grain	14 21 28	0.13, 0.15, 0.15 (0.14) 0.089, 0.081, 0.087 (0.086) 3× < 0.020	3× < 0.02 3× < 0.02 3× < 0.02	
	SC	3	37.5	5.0	BBCH 59-71	Rice grain	14 21 28	0.19, 0.19, 0.19 (0.19) 0.056, 0.057, 0.056 (0.056) 3× < 0.020	3× < 0.02 3× < 0.02 3× < 0.02	
India, Maruteru, Andhra Pradesh, 2014 (Swarna-7029)	SC	2	25.0	5.0	BBCH 89	Rice grain	23	0.021, 0.020, 0.021 (<u>0.021</u>)	3× < 0.003	DuPont-40367, Manikandan, (2015, TRIFLUMEZ_047) analytical method DuPont-36348, storage period: <6 month Samples from 3 replicate plots
	SC	2	50.0	10.0	BBCH 89	Rice grain	23	0.071, 0.069, 0.072 (0.071)	3× < 0.003	
India, Palem, Telangana, 2014	SC	2	25.0	5.0	BBCH 89	Rice grain	19	0.087, 0.085, 0.088 (<u>0.087</u>)	3× < 0.003	DuPont-40367, Manikandan, (2015, TRIFLUMEZ_047) analytical method

Location, Year (variety)	Application Form.	No	g ai/ha	g ai/hL	Growth stage	Residues, mg/kg Sample	DALT	Triflumezo-pyrim	IN-RPA16	Report/Trial No., Reference, analytical method, validation data, storage period
(Pusa basmati)	SC	2	50.0	10.0	BBCH 89	Rice grain	19	0.17, 0.17, 0.17 (0.17)	3× < 0.003	DuPont-36348, storage period: <6 month Samples from 3 replicate plots
India, Gangavati, Karnataka, 2014 (BPT-5204)	SC	2	25.0	5.0	BBCH 89	Rice grain	22	0.020, 0.024, 0.023 (0.022)	3× < 0.003	DuPont-40367, Manikandan, (2015, TRIFLUMEZ_047) analytical method DuPont-36348, storage period: <6 month Samples from 3 replicate plots
	SC	2	50.0	10.0	BBCH 89	Rice grain	22	0.032, 0.034, 0.035 (0.034)	3× < 0.003	
India, Shimoga, Karnataka, 2014 (Jyoti)	SC	2	25.0	5.0	BBCH 89	Rice grain	21	0.17, 0.18, 0.18 (0.18)	3× < 0.003	DuPont-40367, Manikandan, (2015, TRIFLUMEZ_047) analytical method DuPont-36348, storage period: <6 month Samples from 3 replicate plots
	SC	2	50.0	10.0	BBCH 89	Rice grain	21	0.17, 0.18, 0.17 (0.17)	3× < 0.003	
India, Bhuvaneshwar, Odisha, 2014 (Swarna)	SC	2	25.0	5.0	BBCH 89	Rice grain	21	3× 0.003	3× < 0.003	DuPont-40367, Manikandan, (2015, TRIFLUMEZ_047) analytical method DuPont-36348, storage period: <6 month Samples from 3 replicate plots
	SC	2	50.0	10.0	BBCH 89	Rice grain	21	3× 0.003	3× < 0.003	
Thailand, Chainat, Muang, 2014 (Kor –Khor 31 (RD31))	SC	2	25.0 26.0	5.2 5.2	BBCH 89	Rice grain	20	0.016	< 0.003	DuPont-38864, Revision No. 1 S13-04756-01, Tandy (2015, TRIFLUMEZ_048) analytical method: DuPont-36348, storage period: <9.4 month (not validated for IN-RPA16) Mean of analytical duplicate samples

Location, Year (variety)	Application Form.	No	g ai/ha	g ai/hL	Growth stage	Residues, mg/kg Sample	DALT	Triflumezo-pyrim	IN-RPA16	Report/Trial No., Reference, analytical method, validation data, storage period
Thailand, Chainat, Manorum, 2014 (Pathum thanee 1)	SC	2	27.0 26.0	5.2 5.2	BBCH 89	Rice grain	21	0.008	< 0.003	DuPont-38864, Revision No. 1 S13-04756-03, Tandy (2015, TRIFLUMEZ_048) analytical method: DuPont-36348, storage period: <9.4 month (not validated for IN-RPA16) Mean of analytical duplicate samples
Thailand, Chainat, Sunburi, 2014 (Kor –Khor 31 (RD31))	SC	2	27.0 23.0	5.2 5.0	BBCH 89	Rice grain	22	0.009	< 0.003	DuPont-38864, Revision No. 1 S13-04756-04, Tandy (2015, TRIFLUMEZ_048) analytical method: DuPont-36348, storage period: <9.4 month (not validated for IN-RPA16) Mean of analytical duplicate samples
Thailand, Chainat, Manorum, 2014 (Kor –Khor 31 (RD31))	SC	2	26.0 27.0	5.3 5.3	BBCH 89	Rice grain	20	0.025	< 0.003	DuPont-38864, Revision No. 1 S13-04756-05, Tandy (2015, TRIFLUMEZ_048) analytical method: DuPont-36348, storage period: <9.4 month (not validated for IN-RPA16) Mean of analytical duplicate samples

DALT: days after last treatment

Table 78 Residues of triflumezopyrim and metabolites IN-RPD47, IN-R3Z91 and IN-Y2186 in rice grain following foliar application

Location, Year (variety)	Application					Residues, mg/kg						Report/Trial No., Reference, analytical method, validation data, storage period
	Form.	No	g ai/ha	g ai/hL	Growth stage	Sample	DALT	Triflumezo-pyrim	IN-RPD47	IN-R3Z91	IN-Y2186	
Thailand, Chainat, Muang, 2014 (Kor – Khor 31 (RD31))	SC	2	25.0 26.0	5.2 5.2	BBCH 89	Rice grain	20	0.010	0.004	< 0.003	< 0.003	DuPont-45169 S13-04756-01, Schernikau (2016, TRIFLUMEZ_049) analytical method: DuPont-45170 , storage period: <19.4 month; not validated for all analytes Mean of duplicate samples from re-analysis of TRIFLUMEZ_048
Thailand, Chainat, Manorum, 2014 (Pathum thanee 1)	SC	2	27.0 26.0	5.2 5.2	BBCH 89	Rice grain	21	0.007	< 0.003	< 0.003	< 0.003	DuPont-45169 S13-04756-03, Schernikau (2016, TRIFLUMEZ_049) analytical method: DuPont-45170, storage period: <19.4 month; not validated for all analytes Mean of duplicate samples from re-analysis of TRIFLUMEZ_048
Thailand, Chainat, Sunburi, 2014 (Kor – Khor 31 (RD31))	SC	2	27.0 23.0	5.2 5.0	BBCH 89	Rice grain	22	0.007	< 0.003	< 0.003	< 0.003	DuPont-45169 S13-04756-04, Schernikau (2016, TRIFLUMEZ_049) analytical method: DuPont-45170, storage period: <19.4 month; not validated for all analytes Mean of duplicate samples from re-analysis of TRIFLUMEZ_048

Location, Year (variety)	Application					Residues, mg/kg						Report/Trial No., Reference, analytical method, validation data, storage period
	Form.	No	g ai/ha	g ai/hL	Growth stage	Sample	DALT	Triflumezo-pyrim	IN-RPD47	IN-R3Z91	IN-Y2186	
Thailand, Chainat, Manorum, 2014 (Kor – Khor 31 (RD31))	SC	2	26.0 27.0	5.3 5.3	BBCH 89	Rice grain	20	0.018	< 0.003	< 0.003	0.005	DuPont-45169 S13-04756-05, Schernikau (2016, TRIFLUMEZ_049) analytical method: DuPont-45170, storage period: <19.4 month, not validated for all analytes Mean of duplicate samples from re-analysis of TRIFLUMEZ_048
Thailand, Chainat, Muang, 2015 (RD41)	SC	1	26.1	6.24	BBCH 89	Rice grain	54	< 0.003	< 0.003	< 0.003	< 0.003	DuPont-45355 S15-05915-01, Plot 2 and 3 Jaekel (2016, TRIFLUMEZ_050) analytical method: DuPont-45170, storage period: <3 month Mean of duplicate samples
	SC	2	23.9 25.0	6.24 6.23	BBCH 89	Rice grain	19	0.057	0.006	< 0.003	0.015	
Thailand, Bang Rachan, Singburi 2015 (RD41)	SC	1	24.6	6.26	BBCH 89	Rice grain	53	< 0.003	< 0.003	< 0.003	< 0.003	DuPont-45355 S15-05915-02, Plot 2 and 3 Jaekel (2016, TRIFLUMEZ_050) analytical method: DuPont-45170, storage period: <3 month Mean of duplicate samples
	SC	2	25.1 25.4	6.26 6.26	BBCH 89	Rice grain	19	0.049	0.005	< 0.003	0.013	
Thailand, Tubtan, Uthai Thani 2015 (Chainat 1)	SC	1	24.6	6.26	BBCH 89	Rice grain	65	< 0.003	< 0.003	< 0.003	< 0.003	DuPont-45355 S15-05915-03, Plot 2 and 3 Jaekel (2016, TRIFLUMEZ_050) analytical method: DuPont-45170, storage period: <3 month Mean of duplicate samples
	SC	2	24.9 24.4	6.26 6.24	BBCH 89	Rice grain	21	0.064	0.009	< 0.003	0.016	
Thailand, Sam Ko, Ang Thong 2015	SC	1	23.9	6.24	BBCH 89	Rice grain	61	< 0.003	< 0.003	< 0.003	< 0.003	DuPont-45355 S15-05915-04, Plot 2 and 3 Jaekel (2016, TRIFLUMEZ_050)

Location, Year (variety)	Application					Residues, mg/kg						Report/Trial No., Reference, analytical method, validation data, storage period
	Form.	No	g ai/ha	g ai/hL	Growth stage	Sample	DALT	Triflumezo-pyrim	IN-RPD47	IN-R3Z91	IN-Y2186	
(RD57)	SC	2	24.3 25.5	6.25 6.25	BBCH 89	Rice grain	20	0.054	0.010	< 0.003	0.017	analytical method: DuPont-45170, storage period: <3 month Mean of duplicate samples

Table 79 Residues of triflumezopyrim and IN-RPA16 in rice hulls following foliar application

