BICYCLOPYRONE (295)

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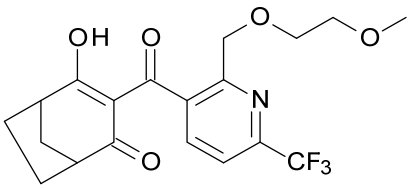
EXPLANATION

Bicyclopyrone is a selective herbicide for the control of broadleaf weeds and perennial grasses in corn, wheat, barley and sugar cane. It is a member of the HPPD-inhibitor class of herbicides and belongs to the subclass of the triketone compounds.

Bicyclopyrone was scheduled by the 48th Session of the CCPR as a new compound for consideration by the 2017 JMPR. Residue and analytical aspects were considered for the first time by the present meeting. The Meeting received information on physical and chemical properties, animal and plant metabolism, environmental fate, analytical methods, storage stability, use patterns, supervised trials, processing and farm animal feeding.

IDENTITY

ISO Common Name	Bicyclopyrone	
Chemical name	IUPAC	4-hydroxy-3-[2-(2-methoxy-ethoxymethyl)-6-trifluoromethyl-pyridine-3-carbonyl]-bicyclo[3.2.1]oct-3-en-2-one
	CAS	4-hydroxy-3-[[2-[(2-methoxyethoxy)methyl]-6-(trifluoromethyl)-3-pyridinyl]carbonyl]bicyclo[3.2.1]oct-3-en-2-one-
CIPAC No.	None	
CAS No	352010-68-5	
EEC No.	None	
Structural formula		
Molecular formula	$C_{19}H_{20}F_3NO_5$	
Molecular mass	399.36	

PHYSICAL AND CHEMICAL PROPERTIES

Pure active ingredient

Property	Results	Reference
Appearance	Pure active-White crystalline powder (99.9%) Technical grade-Yellow-beige powder with agglomerates (96.7%) Technical grade (wet paste)-Brown-beige powder with agglomerates (88.4%)	Das R., 2007 (NOA449280/0050) Das R., 2009a (NOA449280_11062) Das R., 2009b (NOA449280_11071)
Vapour pressure	Pure active: At 20 °C: $< 5 \times 10^{-6}$ Pa At 25 °C: $< 5 \times 10^{-6}$ Pa	Geoffroy, A., 2007a (NOA449280/0066)

Property	Results		Reference
	At 40 °C: < 1×10^{-5} Pa		
Boling point & melting point	Boiling point at 101.3kPa >296 °C Melting point 65.3°C		Geoffroy, A., 2007b (NOA449280/0068)
Octanol/Water Partition Coefficient at 25 °C (Log P_{ow})	At pH 5 log P_{ow} = 0.25 At pH 7 log P_{ow} = -1.2 At pH 9 log P_{ow} = -1.9		Weissenfeld, M., 2008 (NOA449280_11000)
Solubility in water at 25 ºC	Pure water: 1.2 g/L (a pH of about 3 was recorded) Aqueous sol.: 38 g/L at pH 4.9 Aqueous sol.: 119 g/L at pH 7.2 Aqueous sol.: 119 g/L at pH 9.2		Weissenfeld, M., 2009 (NOA449280_11013)
Solubility in organic solvents at 25 ºC	Acetone: > 500 g/L Dichloromethane: > 500 g/L Ethyl acetate: > 500 g/L Hexane: 8.9 g/L Methanol: > 500 g/L Octanol: 91 g/L Toluene: > 500 g/L		Vijayakumar, C., 2010 (NOA449280_11083)
Specific gravity/density	Pure substance: 1.503 g/cm3 at 20.5 °C		Weissenfeld M., 2007 (NOA449280/0069)
	Technical grade: 1.41 g/cm3 at 22.0 ± 0.5 ºC		O'Connor, B.J. White, D.F., 2012a (NOA449280_11179)
	Technical wet paste 88.4%: 1.35 g/cm3 at 21.0 ± 0.5 ºC		O'Connor, B.J. White, D.F., 2012b (NOA449280_11168)
Hydrolysis	Bicyclopyrone was shown to be stable to hydrolysis under acidic, neutral and alkaline conditions. After 5 days at 50 °C, the amount of test substance represented 97.7%, 96.0%, 98.0% and 96.4% of the applied radioactivity for pH 4, 5, 7 and 9, respectively. After 31 days at 25 °C, the amount of test item represented 99.0%, 97.6% and 97.6% of the applied radioactivity for pH 5, 7 and 9, respectively. Based on these results, the DT_{50} was extrapolated to be > 1 year at 25 °C.		Adam D., 2008 (NOA449280_10121)
Photolysis	The aqueous photo transformation of bicyclopyrone was studied at 25 ± 1ºC in sterile aqueous citrate (pH 5), phosphate (pH 7) and borate (pH 9) buffers and in natural water at pH 7.33. Bicyclopyrone was extensively degraded under simulated sunlight. Degradation was pH-dependent in the order pH 5 > pH 7/natural water > pH 9. However the definitive tests were not carried out at pH 9 as the preliminary tests indicated that < 20% degradation would occur at this pH. DegT50 values applicable to Europe and North America (latitudes 30°, 40° and 50°) were approximately 10 days at pH 5 and 50 days at pH 7 and in natural water. $DegT_{50}$ values applicable to Japan in Spring (April to June in Tokyo) were approximately 34 and 167 days respectively.		Lewis C.J., Gilbert J., 2009a (NOA449280_11044)
Dissociation constant (pKa)	3.06 at 20 °C		Martin, N., 2007 (NOA449280/0057)
Thermal stability (Conducted on technical substance)	Technical substance 96.7% (OECD 113)	DSC and TGA scans carried out on the test substance in nitrogen and air show that the test substance is stable in nitrogen or air.	Williams C., 2010a (NOA449280_11096)
	Technical wet paste 88.4% (OECD 113)	DSC and TGA scans carried out on the test substance in nitrogen and air show that the test substance is stable in nitrogen or air.	Williams C., 2010b (NOA449280_11095)