Location, Year (variety)	Application					Residues, mg/kg				Report/Trial No., Reference, analytical method, validation data, storage period
	Form.	No	g ai/ha	g ai/hL	Growth stage	Sample	DALT	Triflumezo-pyrim	IN-RPA16	
China Qianjin town Xiaoshan District Hangzhou, Zhejiang 2013 (Xiushui 09)	SC	2	25	3.3	BBCH 59-61	Rice hulls	14 21 28	0.43, 0.43, 0.43 (0.43) 0.30, 0.31, 0.29 (0.30) 0.25, 0.31, 0.31 (0.29)	3× < 0.02 3× < 0.02 3× < 0.02	DuPont-38927, Zhu (2015, TRIFLUMEZ_041) analytical method: DuPont-36348, storage period: <12 month (not validated for IN-RPA16) Samples from 3 replicate plots
	SC	3	25	3.3	BBCH 59-71	Rice hulls	14 21 28	0.42, 0.41, 0.43 (0.42) 0.32, 0.35, 0.32 (0.33) 0.34, 0.34, 0.26 (0.31)	3× < 0.02 3× < 0.02 3× < 0.02	
	SC	2	37.5	5.0	BBCH 59-61	Rice hulls	14 21 28	0.60, 0.61, 0.63 (0.61) 0.47, 0.47, 0.45 (0.46) 0.37, 0.34, 0.38 (036)	3× < 0.02 3× < 0.02 3× < 0.02	
	SC	3	37.5	5.0	BBCH 59-71	Rice hulls	14 21 28	0.63, 0.60, 0.63 (0.62) 0.44, 0.45, 0.43 (0.44) 0.47, 0.49, 0.49 (0.48)	3× < 0.02 3× < 0.02 3× < 0.02	
China Qianjin town Xiaoshan District Hangzhou, Zhejiang 2014 (Zhe 108)	SC	2	25	3.3	BBCH 59-61	Rice hulls	14 21 28	0.14, 0.14, 0.11 (0.13) 0.13, 0.11, 0.12 (0.12) 0.16, 0.13, 0.15 (0.15)	3× < 0.02 3× < 0.02 3× < 0.02	DuPont-38927, Zhu (2015, TRIFLUMEZ_041) analytical method: DuPont-36348, storage period: <12 month (not validated for IN-RPA16) Samples from 3 replicate plots
	SC	3	25	3.3	BBCH 59-71	Rice hulls	14 21 28	0.26, 0.31, 0.30 (0.29) 0.18, 0.18, 0.21 (0.19) 0.22, 0.23, 0.23 (0.23)	3× < 0.02 3× < 0.02 3× < 0.02	

Location, Year (variety)	Application Form.	No	g ai/ha	g ai/hL	Growth stage	Residues, mg/kg Sample	DALT	Triflumezo-pyrim	IN-RPA16	Report/Trial No., Reference, analytical method, validation data, storage period
	SC	2	37.5	5.0	BBCH 59-71	Rice hulls	14	0.22, 0.22, 0.23 (0.22)	3× < 0.02	
							21	0.14, 0.13, 0.16 (0.14)	3× < 0.02	
							28	0.15, 0.14, 0.11 (0.13)	3× < 0.02	
	SC	3	37.5	5.0	BBCH 59-71	Rice hulls	14	0.19, 0.21, 0.23 (0.21)	3× < 0.02	
							21	0.16, 0.18, 0.18 (0.17)	3× < 0.02	
							28	0.26, 0.30, 0.29 (0.28)	3× < 0.02	
China Dalu village Zhaodian town Gaoqing county Zibo Shandong 2013 (Yanfeng 47)	SC	2	25	3.3	BBCH 59-61	Rice hulls	14	0.21, 0.29, 0.29 (0.26)	3× < 0.02	DuPont-38927, Zhu (2015, TRIFLUMEZ_041) analytical method: DuPont-36348, storage period: <12 month (not validated for IN-RPA16) Samples from 3 replicate plots
							21	0.19, 0.18, 0.20 (0.19)	3× < 0.02	
							28	0.12, 0.13, 0.14 (0.13)	3× < 0.02	
	SC	3	25	3.3	BBCH 59-71	Rice hulls	14	0.33, 0.36, 0.39 (0.36)	3× < 0.02	
							21	0.18, 0.21, 0.20 (0.20)	3× < 0.02	
							28	0.23, 0.26, 0.24 (0.24)	3× < 0.02	
	SC	2	37.5	5.0	BBCH 59-61	Rice hulls	14	0.42, 0.39, 0.40 (0.40)	3× < 0.02	
							21	0.28, 0.29, 0.30 (0.29)	3× < 0.02	
							28	0.36, 0.38, 0.38 (0.37)	3× < 0.02	
	SC	3	37.5	5.0	BBCH 59-71	Rice hulls	14	0.66, 0.65, 0.68 (0.66)	3× < 0.02	
							21	0.41, 0.35, 0.40 (0.39)	3× < 0.02	
							28	0.20, 0.20, 0.20 (0.20)	3× < 0.02	
China Dalu village Zhaodian town Gaoqing county Zibo Shandong 2014 (Yanfeng 47)	SC	2	25	3.3	BBCH 59-61	Rice hulls	14	0.086, 0.089, 0.086 (0.087)	3× < 0.02	DuPont-38927, Zhu (2015, TRIFLUMEZ_041) analytical method: DuPont-36348, storage period: <12 month (not validated for IN-RPA16) Samples from 3 replicate plots
							21	0.068, 0.046, 0.066 (0.060)	3× < 0.02	
							28	0.069, 0.074, 0.073 (0.072)	3× < 0.02	
	SC	3	25	3.3	BBCH 59-71	Rice hulls	14	0.073, 0.072, 0.069 (0.071)	3× < 0.02	
							21	0.064, 0.051, 0.064 (0.060)	3× < 0.02	
							28	0.089, 0.083, 0.091 (0.088)	3× < 0.02	
	SC	2	37.5	5.0	BBCH 59-71	Rice hulls	14	0.15, 0.15, 0.15 (0.15)	3× < 0.02	
							21	0.096, 0.084, 0.094 (0.091)	3× < 0.02	
							28	0.12, 0.11, 0.12 (0.12)	3× < 0.02	

Location, Year (variety)	Application Form.	No	g ai/ha	g ai/hL	Growth stage	Residues, mg/kg Sample	DALT	Triflumezo-pyrim	IN-RPA16	Report/Trial No., Reference, analytical method, validation data, storage period
	SC	3	37.5	5.0	BBCH 59-71	Rice hulls	14	0.16, 0.14, 0.16 (0.15)	3× < 0.02	
							21	0.12, 0.12, 0.13 (0.12)	3× < 0.02	
							28	0.083, 0.12, 0.098 (0.10)	3× < 0.02	
China Education and Research Experimental Base Hunan Agricultural University Changsha Hunan 2013 (Xiannong 1)	SC	2	25	3.3	BBCH 59-61	Rice hulls	14	0.33, 0.34, 0.34 (0.34)	3× < 0.02	DuPont-38927, Zhu (2015, TRIFLUMEZ_041) analytical method: DuPont-36348, storage period: <12 month (not validated for IN-RPA16) Samples from 3 replicate plots
							21	0.31, 0.30, 0.31 (0.31)	3× < 0.02	
							28	0.20, 0.24, 0.23 (0.22)	3× < 0.02	
	SC	3	25	3.3	BBCH 59-71	Rice hulls	14	0.41, 0.76, 0.54 (0.57)	3× < 0.02	
							21	0.43, 0.32, 0.39 (0.38)	3× < 0.02	
							28	0.31, 0.35, 0.33 (0.33)	3× < 0.02	
	SC	2	37.5	5.0	BBCH 59-61	Rice hulls	14	0.87, 0.75, 0.83 (0.82)	3× < 0.02	
							21	0.62, 0.39, 0.50 (0.50)	3× < 0.02	
							28	0.38, 0.41, 0.41 (0.40)	3× < 0.02	
	SC	3	37.5	5.0	BBCH 59-71	Rice hulls	14	0.86, 0.67, 0.78 (0.77)	3× < 0.02	
							21	0.44, 0.66, 0.56 (0.55)	3× < 0.02	
							28	0.24, 0.36, 0.30 (0.30)	3× < 0.02	
China Education and Research Experimental Base Hunan Agricultural University Changsha Hunan 2014 (Huanghuajing)	SC	2	25	3.3	BBCH 59-61	Rice hulls	14	0.070, 0.087, 0.072 (0.076)	3× < 0.02	DuPont-38927, Zhu (2015, TRIFLUMEZ_041) analytical method: DuPont-36348, storage period: <12 month (not validated for IN-RPA16) Samples from 3 replicate plots
							21	0.045, 0.048, 0.054 (0.049)	3× < 0.02	
							28	3× < 0.020	3× < 0.02	
	SC	3	25	3.3	BBCH 59-71	Rice hulls	14	0.085, 0.11, 0.10 (0.098)	3× < 0.02	
							21	0.083, 0.095, 0.095 (0.091)	3× < 0.02	
							28	3× < 0.020	3× < 0.02	
	SC	2	37.5	5.0	BBCH 59-71	Rice hulls	14	0.28, 0.39, 0.38 (0.35)	3× < 0.02	
							21	0.20, 0.22, 0.26 (0.23)	3× < 0.02	
							28	3× < 0.020	3× < 0.02	
	SC	3	37.5	5.0	BBCH 59-71	Rice hulls	14	0.48, 0.53, 0.53 (0.51)	3× < 0.02	
							21	0.15, 0.15, 0.15 (0.15)	3× < 0.02	
							28	3× < 0.020	3× < 0.02	

DALT: days after last treatment

Table 80 Residues of triflumezopyrim and IN-RPA16 in rice straw following foliar application

Location, Year (variety)	Application					Residues, mg/kg				Report/Trial No., Reference, analytical method, validation data, storage period
	Form.	No	g ai/ha	g ai/hL	Growth stage	Sample	DALT	Triflumezo-pyrim	IN-RPA16	
China Qianjin town Xiaoshan District Hangzhou, Zhejiang 2013 (Xiushui 09)	SC	2	25	3.3	BBCH 59-61	Rice straw	14 21 28	0.083, 0.080, 0.081 (0.081) 0.093, 0.10, 0.11 (<u>0.10</u>) 0.074, 0.083, 0.085 (0.081)	3× < 0.02 3× < 0.02 3× < 0.02	DuPont-38927, Zhu (2015, TRIFLUMEZ_041) analytical method: DuPont-36348, storage period: <12 month (not validated for IN-RPA16) Samples from 3 replicate plots
	SC	3	25	3.3	BBCH 59-71	Rice straw	14 21 28	0.13, 0.13, 0.13 (0.13) 0.082, 0.088, 0.088 (0.086) 0.11, 0.12, 0.11 (0.11)	3× < 0.02 3× < 0.02 3× < 0.02	
	SC	2	37.5	5.0	BBCH 59-61	Rice straw	14 21 28	0.23, 0.23, 0.24 (0.23) 0.14, 0.14, 0.15 (0.14) 0.12, 0.12, 0.13 (0.12)	3× < 0.02 3× < 0.02 3× < 0.02	
	SC	3	37.5	5.0	BBCH 59-71	Rice straw	14 21 28	0.25, 0.24, 0.25 (0.25) 0.14, 0.15, 0.15 (0.15) 0.17, 0.18, 0.18 (0.18)	3× < 0.02 3× < 0.02 3× < 0.02	
China Qianjin town Xiaoshan District Hangzhou, Zhejiang 2014 (Zhe 108)	SC	2	25	3.3	BBCH 59-61	Rice straw	14 21 28	3× < 0.02 3× < <u>0.02</u> 3× < 0.02	3× < 0.02 3× < 0.02 3× < 0.02	DuPont-38927, Zhu (2015, TRIFLUMEZ_041) analytical method: DuPont-36348, storage period: <12 month (not validated for IN-RPA16) Samples from 3 replicate plots
	SC	3	25	3.3	BBCH 59-71	Rice straw	14 21 28	0.037, 0.045, 0.041 (0.041) 3× < 0.02 2x < 0.02, 0.027 (0.022)	3× < 0.02 3× < 0.02 3× < 0.02	
	SC	2	37.5	5.0	BBCH 59-71	Rice straw	14 21 28	0.033, 0.028, 0.030 (0.030) 3× < 0.02 2x < 0.02, 0.023 (0.021)	3× < 0.02 3× < 0.02 3× < 0.02	
	SC	3	37.5	5.0	BBCH 59-71	Rice straw	14 21 28	0.048, 0.037, 0.043 (0.043) < 0.02, 0.020, 0.020 (0.020) 3× < 0.02	3× < 0.02 3× < 0.02 3× < 0.02	
China Dalu village Zhaodian town Gaoqing county Zibo Shandong 2013 (Yanfeng 47)	SC	2	25	3.3	BBCH 59-61	Rice straw	14 21 28	0.090, 0.10, 0.10 (0.10) 0.086, 0.11, 0.10 (<u>0.099</u>) 0.072, 0.072, 0.075 (0.073)	3× < 0.02 3× < 0.02 3× < 0.02	DuPont-38927, Zhu (2015, TRIFLUMEZ_041) analytical method: DuPont-36348, storage period: <12 month (not validated for IN-RPA16) Samples from 3 replicate plots
	SC	3	25	3.3	BBCH 59-71	Rice straw	14 21 28	0.15, 0.14, 0.15 (0.15) 0.14, 0.15, 0.14 (0.14) 0.15, 0.16, 0.16 (0.16)	3× < 0.02 3× < 0.02 3× < 0.02	

Location, Year (variety)	Application					Residues, mg/kg				Report/Trial No., Reference, analytical method, validation data, storage period
	Form.	No	g ai/ha	g ai/hL	Growth stage	Sample	DALT	Triflumezo-pyrim	IN-RPA16	
	SC	2	37.5	5.0	BBCH 59-61	Rice straw	14 21 28	0.13, 0.11, 0.12 (0.12) 0.13, 0.15, 0.15 (0.14) 0.20, 0.19, 0.19 (0.19)	3× < 0.02 3× < 0.02 3× < 0.02	
	SC	3	37.5	5.0	BBCH 59-71	Rice straw	14 21 28	0.20, 0.19, 0.19 (0.19) 0.21, 0.22, 0.21 (0.21) 0.26, 0.26, 0.26 (0.26)	3× < 0.02 3× < 0.02 3× < 0.02	
China Dalu village Zhaodian town Gaoqing county Zibo Shandong 2014 (Yanfeng 47)	SC	2	25	3.3	BBCH 59-61	Rice straw	14 21 28	0.061, 0.086, 0.070 (0.072) 0.17, 0.13, 0.16 (0.15) 0.035, 0.022, 0.030 (0.029)	3× < 0.02 3× < 0.02 3× < 0.02	DuPont-38927, Zhu (2015, TRIFLUMEZ_041) analytical method: DuPont-36348, storage period: <12 month (not validated for IN-RPA16) Samples from 3 replicate plots
	SC	3	25	3.3	BBCH 59-71	Rice straw	14 21 28	0.027, 0.045, 0.040 (0.037) 0.040, 0.031, 0.035 (0.035) 0.060, 0.066, 0.057 (0.061)	3× < 0.02 3× < 0.02 3× < 0.02	
	SC	2	37.5	5.0	BBCH 59-71	Rice straw	14 21 28	0.12, 0.11, 0.12 (0.12) 0.15, 0.16, 0.17 (0.16) 0.099, 0.058, 0.074 (0.077)	3× < 0.02 3× < 0.02 3× < 0.02	
	SC	3	37.5	5.0	BBCH 59-71	Rice straw	14 21 28	0.047, 0.069, 0.078 (0.065) 0.30, 0.26, 0.30 (0.29) 0.047, 0.064, 0.056 (0.056)	3× < 0.02 3× < 0.02 3× < 0.02	
China Education and Research Experimental Base Hunan Agricultural University Changsha Hunan 2013 (Xiannong 1)	SC	2	25	3.3	BBCH 59-61	Rice straw	14 21 28	0.075, 0.080, 0.079 (0.078) 0.061, 0.058, 0.065 (0.061) 0.061, 0.067, 0.062 (0.063)	3× < 0.02 3× < 0.02 3× < 0.02	DuPont-38927, Zhu (2015, TRIFLUMEZ_041) analytical method: DuPont-36348, storage period: <12 month (not validated for IN-RPA16) Samples from 3 replicate plots
	SC	3	25	3.3	BBCH 59-71	Rice straw	14 21 28	0.066, 0.073, 0.072 (0.070) 0.064, 0.059, 0.060 (0.061) 0.078, 0.079, 0.078 (0.078)	3× < 0.02 3× < 0.02 3× < 0.02	
	SC	2	37.5	5.0	BBCH 59-61	Rice straw	14 21 28	0.10, 0.10, 0.10 (0.10) 0.082, 0.078, 0.090 (0.083) 0.053, 0.051, 0.053 (0.052)	3× < 0.02 3× < 0.02 3× < 0.02	
	SC	3	37.5	5.0	BBCH 59-71	Rice straw	14 21 28	0.18, 0.18, 0.18 (0.18) 0.045, 0.051, 0.049 (0.048) 0.073, 0.077, 0.077 (0.76)	3× < 0.02 3× < 0.02 3× < 0.02	

Location, Year (variety)	Application					Residues, mg/kg				Report/Trial No., Reference, analytical method, validation data, storage period
	Form.	No	g ai/ha	g ai/hL	Growth stage	Sample	DALT	Triflumezo-pyrim	IN-RPA16	
China Education and Research Experimental Base Hunan Agricultural University Changsha Hunan 2014 (Huanghuajing)	SC	2	25	3.3	BBCH 59-61	Rice straw	14 21 28	3× < 0.02 3× < 0.02 3× < 0.02	3× < 0.02 3× < 0.02 3× < 0.02	DuPont-38927, Zhu (2015, TRIFLUMEZ_041) analytical method: DuPont-36348, storage period: <12 month (not validated for IN-RPA16) Samples from 3 replicate plots
	SC	3	25	3.3	BBCH 59-71	Rice straw	14 21 28	0.035, 0.030, 0.035 (0.033) 3× < 0.02 3× < 0.02	3× < 0.02 3× < 0.02 3× < 0.02	
	SC	2	37.5	5.0	BBCH 59-71	Rice straw	14 21 28	0.030, 0.019, 0.026 (0.025) 3× < 0.02 3× < 0.02	3× < 0.02 3× < 0.02 3× < 0.02	
	SC	3	37.5	5.0	BBCH 59-71	Rice straw	14 21 28	0.036, 0.039, 0.038 (0.038) 3× < 0.02 3× < 0.02	3× < 0.02 3× < 0.02 3× < 0.02	
India, Maruteru, Andhra Pradesh, 2014 (Swarna-7029)	SC	2	25.0	5.0	BBCH 89	Rice straw	23	0.057, 0.059, 0.056 (0.057)	3× < 0.003	DuPont-40367, Manikandan, (2015, TRIFLUMEZ_047) analytical method DuPont-36348, storage period: <6 month Samples from 3 replicate plots
	SC	2	50.0	10.0	BBCH 89	Rice straw	23	0.096, 0.092, 0.094 (0.094)	3× < 0.003	
India, Palem, Telangana, 2014 (Pusa basmati)	SC	2	25.0	5.0	BBCH 89	Rice straw	19	0.13, 0.15, 0.15 (0.14)	3× < 0.003	DuPont-40367, Manikandan, (2015, TRIFLUMEZ_047) analytical method DuPont-36348, storage period: <6 month Samples from 3 replicate plots
	SC	2	50.0	10.0	BBCH 89	Rice straw	19	0.16, 0.16, 0.16 (0.16)	3× < 0.003	
India, Gangavati, Karnataka, 2014 (BPT-5204)	SC	2	25.0	5.0	BBCH 89	Rice straw	22	0.071, 0.072, 0.072 (0.072)	3× < 0.003	DuPont-40367, Manikandan, (2015, TRIFLUMEZ_047) analytical method DuPont-36348, storage period: <6 month Samples from 3 replicate plots
	SC	2	50.0	10.0	BBCH 89	Rice straw	22	0.16, 0.15, 0.15 (0.15)	3× < 0.003	
India, Shimoga, Karnataka, 2014	SC	2	25.0	5.0	BBCH 89	Rice straw	21	0.16, 0.16, 0.16 (0.16)	3× < 0.003	DuPont-40367, Manikandan, (2015, TRIFLUMEZ_047) analytical method

Location, Year (variety)	Application					Residues, mg/kg				Report/Trial No., Reference, analytical method, validation data, storage period
	Form.	No	g ai/ha	g ai/hL	Growth stage	Sample	DALT	Triflumezo-pyrim	IN-RPA16	
(Jyoti)	SC	2	50.0	10.0	BBCH 89	Rice straw	21	0.17, 0.17, 0.17 (0.17)	3× < 0.003	DuPont-36348, storage period: <6 month Samples from 3 replicate plots
India, Bhuvaneshwar, Odisha, 2014 (Swarna)	SC	2	25.0	5.0	BBCH 89	Rice straw	21	0.007, 0.007, 0.009 (<u>0.008</u>)	3× < 0.003	DuPont-40367, Manikandan, (2015, TRIFLUMEZ_047) analytical method DuPont-36348, storage period: <6 month Samples from 3 replicate plots
	SC	2	50.0	10.0	BBCH 89	Rice straw	21	0.016, 0.017, 0.017 (0.017)	3× < 0.003	
Thailand, Chainat, Muang, 2014 (Kor –Khor 31 (RD31))	SC	2	25.0 26.0	5.2 5.2	BBCH 89	Rice straw	20	<u>0.028</u>	< 0.003	DuPont-38864, Revision No. 1 S13-04756-01, Tandy (2015, TRIFLUMEZ_048) analytical method: DuPont-36348, storage period: <9.4 month (not validated for IN-RPA16) Mean of analytical duplicate samples
Thailand, Chainat, Manorum, 2014 (Pathum thanee 1)	SC	2	27.0 26.0	5.2 5.2	BBCH 89	Rice straw	21	<u>0.010</u>	< 0.003	DuPont-38864, Revision No. 1 S13-04756-03, Tandy (2015, TRIFLUMEZ_048) analytical method: DuPont-36348, storage period: <9.4 month (not validated for IN-RPA16) Mean of analytical duplicate samples
Thailand, Chainat, Sunburi, 2014 (Kor –Khor 31 (RD31))	SC	2	27.0 23.0	5.2 5.0	BBCH 89	Rice straw	22	<u>0.009</u>	< 0.003	DuPont-38864, Revision No. 1 S13-04756-04, Tandy (2015, TRIFLUMEZ_048) analytical method: DuPont-36348, storage period: <9.4 month (not validated for IN-RPA16) Mean of analytical duplicate samples