Technical material

Property	Results	Reference
Minimum purity	Minimum 95% w/w (for theoretical dry weight material) Minimum 80% w/w (for technical wet paste, which contains up to 20% w/w water)	Mordente A, 2012 (NOA449280_11472)
Melting range	See above for pure substance	
Stability	Technical substance 96.7%: 12 months at 20 °C	De Benedictis S., 2012a (NOA449280_11170)
	Technical wet paste 88.4%: 12 months at 20 °C	De Benedictis S., 2012b (NOA449280_11172)
Property	Results	Reference
Minimum purity	Minimum 95% w/w (for theoretical dry weight material) Minimum 80% w/w (for technical wet paste, which contains up to 20% w/w water)	Mordente A, 2012 (NOA449280_11472)
Melting range	See above for pure substance	
Stability	Technical substance 96.7%: 12 months at 20 °C	De Benedictis S., 2012a (NOA449280_11170)
	Technical wet paste 88.4%: 12 months at 20 °C	De Benedictis S., 2012b (NOA449280_11172)

Formulation

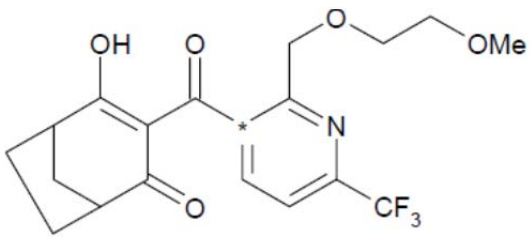
Bicyclopyrone is primarily available in the following formulations:

- Soluble concentrate (SL) formulations containing 200 g/L bicyclopyrone
- Mixed formulation of capsule suspension (CS) and suspension concentrate (SC) containing 7.13g/L bicyclopyrone, 28.5 g/L mesotrione, 119.7 atrazine and 256 g/L S-metolachlor.
- Emulsion concentrate (EC) formulation containing 37.5 g/L bicyclopyrone and 175 g/L Bromoxynil (as Bromoxynil octanoate 255 g/L).

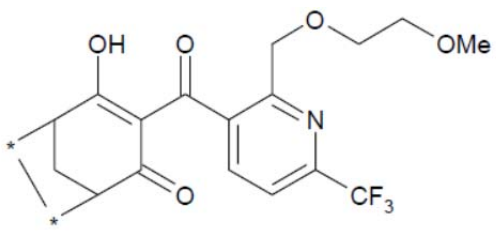
METABOLISM AND ENVIRONMENTAL FATE

The Meeting received bicyclopyrone metabolism studies on plants (corn, soya bean and sugarcane), animals (lactating goats, laying hens), soil and rotational crops (Radish, spinach and wheat).