Location, Year (variety)	Application					Residues, mg/kg				Report/Trial No., Reference, analytical method, validation data, storage period
	Form.	No	g ai/ha	g ai/hL	Growth stage	Sample	DALT	Triflumezo-pyrim	IN-RPA16	
Thailand, Chainat, Manorum, 2014 (Kor –Khor 31 (RD31))	SC	2	26.0 27.0	5.3 5.3	BBCH 89	Rice straw	20	0.077	< 0.003	DuPont-38864, Revision No. 1 S13-04756-05, Tandy (2015, TRIFLUMEZ_048) analytical method: DuPont-36348, storage period: <9.4 month (not validated for IN-RPA16) Mean of analytical duplicate samples

DALT: days after last treatment

Table 81 Residues of triflumezopyrim and metabolites IN-RPD47, IN-R3Z91 and IN-Y2186 in rice straw following foliar application

Location Year (variety)	Application					Residues, mg/kg						Report/Trial No., Reference, analytical method, validation data, storage period
	Form.	No	g ai/ha	g ai/hL	Growth stage	Sample	DALT	Triflumezo-pyrim	IN-RPD47	IN-R3Z91	IN-Y2186	
Thailand, Chainat, Muang, 2014 (Kor – Khor 31 (RD31))	SC	2	25.0 26.0	5.2 5.2	BBCH 89	Rice straw	20	0.022	< 0.003	< 0.003	0.009	DuPont-45169 S13-04756-01, Schernikau (2016, TRIFLUMEZ_049) analytical method: DuPont-45170, storage period: <19.4 month (not validated for all analytes) Mean of duplicate samples from re-analysis of TRIFLUMEZ_048
Thailand, Chainat, Manorum, 2014 (Pathum thanee 1)	SC	2	27.0 26.0	5.2 5.2	BBCH 89	Rice straw	21	0.008	< 0.003	0.005	< 0.003	DuPont-45169 S13-04756-03, Schernikau (2016, TRIFLUMEZ_049) analytical method: DuPont-45170, storage period: <19.4 month (not validated for all analytes) Mean of duplicate samples from re-analysis of TRIFLUMEZ_048

Location	Application					Residues, mg/kg						Report/Trial No., Reference,
Year (variety)	Form.	No	g ai/ha	g ai/hL	Growth stage	Sample	DALT	Triflumezo-pyrim	IN-RPD47	IN-R3Z91	IN-Y2186	analytical method, validation data, storage period
Thailand, Chainat, Sunburi, 2014 (Kor – Khor 31 (RD31))	SC	2	27.0 23.0	5.2 5.0	BBCH 89	Rice straw	22	0.007	< 0.003	0.004	< 0.003	DuPont-45169 S13-04756-04, Schernikau (2016, TRIFLUMEZ_049) analytical method: DuPont-45170, storage period: <19.4 month (not validated for all analytes) Mean of duplicate samples from re-analysis of TRIFLUMEZ_048
Thailand, Chainat, Manorum, 2014 (Kor – Khor 31 (RD31))	SC	2	26.0 27.0	5.3 5.3	BBCH 89	Rice straw	20	0.062	0.004	0.006	0.010	DuPont-45169 S13-04756-05, Schernikau (2016, TRIFLUMEZ_049) analytical method: DuPont-45170, storage period: <19.4 month (not validated for all analytes) Mean of duplicate samples from re-analysis of TRIFLUMEZ_048
Thailand, Chainat, Muang, 2015 (RD41)	SC	1	26.1	6.24	BBCH 89	Rice straw	54	0.004	< 0.003	< 0.003	0.009	DuPont-45355 S15-05915-01, Plot 2 and 3 Jaekel (2016, TRIFLUMEZ_050) analytical method: DuPont-45170, storage period: <3 month Mean of duplicate samples
	SC	2	23.9 25.0	6.24 6.23	BBCH 89	Rice straw	19	0.15	0.010	0.011	0.027	
Thailand, Bang Rachan, Singburi 2015 (RD41)	SC	1	24.6	6.26	BBCH 89	Rice straw	53	0.004	< 0.003	< 0.003	0.006	DuPont-45355 S15-05915-02, Plot 2 and 3 Jaekel (2016, TRIFLUMEZ_050) analytical method: DuPont-45170, storage period: <3 month Mean of duplicate samples
	SC	2	25.1 25.4	6.26 6.26	BBCH 89	Rice straw	19	0.12	0.008	0.010	0.024	

Location Year (variety)	Application Form.	No	g ai/ha	g ai/hL	Growth stage	Residues, mg/kg Sample	DALT	Triflumezo-pyrim	IN-RPD47	IN-R3Z91	IN-Y2186	Report/Trial No., Reference, analytical method, validation data, storage period
Thailand, Tubtan, Uthai Thani 2015 (Chainat 1)	SC	1	24.6	6.26	BBCH 89	Rice straw	65	< 0.003	< 0.003	< 0.003	0.005	DuPont-45355 S15-05915-03, Plot 2 and 3 Jaekel (2016, TRIFLUMEZ_050) analytical method: DuPont-45170, storage period: <3 month Mean of duplicate samples
	SC	2	24.9 24.4	6.26 6.24	BBCH 89	Rice straw	21	0.21	0.019	0.022	0.070	
Thailand, Sam Ko, Ang Thong 2015 (RD57)	SC	1	23.9	6.24	BBCH 89	Rice straw	61	< 0.003	< 0.003	< 0.003	< 0.003	DuPont-45355 S15-05915-04, Plot 2 and 3 Jaekel (2016, TRIFLUMEZ_050) analytical method: DuPont-45170, storage period: <3 month Mean of duplicate samples
	SC	2	24.3 25.5	6.25 6.25	BBCH 89	Rice straw	20	0.20	0.017	0.010	0.028	

DALT: days after last treatment

Table 82 Residues of additional metabolites IN-RPA19 and IN-R6U72 in rice straw following foliar application

Location, Year (variety)	Application Form.	No	g ai/ha	g ai/hL	Growth stage	Residues, mg/kg Sample	DALT	IN-RPA19	IN-R6U72	Report/Trial No., Reference, analytical method, validation data, storage period
Thailand, Chainat, Muang, 2015 (RD41)	SC	2	23.9 25.0	6.24 6.23	BBCH 89	Rice straw	19	0.026	< 0.003	DuPont-45355 S15-05915-01, Plot 3 Jaekel (2016, TRIFLUMEZ_050) analytical method: DuPont-45170, storage period: <3 month Mean of duplicate samples

Location, Year (variety)	Application					Residues, mg/kg				Report/Trial No., Reference, analytical method, validation data, storage period
	Form.	No	g ai/ha	g ai/hL	Growth stage	Sample	DALT	IN-RPA19	IN-R6U72	
Thailand, Bang Rachan, Singburi 2015 (RD41)	SC	2	25.1 25.4	6.26 6.26	BBCH 89	Rice straw	19	0.018	< 0.003	DuPont-45355 S15-05915-02, Plot 3 Jaekel (2016, TRIFLUMEZ_050) analytical method: DuPont-45170, storage period: <3 month Mean of duplicate samples
Thailand, Tubtan, Uthai Thani 2015 (Chainat 1)	SC	2	24.9 24.4	6.26 6.24	BBCH 89	Rice straw	21	0.023	< 0.003	DuPont-45355 S15-05915-03, Plot 3 Jaekel (2016, TRIFLUMEZ_050) analytical method: DuPont-45170, storage period: <3 month Mean of duplicate samples
Thailand, Sam Ko, Ang Thong 2015 (RD57)	SC	2	24.3 25.5	6.25 6.25	BBCH 89	Rice straw	20	0.049	< 0.003	DuPont-45355 S15-05915-04, Plot 3 Jaekel (2016, TRIFLUMEZ_050) analytical method: DuPont-45170, storage period: <3 month Mean of duplicate samples

FATE OF RESIDUES IN STORAGE AND PROCESSING

Nature of residue during processing

The hydrolysis of triflumezopyrim under processing conditions was investigated by Anand (2013, TRIFLUMEZ_017). [pyridine-^{14}C]-, [methylene-^{14}C]- and [pyrimidine-^{14}C]-radiolabelled triflumezopyrim was incubated in aqueous buffer solutions at a nominal concentration of 5 mg/L under three sets of conditions, each designed to simulate an appropriate process: 90 °C (pH 4, 20 minutes) to simulate pasteurisation, 100 °C (pH 5, 60 minutes), to simulate boiling, baking and brewing, and 120 °C (pH 6, 20 minutes) to simulate sterilisation.

Total recovered radioactivity was measured for each test solution by LSC. Radioactive components were characterised by fractionation and co-chromatography with authenticated reference compounds using HPLC and LC-MS.

Table 83 Hydrolysis of triflumezopyrim under simulated processing conditions

Compound	% applied radioactivity recovered as		
	[pyridine-^{14}C] triflumezopyrim	[pyrimidine-^{14}C] triflumezopyrim	[methylene-^{14}C] triflumezopyrim
pH 4 90 °C 20 mins			
Triflumezopyrim	97.2	99.3	102.4
Others	0.0	0.0	0.0
Total	97.2	99.3	102.4
pH 5 100 °C 60 mins			
Triflumezopyrim	99.3	100.0	100.5
Others	1.1	1.1	0.0
Total	100.4	101.1	100.5
pH 6 120 °C 20 mins			
Triflumezopyrim	101.8	103.4	102.9
Others	0.0	0.0	0.0
Total	101.8	103.4	12.9

Residues after processing

The fate of triflumezopyrim during processing of raw agricultural commodity (RAC) was investigated in rice. As a measure of the transfer of residues into processed products, a processing factor was used, which is defined as:

Processing factor = Residue in processed product (mg/kg) ÷ Residue in raw agricultural commodity (mg/kg)

In case of residues below the LOQ in the processed product, the numeric value of the LOQ was used for the calculation and the PF was expressed as "less than" (e.g. < 0.5).

The transfer of residues of triflumezopyrim and its metabolite IN-RPA16 were investigated in rice from three supervised field trial conducted in the USA by Thiel (2015, TRIFLUMEZ_053). The trials were performed with two treatments at exaggerated rates of 75 g ai/ha and harvest at 21 DALT. Rice grains with hulls (rough rice) were processed into brown rice, polished rice, bran and hulls using common commercial practices. All samples were analysed according to method DuPont-36348. Residues of IN-RPA16 were <LOQ in both, rough rice and any processed commodities.