The metabolism and distribution of bicyclopyrone in animals and plants and the fate of bicyclopyrone in the environment were investigated using bicyclopyrone radiolabelled in either the 3-position of the pyridinyl ring or the 6,7-positions of the bicyclooctenone moiety. The label positions (*) are shown below:



[Pyridine-3-^{14}C] label

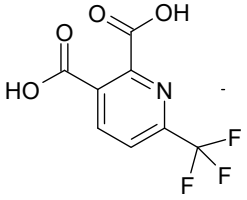
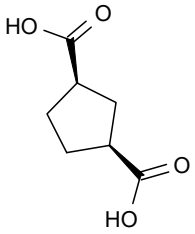
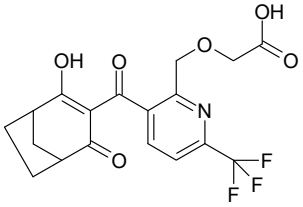
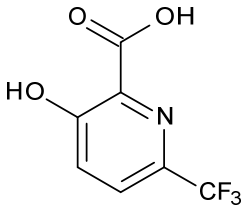
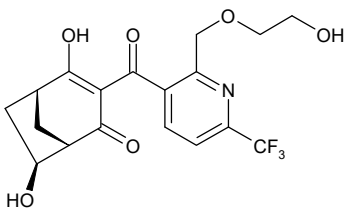
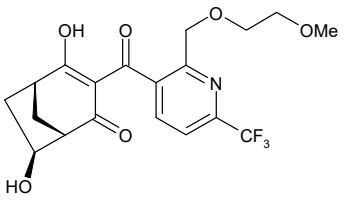


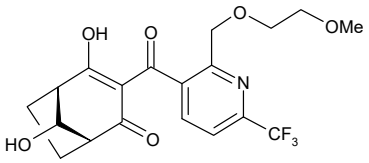
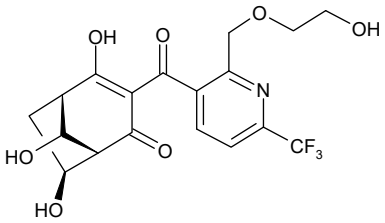
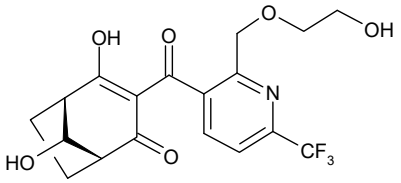
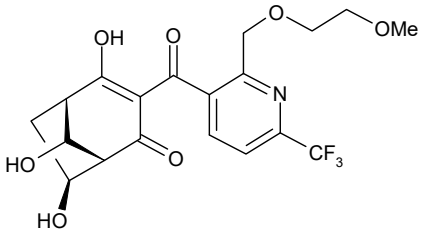
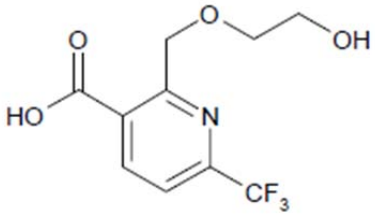
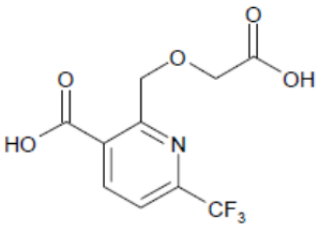
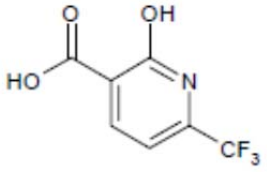
[Bicyclooctenone-6,7-^{14}C2 label

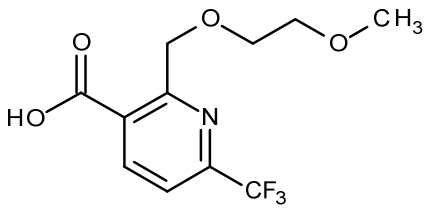
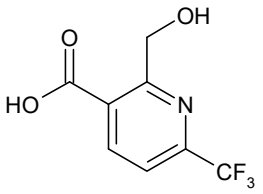
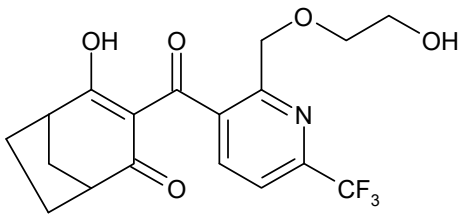
Figure 1 [^{14}C]-Labelled test materials used in animal metabolism, plant metabolism, and environmental fate studies.

The chemical structures of the major degradation compounds from the metabolism of bicyclopyrone are provided below in Table 1.

Table 1 Structure of compounds appearing in metabolism and environmental fate studies

Compound Name/Code	Chemical name (IUPAC)	Structure	Occurrence in metabolism studies
CSCC163768 SYN504810	6-(trifluoromethyl)pyridine-2,3-dicarboxylic acid		Plants Soil Aqueous photolysis
CSAA589691 (NOA412101)	(1S,3R)-cyclopentane-1,3-dicarboxylic acid		Plants Soil Aqueous photolysis Rat cage wash
CSCD642512 (SYN545859)	2-[[3-(2-hydroxy-4-oxo-bicyclo[3.2.1]oct-2-ene-3-carbonyl)-6-(trifluoromethyl)-2-pyridyl]methoxy]acetic acid		Plants Soil
CSCD656832 (SYN545680)	3-hydroxy-6-(trifluoromethyl)pyridine-2-carboxylic acid		Plants Soil
CSCD675162	*rac*-(1R,5S,6S)-2,6-dihydroxy-3-[2-(2-hydroxyethoxymethyl)-6-(trifluoromethyl)pyridine-3-carbonyl]bicyclo[3.2.1]oct-2-en4-one		Plants Rat Goat Hen
CSCD675164	*rac*-(1R,5S,6S)-2,6-dihydroxy-3-[2-(2-methoxyethoxymethyl)-6-(trifluoromethyl)pyridine-3-carbonyl]bicyclo[3.2.1]oct-2-en-4-one		Plants Rat Goat Hen

Compound Name/Code	Chemical name (IUPAC)	Structure	Occurrence in metabolism studies
CSCD677306	*rac*-(1S,5R)-2,8-dihydroxy-3-[2-(2-methoxyethoxymethyl)-6-(trifluoromethyl)pyridine-3-carbonyl]bicyclo[3.2.1]oct-2-en-4-one		Plants Rat Goat Hen
CSCD677692	*rac*-(1S,5R,6S)-2,6,8-trihydroxy-3-[2-(2-hydroxyethoxymethyl)-6-(trifluoromethyl)pyridine-3-carbonyl]bicyclo[3.2.1]oct-2-en-4-one		Plants Rat
CSCD677693	*rac*-(1S,5R)-2,8-dihydroxy-3-[2-(2-hydroxyethoxymethyl)-6-(trifluoromethyl)pyridine-3-carbonyl]bicyclo[3.2.1]oct-2-en-4-one		Plants Rats Goat Hen
CSCD677694	*rac*-(1S,5R,6S)-2,6,8-trihydroxy-3-[2-(2-methoxyethoxymethyl)-6-(trifluoromethyl)pyridine-3-carbonyl]bicyclo[3.2.1]oct-2-en-4-one		Plants
CSCD686480 (SYN545910)	2-(2-hydroxyethoxymethyl)-6-(trifluoromethyl)pyridine-3-carboxylic acid		Plants Goat
CSCD686481 (SYN545911)	2-(carboxymethyloxymethyl)-6-(trifluoromethyl)pyridine-3-carboxylic acid		Plants
CSAA757083 (SYN510579)	2-hydroxy-6-(trifluoromethyl)pyridine-3-carboxylic acid		Plants Soil

Compound Name/Code	Chemical name (IUPAC)	Structure	Occurrence in metabolism studies
CSAA794148 (SYN503780)	2-(2-methoxyethoxymethyl)-6-(trifluoromethyl)pyridine-3-carboxylic acid		Rat Soil Aqueous photolysis
CSAA806573 (NOA451778)	2-(hydroxymethyl)-6-(trifluoromethyl)pyridine-3-carboxylic acid		Plants Rat Soil Aqueous photolysis
CSAA915194 NOA454598	2-hydroxy-3-[2-(2-hydroxyethoxymethyl)-6-(trifluoromethyl)pyridine-3-carbonyl]bicyclo[3.2.1]oct-2-en-4-one		Plants Rat Goat Hen

Plant metabolism

The Meeting received plant metabolism studies on maize, sugar cane and soya bean following applications of [^{14}C]- bicyclopyrone.