Table 84 Summary of triflumezopyrim residues in rice and processed commodities

Trial Identification (City, State/Region, Country, Year)	From.	Crop/ Variety	Commodity or Matrix	Total Rate (g ai/ha)	PHI (days)	Average Residues (mg/kg) (Individual Values)	Processing Factor
Trial 01 (Fisk, MO, USA, 2013)	SC	Rice/ CL 111	Rice grain (RAC)	146	22	0.12 (0.11, 0.12, 0.12)	-
			Brown Rice			< 0.010	< 0.086
			Polished Rice			< 0.010	< 0.086
			Bran			0.072	0.62
			Hulls			0.54	4.6
Trial 02 (Proctor, AR, USA, 2013)	SC	Rice/ CL151	Rice grain (RAC)	145	21	0.040 (0.037, 0.044, 0.040)	-
			Brown Rice			< 0.010	<0.25
			Polished Rice			< 0.010	<0.25
			Bran			0.015	0.37
			Hulls			0.16	3.9
Trial 03 (Louise, TX, USA, 2013)	SC	Rice/ Dixie Bell	Rice grain (RAC)	152	22	0.10 (0.091, 0.10, 0.12)	-
			Brown Rice			< 0.010	< 0.096
			Polished Rice			< 0.010	< 0.096
			Bran			0.052	0.50
			Hulls			0.36	3.5

RAC: raw agricultural commodity

n.p. not possible

Table 85 Summary of processing factors

Matrix	Processing factors	Median or best estimate
Brown Rice	<u>≤ 0.086</u>, < 0.025, < 0.096	< 0.086
Polished Rice	<u>≤ 0.086</u>, < 0.025, < 0.096	< 0.086
Bran	0.62, 0.37, <u>0.50</u>	0.50
Hulls	4.6, <u>3.9</u>, 3.5	3.9

RESIDUES IN ANIMAL COMMODITIES

Farm animal feeding studies

Lactating cows

The estimation of residues of triflumezopyrim in animal matrices was investigated by Wen (2015, TRIFLUMEZ_054) and in the supplement by Sears (2016, TRIFLUMEZ_055). The study was conducted at treatment rates of 1.34 (1×), 4.03 (3×), and 13.48 (10×) mg/kg feed (0.038, 0.115 and 0.392 mg/kg bw) for 30 days.

The cows in the treatment groups (three animals per group, plus two animals in the depuration group) were treated with triflumezopyrim (gelatine capsules) twice daily. Milk samples were collected twice daily throughout the dosing period. Skim milk and cream samples were prepared from milk collected from the three cows in the 10 mg/kg treatment group on days 14 and 21. All cows were sacrificed ca. 17–21 hours after the last dose, except for the depuration group and the control cow included in the depuration phase. The depuration group cows were sacrificed on day 34 and day 38. Samples of liver, kidney, muscle, and fat were collected and taken for analysis.

All samples were analysed by using method DuPont-36347 with a validated LOQ for all matrices at 0.01 mg/kg. Skim milk, cream, fat and muscle were analysed within less than 30 days, while the maximum frozen storage period was 49 days for whole milk and 56 days for kidney and liver.

With the exception of one liver sample (0.004 mg/kg), no detectable residues of triflumezopyrim were found in the control group. The findings in milk and tissues are summarised in Table 86.

Table 86 Residues of triflumezopyrim in cow tissues and milk

Commodity	Sampling Interval (days)	Individual residues in mg/kg (mean)			
		1× group (1.34 ppm)	3× group (4.03 ppm)	10× group (13.48 ppm)	10× depuration group (13.48 ppm)
Milk	-1	< 0.003, < 0.003, < 0.003 (< 0.003)	< 0.003, < 0.003, < 0.003 (< 0.003)	< 0.003, < 0.003, < 0.003 (< 0.003)	NS
	1	< 0.003, < 0.003, < 0.003 (< 0.003)	0.004, < 0.003, < 0.003 (0.003)	0.013, 0.015, 0.012 (0.014)	NS
	3	< 0.003, < 0.003, 0.003 (< 0.003)	0.010, 0.005, 0.005 (0.007)	0.021, 0.022, 0.017 (0.020)	NS
	5	< 0.003, < 0.003, 0.004 (< 0.003)	0.010, 0.004, 0.006 (0.006)	0.019, 0.022, 0.018 (0.020)	NS
	7	< 0.003, 0.004, 0.003 (0.003)	0.008, 0.004, 0.004 (0.005)	0.015, 0.017, 0.022, 0.019 (0.018)	NS
	10	< 0.003, 0.003, < 0.003 (< 0.003)	0.008, 0.004, 0.004 (0.006)	0.021, 0.023, 0.018 (0.020)	NS
	14	0.003, 0.003, < 0.003 (< 0.003)	0.007, 0.004, 0.004 (0.005)	0.021, 0.021, 0.025 (0.022)	NS
	21	< 0.003, < 0.003,	0.007, 0.003, 0.005	0.022, 0.020, 0.021	NS

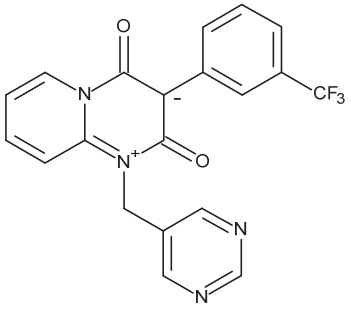
Commodity	Sampling Interval (days)	Individual residues in mg/kg (mean) 1× group (1.34 ppm)	3× group (4.03 ppm)	10× group (13.48 ppm)	10× depuration group (13.48 ppm)
		0.003 (< 0.003)	(0.005)	(0.021)	
	24	NS	NS	0.018, 0.020, 0.018 (0.020)	NS
	28	< 0.003, 0.003, 0.003 (0.003)	0.006, < 0.003, 0.005 (0.004)	0.018, 0.021, 0.020, 0.017, 0.017 (0.018)	NA
	29	NA	NA	NA	0.034, 0.027 (0.030)
	30	NA	NA	NA	0.029, 0.029 (0.029)
	31	NS	NS	NS	0.012, 0.012 (0.012)
	32	NS	NS	NS	0.021, < 0.003 (0.011)
	33	NS	NS	NS	< 0.003, 0.006 (0.003)
	34	NS	NS	NS	< 0.003, < 0.003 (< 0.003)
	35	NS	NS	NS	< 0.003, < 0.003 (< 0.003)
	36	NS	NS	NS	< 0.003, < 0.003 (< 0.003)
	37	NS	NS	NS	< 0.003, < 0.003 (< 0.003)
Milk – skim milk	14	NS	NS	0.018, 0.019, 0.021 (0.019)	NS
	21	NS	NS	0.019, 0.021, 0.017 (0.019)	NS
Milk – cream	14	NS	NS	0.022, 0.027, 0.029 (0.026)	NS
	21	NS	NS	0.023, 0.020, 0.026 (0.023)	NS
Muscle	31	NS	NS	< 0.003, < 0.003, < 0.003 (< 0.003)	NS
	34	NS	NS	NS	< 0.003
	38	NS	NS	NS	< 0.003
Liver	31	0.006, 0.008, 0.005, 0.008, 0.007, 0.010, 0.010, 0.010, 0.011 (0.008)	0.005, 0.008, 0.005, 0.007, 0.008, 0.008, 0.006, 0.009, 0.010 0.007	0.031, 0.036, 0.035 (0.034)	NS
	34	NS	NS	NS	< 0.003
	38	NS	NS	NS	< 0.003
Kidney	31	0.004, 0.008, 0.006, 0.005, 0.009, 0.013, 0.008, 0.006, 0.010 (0.008)	< 0.003, 0.006, 0.008, 0.007, 0.007, 0.008, 0.006, 0.007, 0.008 (0.007)	0.022, 0.024, 0.024 (0.023)	NS
	34	NS	NS	NS	0.004
	38	NS	NS	NS	< 0.003
Fat	31	NS	NS	< 0.003, < 0.003, < 0.003 (< 0.003)	NS
	34	NS	NS	NS	< 0.003
	38	NS	NS	NS	< 0.003

NS: no sample

NA: not applicable

APPRAISAL

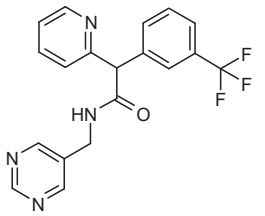
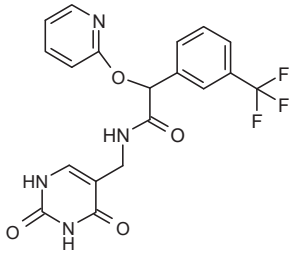
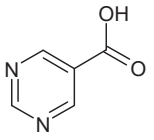
Triflumezopyrim (ISO common name) is an insecticide used to control planthoppers in rice. Triflumezopyrim was scheduled by the 48th Session of the CCPR for evaluation of residues and toxicology for the first time by the present Meeting. The 2017 Meeting received information and studies on the environmental fate in soil and water, plant metabolism in rice, confined rotational crop metabolism, animal metabolism in lactating goats and laying hen, analytical methods, storage stability, supervised field trials on rice, processing data on rice and animal feeding. Triflumezopyrim is registered by several countries for use on rice.

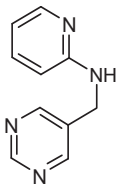
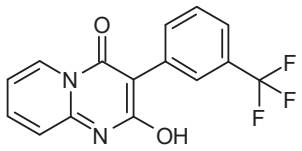
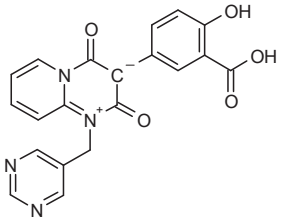
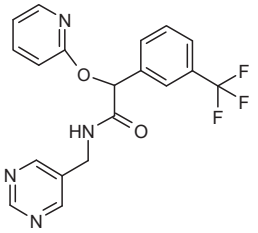
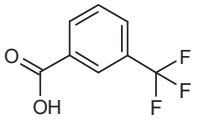
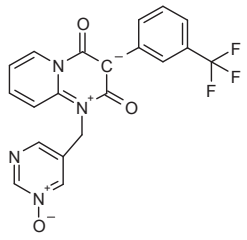
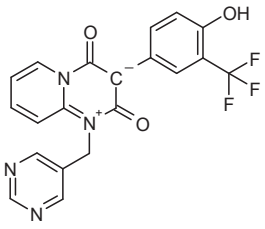


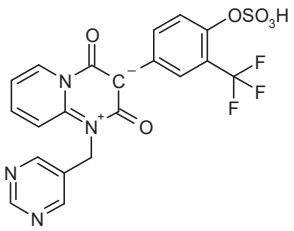
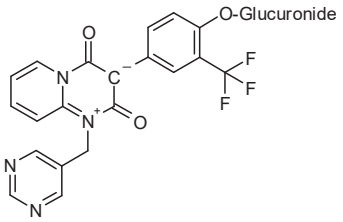
The IUPAC and CA name of triflumezopyrim is 3,4-dihydro-2,4-dioxo-1-(pyrimidin-5-ylmethyl)-3-(α,α,α-trifluoro-*m*-tolyl)-2*H*-pyrido[1,2-*a*]pyrimidin-1-ium-3-ide.

Metabolism and environmental fate studies were conducted using [fused pyrimidine-3-^{14}C]triflumezopyrim, [methylene-^{14}C]triflumezopyrim and [pyridine-2,6-^{14}C]triflumezopyrim. Moreover, [fused pyrimidine-3-^{13}C]triflumezopyrim was used.