Maize

The metabolic fate and distribution of bicyclopyrone was studied outdoors in maize after either a pre-emergence application (at 200 g ai/ha) or pre-emergence application (at 200 g ai/ha) followed by a post-emergence treatment (at 200 g ai/ha) at the 8 to 9 leaf stage for a second treatment group [Chapleo, 2010a, NOA449290_11081]. The test item used was [bicyclooctenone-6,7-^{14}C2]- and [pyridine-3-^{14}C]-bicyclopyrone. Plants were harvested at three stages: early foliage (28 days after the post-emergence application; foliage only), forage (BBCH 75–79; foliage immature cobs and immature grain) and maturity (BBCH 89; stover, cobs and grain). All samples were homogenised in the presence of dry ice and stored frozen (at -20 °C) until required for analysis.

Homogenised samples were analysed by combustion/LSC. The TRRs for each commodity in which the TRR by combustion was > 0.01 mg/kg were determined by summation of activity in the extracts by LSC and in the non-extractable debris as determined by combustion/LSC.

The nature of the residue in early foliage, forage, stover and grain was investigated by extraction using acetonitrile/water (4:1 v/v and 3:7 v/v), followed by acetonitrile. Where necessary (debris samples after extraction of forage and stover from plants receiving both applications), additional, more exhaustive extraction techniques were employed (acid hydrolysis in 1M HCl at approximately 60 °C or 90 °C (each approximately 2h). The extracts were combined and analysed by HPLC and LC-MS. Identification of metabolites was achieved by co-chromatographing metabolite fractions against reference standards by TLC, HPLC or LC-MS. Samples were analysed within approximately 5 to 6 months of sampling.

Total radioactive residues in early foliage, forage and stover receiving only the pre-emergence application were 0.033, 0.023 and 0.032 mg eq/kg, respectively, for the [bicyclooctenone-6,7-^{14}C2]-labelled experiment and 0.042, 0.083 and 0.077 mg eq/kg, respectively, for the [pyridine-3-^{14}C]-labelled experiment. Values in immature cobs, immature grain, mature cobs and mature grain were ≤ 0.003 mg eq/kg for the [bicyclooctenone-6,7-^{14}C2]-labelled experiment and ≤ 0.005 mg eq/kg for the [pyridine-3-^{14}C]-labelled experiment.

Total radioactive residues in early foliage, forage and stover from the combined pre- and post-emergence application regime were 0.354, 0.459 and 0.455 mg eq/kg, respectively, for the [bicyclooctenone-6,7-^{14}C2]-labelled experiment and 0.440, 0.925 and 0.762 mg eq/kg, respectively, for the [pyridine-3-^{14}C]-labelled experiment. Values in immature cobs, immature grain, mature cobs and mature grain were 0.029, 0.037, 0.036 and 0.058 mg eq/kg, respectively, for the [bicyclooctenone-6,7-^{14}C2]-labelled experiment and 0.033, 0.020, 0.018 and 0.025 mg eq/kg, respectively, for the [pyridine-3-^{14}C]-labelled experiment.