The following abbreviations are used for the metabolites discussed below:

IN-RUB93	2-(2-pyridyl)-N-(pyrimidin-5-ylmethyl)-2-[3-(trifluoromethyl)phenyl]acetamide	
IN-SBY68	N-[(2,4-dioxo-1H-pyrimidin-5-yl)methyl]-2-(2-pyridyloxy)-2-[3-(trifluoromethyl)phenyl]acetamide	
IN-RPA16	pyrimidine-5-carboxylic acid	

IN-RPA19	N-(pyrimidin-5-ylmethyl)pyridin-2-amine	
IN-RPD47	2-hydroxy-3-[3-(trifluoromethyl)phenyl]pyrido[1,2-a]pyrimidin-4-one	
IN-R6U72 (hydroxy acid)	5-[2,4-dioxo-1-(pyrimidin-5-ylmethyl)pyrido[1,2-a]pyrimidin-1-ium-3-id-3-yl]-2-hydroxy-benzoic acid	
IN-SBV06	2-(2-pyridyloxy)-N-(pyrimidin-5-ylmethyl)-2-[3-(trifluoromethyl)phenyl]acetamide	
IN-Y2186	3-(trifluoromethyl)benzoic acid	
IN-R3Z91 (N-oxide)	1-[(1-oxidopyrimidin-1-ium-5-yl)methyl]-3-[3-(trifluoromethyl)phenyl]pyrido[1,2-a]pyrimidin-1-ium-3-ide-2,4-dione	
IN-R6U70	3-[4-hydroxy-3-(trifluoromethyl)phenyl]-1-(pyrimidin-5-ylmethyl)pyrido[1,2-a]pyrimidin-1-ium-3-ide-2,4-dione	

R6U70 sulfate (sulphate conjugate of IN-R6U70)	[4-[2,4-dioxo-1-(pyrimidin-5-ylmethyl)pyrido[1,2-a]pyrimidin-1-ium-3-id-3-yl]-2-(trifluoromethyl)phenyl] hydrogen sulfate	
R6U70 glucuronide (glucuronic acid conjugate of IN-R6U70)	6-[4-[2,4-dioxo-1-(pyrimidin-5-ylmethyl)pyrido[1,2-a]pyrimidin-1-ium-3-id-3-yl]-2-(trifluoromethyl)phenoxy]-3,4,5-trihydroxy-tetrahydropyran-2-carboxylic acid	

Environmental fate in soil & water

The Meeting received information for triflumezopyrim on soil and aqueous photolysis, aqueous hydrolysis and aerobic soil metabolism.

Half-lives of ^{14}C-triflumezopyrim for soil and aqueous photolysis were estimated at 12 days and 2–3 days, respectively assuming of 1st order kinetics. During aqueous photolysis, metabolite IN-RUB93 was identified at up to 66–85%.

Degradation in water and water/sediment systems was investigated under dark and irradiated conditions. When kept in the dark, half-lives for triflumezopyrim in water alone and in the water/sediment system were estimated to be between 23–41 days and 283–320 days, respectively, while in irradiated systems, half-live times were estimated to be between 5–9 days and 33–36 days, respectively.

In aerobic soil metabolism studies, moderate degradation of triflumezopyrim was observed with estimated half-lives in various soils ranging from 53–133 days. Several metabolites were identified, but only IN-SBY68 and IN-RPD47 occurred in significant amounts of 5–9% AR.Under the more realistic conditions of flooded soil the half-lives were estimated at 184 days. In sterile soil half-lives were longer at an estimated 740 days.

The Meeting received one confined rotational crop metabolism study.

The study was conducted with lettuce, radish and wheat with triflumezopyrim applied at a rate equivalent to 0.1 kg ai/ha to a sandy loam soil under glasshouse conditions with plant-back intervals (PBIs) of 30, 120 and 268 days. Only wheat straw samples (from all PBIs) and one wheat hay sample at 30-day PBI contained total residues > 0.010 mg eq/kg and were further analysed. Parent triflumezopyrim and several metabolites were identified in these samples, but levels were consistently < 0.01 mg eq/kg.

In summary the Meeting concluded that triflumezopyrim is persistent in soil suggesting a potential for accumulation. It should be noted that metabolite IN-SBY68 is a soil metabolite only. As it was not detected in the rotational crop study it was not considered relevant for plant commodities.

The Meeting concluded that a significant transfer of triflumezopyrim residues from soil to succeeding crops is not expected.

Plant metabolism

The Meeting received two rice plant metabolism studies for triflumezopyrim following soil and foliar application of ^{14}C- pyrimidine-, ^{14}C-methylene- and ^{14}C-pyridine-radiolabelled active substances.

For the soil regime, triflumezopyrim was applied at a rate equivalent to 0.3 kg ai/ha to the soil around emerged rice plants (BBCH 13, 3 leaves unfolded) grown in pots. The plant pots were flooded two days after the soil treatment and kept under flooded conditions for the duration of the study. Samples were collected at 44 DAT (foliage, roots) and at grain maturity, 127/131 DAT (straw, chaff, grain and root).

Maximum TRR levels found for the different labels were highest in roots (0.40 mg eq/kg), followed by foliage (0.12 mg eq/kg), straw, (0.073 mg eq/kg), chaff (0.064 mg eq/kg) and grain (0.014 mg eq/kg).

Samples were sequentially extracted with methanol followed by methanol/water at various ratios. Extracted radioactivity ranged between 37–49% TRR in foliage, 38–43% TRR in straw, 41–54% TRR in chaff and 19–37% TRR in grain.

Among the identified components, parent triflumezopyrim was present at 8–19% TRR (0.001–0.002 mg eq/kg) in rice grain. In foliage, straw and chaff triflumezopyrim ranged between 11–23% TRR (0.005–0.015 mg eq/kg). Other metabolites were identified but ranged individually between 0.4–7.8% TRR (< 0.001–0.007 mg eq/kg).

For the foliar regime, two spray applications (BBCH 23, 3 tillers detectable; BBCH 69, end of flowering) were performed at a rate of 0.035 kg ai/ha each (total 0.07 kg ai/ha). Plants were sampled at 0, 7 (all labels) and 14 days after the last application (DALA) (pyridine label only) and at grain maturity, 64/68 DALA (straw, chaff, grain and root).

TRR levels found were highest in chaff (up to 0.55 mg eq/kg), followed by foliage (up to 0.28 mg eq/kg), straw, (up to 0.12 mg eq/kg), grain (up to 0.12 mg eq/kg) and roots (up to 0.043 mg eq/kg).

Samples were sequentially extracted with methanol followed by methanol/water at various ratios. Extracted radioactivity ranged between 79–95% TRR for foliage (0, 7 DAT), 56% TRR for foliage (14 DALA), 40–54% TRR for straw, 30–43% TRR for chaff and 21–52% TRR for grain.

Among the identified components in the initial solvent extracts, parent triflumezopyrim was present at 2.9–9.1% TRR (0.003–0.006 mg eq/kg) in rice grain.

In initial solvent extracts of feed commodities, parent triflumezopyrim was present in foliage (0, 7, 14 DALA) at 26–82% TRR (0.027–0.23 mg eq/kg), in straw at 4.8–7.3% TRR (0.004–0.008 mg eq/kg), in chaff at 12–15% TRR (0.043–0.083 mg eq/kg). Additionally, parent triflumezopyrim was detected in the solubilizates of the post-extraction solids of chaff at 0.4–8.5% TRR (0.002–0.047 mg eq/kg). A notable identified metabolite was IN-RPA19 in foliage (0, 7 DALA) at up to 19% TRR (0.030 mg eq/kg). Moreover, conjugates of IN-R3Z91 were detected in chaff at significant amounts after alkaline hydrolysis at 13% TRR (0.041 mg eq/kg). Additional metabolites were identified at much lower levels.

In a second study, the metabolic fate of radiolabelled triflumezopyrim was investigated following soil and foliar application. Application rates and test design were identical to the first study with the exception of sampling times. Additionally, post extraction solids were subjected additionally to a 10N base reflux with subsequent lignin precipitation.

Plants receiving the soil treatment were sampled at 51 DAT (foliage, roots) and at maturity, 119 DAT (straw, chaff, grain and root).

Maximum TRR levels found were highest in roots (0.12 mg eq/kg), followed by straw (0.11 mg eq/kg), chaff (0.093 mg eq/kg), foliage (0.066 mg eq/kg), and grain (0.013 mg eq/kg).

Samples were sequentially extracted with methanol followed by methanol/water (7:3, v/v), resulting in extraction rates of 47–49% TRR for foliage, 38–46% TRR for straw, 26–39% TRR for chaff and below LOQ for grain.

In foliage, straw and chaff, triflumezopyrim ranged between 5–24% TRR (0.002–0.016 mg eq/kg). Other metabolites were identified but ranged individually between 0.3–4.6% TRR (< 0.001–0.004 mg eq/kg).

Plants receiving the foliar treatments were sampled at 14 days after the first treatment and, in agreement with the critical GAP, 21 days after the second treatment (straw, chaff, grain and root).

TRR levels found were highest in chaff (up to 0.94 mg eq/kg), followed by straw (up to 0.34 mg eq/kg), foliage, (up to 0.13 mg eq/kg), roots (up to 0.10 mg eq/kg) and grain (up to 0.076 mg eq/kg).

Samples were sequentially extracted with methanol followed by methanol/water (7:3, v/v), resulting in extraction rates of 64–78% TRR for foliage, 55–71% TRR for straw, 43–53% TRR for chaff and 47–57% TRR for grain.

Among the identified components in the solvent extracts, parent triflumezopyrim was present at 22% TRR (0.009–0.017 mg eq/kg) in rice grain at 21 DALA. Moreover, metabolite IN-Y2186 was quantified at 12% TRR (0.009 mg eg/kg)

In the solvent extracts of feed commodities parent triflumezopyrim was present in foliage at 18–22% TRR (0.017–0.028 mg eq/kg), in straw at 19–20% TRR (0.044–0.064 mg eq/kg), in chaff at 17–25% TRR (0.15–0.16 mg eq/kg). Notable identified metabolites in feed commodities were IN-RPA19 in foliage, straw and chaff at up to 9%TRR (0.039 mg eq/kg) and IN-R6U72 (not detected in the first study) in foliage, straw and chaff at up to 16% TRR (0.032 mg eq/kg). Additional metabolites were identified at much lower levels.

Up to about 30% TRR in straw was released from PES using aggressive extraction techniques indicating that these residues are likely from the incorporation of ^{14}C into natural products.

Within the plants, parent triflumezopyrim was the predominant identified residue is in all matrices. Nevertheless, a large fraction of the active substance did degrade rather quickly into numerous metabolites before some of the observed radioactivity was incorporated into natural products. Among the metabolites identified, IN-RPA19 in foliage, IN-R6U72 in foliage and straw, IN-Y2186 in grain and conjugates of IN-R3Z91 in chaff can be considered as major metabolites, while all other identified metabolites can be considered as minor. All major identified metabolites were also found in the rat.

Animal metabolism

Information was available on the metabolism of triflumezopyrim in laboratory animals, lactating goats and laying hens. The evaluation of the metabolism studies in rats was carried out by the WHO group.