Table 2 Extractability of residues from maize matrices and Total Radioactive Residues

Radiolabel	Relative maturity	Sample/ Commodity	Pre-emergence application			Pre- and post- emergence application		
			TRR (mg eq/kg)	% TRR extracted	% TRR unextracted	TRR (mg eq/kg)	% TRR extracted	% TRR unextracted
Bicyclooctenone	Early foliage	Foliage	0.033	77.7	21.8	0.354	83.2	16.8
	Forage	Forage	0.023	78.3	21.7	0.459	84	16
		Immature Cobs	< 0.003[(a)]	NE	NE	0.029	89.1	11
		Immature Grain	< 0.003[(a)]	NE	NE	0.037	91.9	8.2
	Maturity	Stover	0.032	79.1	20.9	0.455	80.8	19.2
		Cobs	< 0.003[(a)]	NE	NE	0.036	73.2	26.9
		Grain	< 0.003[(a)]	NE	NE	0.058	76.6	23.4
Pyridine	Early foliage	Foliage	0.042	83.5	16.5	0.44	93.1	6.9
	Forage	Forage	0.083	88.1	11.9	0.925	90.6	9.3
		Immature Cobs	< 0.003[(a)]	NE	NE	0.033	69.7	30.4
		Immature Grain	< 0.003[(a)]	NE	NE	0.02	88.8	11.2
	Maturity	Stover	0.077	80.7	19.3	0.762	83.9	16.1
		Cobs	< 0.003[(a)]	NE	NE	0.018	77.4	22.6
		Grain	< 0.003[(a)]	NE	NE	0.025	78.8	21.2

(a) Determined by direct combustion

NE – Not extracted

Analysis of forage, stover and grain samples showed that bicyclopyrone is extensively metabolised and that no or only very minor residues of bicyclopyrone, were present (≤4.3% TRR; ≤ 0.009 mg/kg). At least four desmethyl dihydroxylated bicyclopyrone isomers were shown to be present which collectively accounted for up to 35.7% TRR (0.331 mg eq/kg; all in the free metabolite form) and individually up to 20.6% TRR (CSCD677692: 0.191 mg eq/kg). Two desmethyl monohydroxy isomers of bicyclopyrone were shown to be present which collectively accounted for up to 21.7% TRR (0.200 mg eq/kg) and individually up to 7.6% TRR (CSCD677693: 0.070 mg eq/kg; as the free metabolite) or up to 14.1% TRR (CSCD675162: 0.130 mg eq/kg; total for the free and glycoside conjugated forms). A cyclopentane dicarboxylic acid metabolite, CSAA589691, was shown to be present in immature and mature grain at levels up to 49.4% TRR (0.024 mg eq/kg). Comparison of the qualitative profile of metabolites present in samples from the pre-emergence only application with those from the combined pre- and post-emergence applications demonstrated a high degree of similarity.

Table 3 Distribution of extracted ^{14}C residue in the maize matrices following application of [^{14}C] bicyclopyrone Pre- and Post-emergence Applications (each 200 g ai ha [a])

Maize Sample/Commodity	Component	Bicyclooctenone-^{14}C		Pyridine -^{14}C	
		% of TRR	Residue (mg eq/kg)	% of TRR	Residue (mg eq/kg)
Forage	Bicyclopyrone	1.6	0.007	ND	ND
	CSAA806573 glycoside	NA	NA	4.6	0.042
	CSCD686480 glycoside	NA	NA	1.8	0.017
	CSCD686481	NA	NA	3.0	0.027
	CSAA589691	4.3	0.020	NA	NA
	CSCD677692 Desmethyl dihydroxy bicyclopyrone isomer A (undefined stereochemistry) Desmethyl dihydroxy bicyclopyrone isomer B (undefined stereochemistry) Total desmethyl dihydroxy bicyclopyrone isomers [a]	8.3 3.1 4.0 15.4	0.0.38 0.014 0.018 0.070	20.6 7.9 7.2 35.7	0.191 0.073 0.067 0.331
	CSCD675162 CSCD675162 glycoside CSCD677693 Total desmethyl monohydroxy bicyclopyrone isomers[1]	3.8 6.5 5.0 15.3	0.018 0.030 0.023 0.071	5.6 8.5 7.6 21.7	0.052 0.078 0.070 0.200
	Total monohydroxy NO449280 isomers[a]	4.1	0.019	2.4	0.022
	CSCD677694	ND	ND	1.8	0.017
	CSCD642512	2.0	0.009	ND	ND
	TRR by summation mg /kg	0.459		0.925	
	TRR by quantification mg /kg	0.444		0.877	
	Percentage of TRR analysed by chromatography, %	77.9		90.1	
	Organosoulble extracted	0.2	0.001	0.3	0.003
	Acid extracted	4.8	0.022	3.9	0.036
	unextracted	5.8	0.027	4.0	0.049
	Losses/gains on fractionation	11.7 (loss)	0.052 (loss)	7.4 (gain)	0.077 (gain)
Stover	Total CSAA806573 (includes conjugates)	NA	NA	6.1	0.046
	CSCD686480 glycoside	NA	NA	3.1	0.024
	CSCD686481	NA	NA	0.8	0.006
	CSAA589691	3.8	0.017	NA	NA
	CSCD677692 Desmethyl dihydroxy bicyclopyrone isomer A (undefined stereochemistry) Desmethyl dihydroxy bicyclopyrone isomer B (undefined stereochemistry) Total desmethyl dihydroxy bicyclopyrone isomers[a]	6.0 4.2 1.1 11.3	0.027 0.019 0.005 0.051	12.0 5.2 4.2 21.4	0.091 0.040 0.032 0.163
	CSCD675162 CSCD675162 glycoside CSCD677693 Total desmethyl monohydroxy bicyclopyrone isomers[1]	2.4 5.1 3.5 11.0	0.011 0.023 0.016 0.050	2.4 6.4 2.9 11.7	0.018 0.049 0.022 0.089
	Total monohydroxy NO449280 isomers[a]	2.1	0.010	4.5	0.034
	CSCD677694	1.6	0.007	ND	ND
	CSCD642512	2.2	0.010	2.6	0.020
	Unassigned	27.8	0.127	23.1	0.174
	Solvent front	11.7	0.053	4.2	0.032