In lactating goats, the metabolic fate of triflumezopyrim was investigated using ^{14}C-radiolabelled triflumezopyrim. The compound was administered for seven consecutive days to three lactating goats (one per label) in gelatine capsules at 22 ppm (0.67 mg/kg bw) for [pyrimidine-^{14}C]-, 25 ppm (0.60 mg/kg bw) for [methylene-^{14}C]- or 20 ppm (0.58 mg/kg bw) for [pyridine-^{14}C]-triflumezopyrim.

Most of the administered radioactivity was recovered from faeces (36–53% AR) and urine (19–29% AR). For all three labels, kidney gave the highest TRR (0.58–0.93 mg eq/kg), followed by liver (0.48–0.81 mg eq/kg), milk (0.28–0.60 mg eq/kg), muscle (0.024–0.041 mg eq/kg) and fat (0.007–0.044 mg eq/kg).

TRRs in milk did not reach a plateau over the investigated timeframe of 7 days.

Milk and tissue samples were sequentially extracted with acetonitrile followed by acetonitrile/water in various ratios, with the exception of fat, where dichloromethane was used prior to acetonitrile followed by acetonitrile/water. Resulting extraction rates were 99% TRR in milk, 78–83% TRR in liver, 96–98% TRR in kidney and 91–95% TRR in muscle and 84–95% TRR in fat.

Triflumezopyrim was the principal extracted component in day 4–6 composite milk (81–83% TRR; 0.23–0.49 mg/kg), liver (37–54% TRR; 0.20–0.37 mg/kg), kidney (70–83% TRR; 0.42–0.73 mg/kg), muscle (64–89% TRR; 0.015–0.035 mg/kg), and fat (70–93% TRR; 0.006–0.031 mg/kg) from all radiolabels.

In solvent extracts, the predominant metabolite in milk, liver and kidney was unconjugated IN-R6U70 and/or its glucuronic acid and sulphate conjugates (total of 12–40% TRR; 0.048–0.22 mg/kg). Other metabolites occurring at lower levels (< 0.027 mg/kg) were also identified.

In laying hens, the metabolic fate of triflumezopyrim was investigated using ^{14}C-radiolabelled triflumezopyrim. Each of the compounds was administered for 14 consecutive days to 3 groups of laying hens (5 hens per group) in gelatine capsules at 14 ppm (7.6 mg/kg bw) for [pyrimidine-^{14}C]-, 14 ppm (7.6 mg/kg bw) for [methylene-^{14}C]- and 15 ppm (7.8 mg/kg bw) for [pyridine-^{14}C]-triflumezopyrim.

Most of the administered radioactivity was recovered from excreta (83–90% AR). For all three labels, liver gave the highest TRR (0.28–0.38 mg eq/kg), followed by muscle (0.005–0.012 mg eq/kg) and fat (0.004–0.014 mg eq/kg).

TRR levels in eggs reached a plateau after approximately one week.

Egg and tissue samples were sequentially extracted with acetonitrile followed by acetonitrile/water in various ratios. Resulting extraction rates were 79–92% TRR in egg, 73–79% TRR in liver, 56–85% TRR in muscle and 93–94% TRR in fat.

Triflumezopyrim was the principal extracted component in day 9–13 composite eggs (48–65% TRR; 0.012–0.016 mg/kg) and liver (50–52% TRR; 0.14–0.20 mg/kg) from all radiolabels.

Among the identified metabolites only IN-R3Z91 in liver occurred in significant amounts (10–14% TRR; 0.027–0.053 mg/kg). Other metabolites occurring at lower levels (< 0.011 mg/kg) were also identified.

In summary, parent triflumezopyrim was the predominant residue in rat, lactating goat and laying hen. Only moderate metabolic degradation of triflumezopyrim was observed. In goat liver and kidney, IN-R6U70 in its conjugated and unconjugated form was the predominant metabolite, as well as in milk in its unconjugated form only. In the tissues of laying hens this metabolite occurred only in minor amounts, while IN-R3Z91 in liver was the only metabolite exceeding 10% TRR or 0.05 mg eq/kg. All major identified metabolites were also found in the rat.

Methods of analysis

The Meeting received analytical methods for the determination of triflumezopyrim, IN-RPA16, IN-RPD47, IN-R3Z91 IN-RPA19, IN-Y2186 and IN-R6U72 in plant matrices as well as for the determination of triflumezopyrim in animal matrices.

For matrices of plant origin, the basic principle employs extraction with methanol/water (70/30, v/v), followed by SPE clean-up using an HLB cartridge. Residues are determined by LC-MS/MS with an LOQ of 0.01 mg/kg per analyte.

In animal matrices, triflumezopyrim was determined in tissues, milk and eggs by extraction with acetonitrile/water (1/1, v/v) (no additional clean-up is performed) and LC-MS/MS detection with a LOQ of 0.01 mg/kg.

For enforcement, the applicability of a multi-residue method was successfully demonstrated for triflumezopyrim (IN-RPA-16 was not successfully validated) in plant and animal matrices with the QuEChERS method, using LC-MS/MS detection with a LOQ of 0.01 mg/kg. Other metabolites were not tested.

The Meeting concluded that suitable data generation and monitoring methods are available to measure triflumezopyrim in plant and animal commodities.

Stability of residues in stored analytical samples

The Meeting received information on the storage stability of triflumezopyrim and metabolites IN-RPA16, IN-RPD47, IN-R3Z91 and IN-Y2186 in rice plant matrices (whole plant, grain, straw) stored at -18 °C.

The storage stability in different frozen rice commodities of triflumezopyrim and all metabolites was demonstrated for at least 16 months and 6 months, respectively.

The storage stability of triflumezopyrim in animal matrices was not tested, with samples from a feeding study with lactating cows analysed within 30 days after collection.

Definition of the residue

From the plant metabolism studies in rice the foliar treatment regime and samples taken at 21 DALT were considered most relevant, as the critical GAP employs the same application method and is in agreement with the PHI of 21 days.

Parent triflumezopyrim was the predominant residue in rice grain at 22% TRR (0.009–0.017 mg/kg) as well as metabolite IN-Y2186 at up to 12% TRR (0.009 mg eq/kg). In feed matrices at 21 DALT, residues of triflumezopyrim ranged from 19–20% TRR in straw and 17–25% TRR in chaff. A metabolite found at significant levels at 21 DALT was IN-R6U72 in straw at up to 14% TRR (0.032 mg eq/kg)

In the confined rotational crop study total radioactive residues were < 0.01 mg eq/kg with the exception of straw and one hay sample. Parent triflumezopyrim (up to 30% TRR) and several metabolites (<10% TRR each) were identified in these samples, but concentrations were consistently < 0.01 mg eq/kg.

The Meeting concluded that triflumezopyrim is the major residue in rice and rotational crops (although at very low levels) and is a suitable marker compound for compliance with MRLs. Analytical multi-residue methods are capable of measuring triflumezopyrim in all plant matrices.

For dietary exposure purposes, the only metabolite found at potentially significant levels in rice grain was IN-Y2186 (up to 12% TRR, 0.009 mg eq/kg). In supervised field trials where IN-Y2186 was measured, the metabolite was found above the LOQ in five out of eight trials, ranging up to 0.017 mg/kg in the grain (parent triflumezopyrim concentrations up to 0.064 mg/kg).

The Meeting concluded that residues of IN-Y2186 may add significantly to the overall dietary exposure of triflumezopyrim residues. Since IN-Y2186 was observed in the rat and is of no greater toxicity than parent triflumezopyrim and is covered by its toxicological reference values, the Meeting decided to include the metabolite into the residue definition for dietary exposure purposes.

In lactating goats, triflumezopyrim was the principal extracted component in day 4–6 composite milk, liver, kidney, muscle and fat ranging from 36–89% TRR. The only major metabolite, IN-R6U70 and its glucuronic acid and sulphate conjugate was identified in milk, liver and kidney at levels ranging between 14–49% of parent.

A cow feeding study was conducted at treatment rates of 1.3, 4.0 and 14 ppm. In the 1.3 and 4.0 ppm treatment groups no residues >0.01 mg/kg were detected, while in the 14 ppm treatment group residues of triflumezopyrim occurred in liver (0.034 mg/kg), kidney (0.023 mg/kg) milk (0.021 mg/kg) and cream (0.026 mg/kg). A plateau for the parent compound in milk was reached after approximately one week. Analysis for metabolites was not performed.

In laying hens, triflumezopyrim was the principal extracted component in day 9–13 composite eggs and liver from all radiolabels ranging from 48–65% TRR. The only major metabolite IN-R3Z91 occurred in liver at 10–14% TRR, however at lower proportions (19–27%) than parent triflumezopyrim, depending on the radiolabel.

Livestock animals may be exposed to metabolites of triflumezopyrim through plant parts utilised for feed purposes. Plant metabolism and supervised field trial studies indicate IN-Y2186, IN-RPA19, IN-R6U72 and IN-R3Z91 to be present at concentrations comparable to the parent compound. The Meeting noted that these metabolites, based on their structures, are expected to have higher water solubilities than parent compound. The Meeting considered that these metabolites would be more readily excreted and hence less likely to accumulate in milk, eggs and tissues than parent. Noting that these compounds were present in rice fodder and forage at comparable levels to the parent compound, it is considered that these metabolites would be found at lower levels than parent

compound in animal matrices after feeding treated rice. Therefore, inclusion in the residue definition for animal commodities is not necessary.

For compliance with MRLs the Meeting concluded that triflumezopyrim is a suitable marker in all animal commodities. Analytical multi-residue methods are capable of measuring triflumezopyrim in all animal matrices.

In muscle and fat tissues of all animals investigated, residue concentrations of parent triflumezopyrim were comparable. In addition, TRR levels found in skim milk and cream did not differ significantly. In whole milk > 80% of the TRR were identified as parent. The log P_{ow} of triflumezopyrim is 1.2. The Meeting decided that residues of triflumezopyrim are not fat soluble.

For dietary exposure purposes, parent triflumezopyrim was the predominant residue in all matrices investigated. In addition, IN-R6U70 and its conjugates were found in goats at relative amounts of up to 49% of parent, while in laying hens the only major metabolite was IN-R3Z91 in liver, being present at relative amounts of up to 27% of the parent. However, in view of the very low livestock animal dietary burden for triflumezopyrim of maximal 0.26 ppm, not resulting in residues at or above the LOQ in animal products, the contribution of both metabolites to the overall dietary exposure was considered as insignificant by the Meeting. Therefore, the Meeting decided that the residue definition for the dietary intake of animal commodities is triflumezopyrim only. Reconsideration may be required if additional uses increase the livestock animal dietary burden significantly.

Definition of the residue (for compliance with the MRL) for plant and animal commodities: *Triflumezopyrim*

Definition of the residue (for the estimation of dietary intake) for plant commodities: *Sum of triflumezopyrim and 3-(trifluoromethyl)benzoic acid (IN-Y2186), expressed as triflumezopyrim.*

Definition of the residue (for the estimation of dietary intake) for animal commodities: T*riflumezopyrim*

The residue is not fat-soluble.