Maize Sample/Commodity	Component	Bicyclooctenone-^{14}C		Pyridine -^{14}C	
		% of TRR	Residue (mg eq/kg)	% of TRR	Residue (mg eq/kg)
	TRR by summation mg /kg	0.455		0.762	
	TRR by quantification mg /kg	0.465		0.845	
	Percentage of TRR analysed by chromatography, %	71.3		77.1	
	Organosoluble extract	0.1	< 0.001	0.1	0.001
	Acid extracted	7.1	0.033	5.9	0.042
	Unextracted	11.2	0.051	8.6	0.066
	Losses/gains on fractionation	10.1	0.046	8.2	0.065
Mature Grain	CSAA589691	41.7	0.024	NA	NA
	CSCD675162 CSCD677693 Total desmethyl monohydroxy bicyclopyrone isomers	ND ND ND	ND ND ND	22.7 5.2 27.9	0.006 0.001 0.007
	CSCD677306 Monohydroxy bicyclopyrone isomers (glycosides; undefined stereochemistries) Total monohydroxy NO449280	ND ND ND	ND ND ND	1.7 17.6 19.3	< 0.001 0.004 0.004
	CSCD642512	ND	ND	5.9	0.001
	Organosoluble extract	0.3	< 0.001	0.9	< 0.001
	Unextracted	23.4	0.014	21.2	0.005
	Losses/gains on fractionation	2.4 (loss)	0.001(Loss)	5.2(Loss)	0.004 (Loss)

ND = not detected

NA = not applicable

[a] Total of all isomers with these structural characteristics including specific metabolites, metabolites of undefined substitution specificity, and conjugates