Results of supervised residue trials on crops

The Meeting received supervised trial data for applications of triflumezopyrim on rice only. The trials were conducted in China, India and Thailand.

The critical GAP is from China with a maximum rate of 2 × 25 g ai/ha with a PHI of 21 days. Supervised field trials from China, India and Thailand matching the cGAP were submitted.

MRL Setting

Rice grain

For MRL setting of rice grain, the ranked order of residues of *triflumezopyrim* following GAP treatment was (n=23): 0.003, 0.007(2), 0.008, 0.009, 0.010, 0.016, 0.018, < 0.020, 0.021, 0.022, 0.025, 0.032 (2), 0.034, 0.049, 0.051, 0.054, 0.057, 0.064, 0.083, 0.087, 0.18 mg/kg.

The Meeting estimated a maximum residue level of 0.2 mg/kg for *triflumezopyrim* in rice grains and a median residue of 0.025 mg/kg for animal dietary burden calculation.

Husked rice

For MRL setting of husked rice, the ranked order of residues of *triflumezopyrim* husked rice from field trials following GAP treatment was (n=6): 6×< 0.01 mg/kg.

Noting that all residues were < 0.01 mg/kg and that even trials with higher treatment rates (2 × 37.5 g ai/ha resulted in residue < 0.01 mg/kg, the Meeting estimated a maximum residue level of 0.01 mg/kg for *triflumezopyrim* in husked rice.

Dietary exposure

For estimating the dietary exposure, no residue data on husked rice according to the residue definition *Sum of triflumezopyrim and 3-(trifluoromethyl)benzoic acid (IN-Y2186), expressed as triflumezopyrim* are available. However, field trials from Thailand determining both, parent triflumezopyrim and IN-Y2186 in rice grain were provided, matching the cGAP. A molecular weight conversion factor of 2.095 ($M_{Triflumezopyrim}/M_{IN-Y2186}$ = 398.3 g/mol/190.1 g/mol) was applied to express IN-Y2186 as triflumezopyrim equivalents. The ranked order of total residue was (n=8): 0.007 (2), 0.010, 0.029, 0.076, 0.088, 0.090, 0.098 mg/kg.

The Meeting estimated a STMR of 0.053 mg/kg for triflumezopyrim and IN-Y2186 in rice grain. As no processing data from rice grain to husked rice and polished rice was available for the sum of triflumezopyrim and IN-Y2186, the Meeting decided to take a conservative approach by assuming that after the respective processing steps the entire residue found in rice grain was also present in husked and polished rice. Application of a weight adjustment factor of 0.8 for rice grain to husked rice resulted in a STMR of 0.066 mg/kg, while a weight adjustment factor of 0.775 for husked rice to polished rice resulted in a STMR of 0.086 mg/kg.

Animal feedstuffs

Rice hulls

Residues following GAP treatment (±25%) were (n=6): 0.049, 0.072, 0.15, 0.19, 0.30, 0.31 mg/kg.

The Meeting estimated a median residue of 0.17 mg/kg for *triflumezopyrim* in rice hulls.

Rice straw

Supervised field trials from China, India and Thailand according to the cGAP were submitted.

For MRL setting of rice straw, residues following GAP treatment (±25%) were (n=23): 0.007, 0.008 (2), 0.009, 0.01, < 0.02 (2), 0.022, 0.028, 0.057, 0.062, 0.063, 0.072, 0.077, 0.099, 0.10 , 0.12, 0.14, 0.15 (2), 0.16, 0.20, 0.21 mg/kg.

The Meeting estimated a maximum residue level of 0.4 mg/kg (DM, based on 90% DM content) for triflumezopyrim in rice straw and a median and highest residue of 0.063 and 0.21 mg/kg (as received), respectively, for animal dietary burden calculation.

Fate of residues during processing

The Meeting received information on the hydrolysis of [pyridine-^{14}C]-, [methylene-^{14}C]- and [pyrimidine-^{14}C]-radiolabelled triflumezopyrim as well as one processing study using unlabelled triflumezopyrim on rice.

In a hydrolysis study using radiolabelled triflumezopyrim typical processing conditions were simulated (pH 4, 5 and 6 with 90 °C, 100 °C and 120 °C for 20, 60 and 20 minutes). No degradation of the parent was observed.

The fate of triflumezopyrim during processing of raw agricultural commodity (RAC) was investigated in rice. However, no processing data was provided for the sum of triflumezopyrim and IN-Y2186. Therefore, only processing factors according to the residue definition for MRL setting (parent triflumezopyrim) could be derived.

The Meeting concluded that no residues are expected in husked and polished rice since residues were < 0.01 mg/kg during processing. In conclusion the Meeting decided to set a maximum residue level of 0.01 mg/kg for polished rice.

Residues in animal commodities

Farm animal feeding studies

The Meeting received one feeding study involving triflumezopyrim on lactating cows. No poultry feeding study was submitted.

Residues were < 0.01 mg/kg in all samples of the 1.3 and 4 ppm treatment rates. In milk, residues of triflumezopyrim in the 13 ppm group were up to 0.025 mg/kg (mean: 0.022 mg/kg). Skim milk and cream were analysed individually in the 13 ppm dosing group only, showing residues of up to 0.021 mg/kg (mean: 0.019 mg/kg) for skim milk and up to 0.029 mg/kg (mean: 0.026 mg/kg) for cream. In tissues, muscle and fat did not contain residues of triflumezopyrim at or above 0.01 mg/kg. Only liver and kidney samples from the 13 ppm dosing group contained residues with maximum at 0.036 mg/kg (mean: 0.034 mg/kg) and 0.024 mg/kg (mean: 0.023 mg/kg), respectively.

Estimated maximum and mean dietary burdens of livestock and animal commodities maximum residue levels

Dietary burden calculations for beef cattle, dairy cattle, broilers and laying poultry are presented in Annex 6. The calculations were made according to the livestock diets from US-Canada, EU, Australia and Japan in the OECD Table (Annex 6 of the 2006 JMPR Report).

	Livestock dietary burden, Triflumezopyrim, ppm of dry matter diet							
	US-Canada		EU		Australia		Japan	
	max.	Mean	max.	mean	max.	Mean	max.	Mean
Beef cattle	0.008	0.008	0.023	0.007	0.16[a]	0.061[b]	0.13	0.041
Dairy cattle	0.008	0.008	0.014	0.006	0.075	0.043	0.06	0.019
Poultry – broiler	0.007	0.01	0.001	0.001	0.017[c]	0.017[d]	0.0007	0.0007
Poultry – layer	0.001	0.012	0.0007	0.001	0.017[c]	0.017[d]	0.003	0.003

[a] Highest maximum beef or dairy cattle burden suitable for MRL estimates for mammalian meat and milk

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

[c] Highest maximum broiler or laying hen burden suitable for MRL estimates for poultry products and eggs

[d] Highest mean broiler or laying hen burden suitable for STMR estimates for poultry products and eggs

none no relevant feed items

Animal commodities maximum residue levels

For beef and dairy cattle a maximum and mean dietary burden of 0.16 ppm and 0.061 ppm were estimated, respectively. The estimated dietary burdens are evaluated against a lactating cow feeding study involving administration of triflumezopyrim at 1.34, 4.03 and 13.48 ppm. At the lowest level of 1.34 ppm no parent residues > 0.01 mg/kg were found in whole milk, skim milk, cream, muscle, liver, kidney or fat.

The Meeting concluded that the dietary burden is 8–22 times lower than the lowest dose administered in the cow feeding study (1.34 ppm). Therefore, no residues > 0.01 mg/kg are expected in milk, cream and cattle tissues.

For poultry no farm animal feeding studies were provided. Laying hen metabolism studies involved administration of up to 14–15 ppm triflumezopyrim in the diet. Residues of triflumezopyrim were up to 0.25 mg/kg in liver. The maximum dietary burden for broiler and layer poultry of 0.017 ppm is at least 824 times lower than the dose administered in the hen metabolism study. Therefore, no residues > 0.01 mg/kg are expected in eggs, egg yolks and hen tissues.

In conclusion, the Meeting decided to set a maximum residue level of 0.01* mg/kg for matrices of animal origin, as well as a STMR and HR of 0 mg/kg.

RECOMMENDATIONS

On the basis of the data from supervised trials the Meeting concluded that the residue levels listed in below are suitable for establishing maximum residue limits and for IEDI/IESTI assessmentThe

Definition of the residue for compliance with MRL for plant and animal commodities: *Triflumezopyrim*

Definition of the residue for the dietary intake for plant commodities: *Sum of triflumezopyrim and 3-(trifluoromethyl)benzoic acid (IN-Y2186), expressed as triflumezopyrim*

Definition of the residue for the dietary intake for animal commodities: *Triflumezopyrim*

The residue is not fat-soluble.

Maximum residue levels and dietary exposure

Commodity		MRL, mg/kg		STMR or STMR-P, mg/kg	HR or highest residue, mg/kg
CCN	Name	New	Previous		
MO 0105	Edible offal (Mammalian)	0.01*	-	0	0
PE 0112	Eggs	0.01*	-	0	0
MF 0100	Mammalian fats (except milk fats)	0.01*	-	0	0
MM 0095	Meat (from mammals other than marine mammals)	0.01*	-	0	0
ML 0106	Milks	0.01*	-	0	0
FM 0183	Milk fats	0.01*	-	0	0
PM 0110	Poultry meat	0.01*	-	0	0
PF 0111	Poultry fats	0.01*	-	0	0
PO 0111	Poultry, Edible offal of	0.01*	-	0	0
GC 0649	Rice	0.2	-	0.053	-
CM 1207	Rice, husked	0.01	-	0.066	-
CM 1205	Rice, polished	0.01	-	0.086	-

Dietary exposure and feed burden

Commodity		MRL, mg/kg		Median, STMR or STMR-P, mg/kg	HR or highest residue, mg/kg
CCN	Name	New	Previous		
CM 1207	Rice hulls	-	-	0.17	
AS 0649	Rice straw and fodder, dry	0.4 dw	-	0.063 (as received)	0.21 (as received)
CM 1206	Rice bran			0.0125	

DIETARY RISK ASSESSMENT

Long-term dietary exposure

The evaluation of triflumezopyrim has resulted in recommendations for MRLs and STMRs for raw and processed commodities. The International Estimated Daily Intakes for the 17 GEMS/Food cluster diets, based on this years estimated STMRs, were in the range 0–0.2% of the maximum ADI of 0.2 mg/kg bw. The results are shown in Annex 3 to the 2017 Report.

The Meeting concluded that the long-term dietary exposure to residues of triflumezopyrim from uses that have been considered by the Meeting is unlikely to present a public health concern.

Short-term dietary exposure

The International Estimated Short Term Intake (IESTI) for triflumezopyrim was calculated from recommendations for STMRs for raw and processed commodities in combination with consumption data for corresponding food commodities. The results are shown in Annex 4.

The IESTI for the diets submitted to the JMPR represented 0% of the ARfD (1 mg/kg bw). The Meeting concluded that the short-term dietary exposure to residues of triflumezopyrim from uses considered by the Meeting is unlikely to present a public health concern.

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