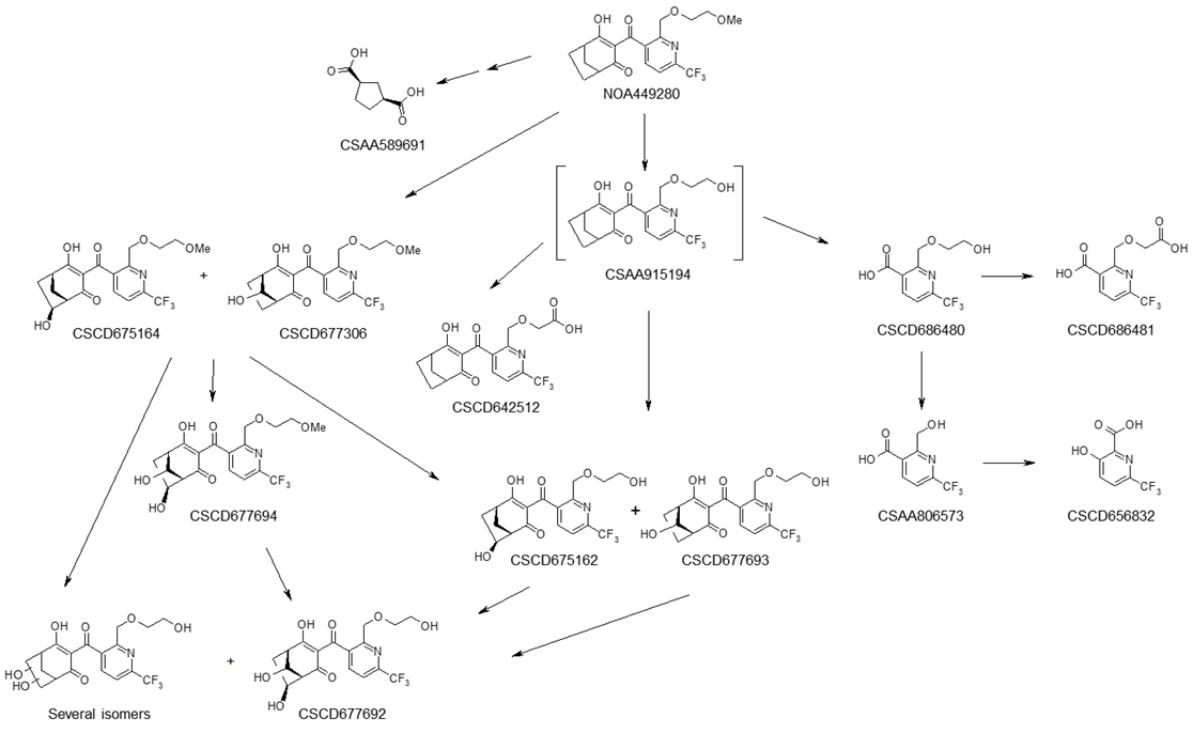


Figure 1 Proposed metabolic pathways of bicyclopyrone in maize

Sugarcane

In a study reported by Chapleo, 2009 [Ref: NOA449280 11056], a single application of either [bicyclooctenone-6,7-^{14}C2]-bicyclopyrone and [pyridine-3-^{14}C]-bicyclopyrone was applied to cane plants at the 7–8 leaf stage (BBCH 17–18) at a nominal rate of 300 g ai/ha post emergence.

Immature foliage was collected at 42 days after treatment (BBCH 23–24). Foliage (all leaves) and cane were collected at maturity 301 days after treatment (BBCH 39) when the maximum stem length had been achieved and estimates of stem sugar content in upper and lower stem internodes were similar. Samples were extracted at ambient temperature by homogenisation with solvents (acetonitrile/water (80:20, v/v), acetonitrile/water (30:70, v/v) and acetonitrile). The solid and liquid phases were separated by centrifugation and aspiration allowing radio-assay of the solid and liquid phases by combustion analysis and LSC respectively. Immature foliage debris, remaining after solvent extraction were further characterised after hydration (overnight soaking in water) by acid hydrolysis (0.1M HCl at approximately 40 °C and 90 °C, each for approximately 4h). The solid and liquid phases were separated by centrifugation and aspiration allowing radio-assay of the solid and liquid phases by combustion analysis and LSC respectively.

The TRR in sugar cane foliage sampled 42 days after treatment were 0.779 mg eq/kg (85.4% TRR) and 0.888 mg eq/kg (88.5% TRR) for the [bicyclooctenone-6,7-^{14}C2] and [pyridine-3-^{14}C]-bicyclopyrone labelled experiments respectively. Residues in foliage at maturity were 0.004 mg eq/kg and 0.003 mg eq/kg respectively. The TRRs in the cane harvested at maturity were 0.002 mg eq/kg and 0.004 mg eq/kg for the [bicyclooctenone-6,7-^{14}C2] and [pyridine-3-^{14}C]-bicyclopyrone labelled experiments respectively. The mature cane and foliage were not extracted since residues were below 0.01 mg/kg.

Table 4 Extractability of residues from sugar cane matrices and total radioactive residues

Radiolabelled experiment	Relative maturity	Sample/ Commodity	TRR mg eq/kg	% TRR Extracted [a]	% TRR Unextracted
Bicyclooctenone	42 DAT	Foliage	0.778	85.4	14.6
	Maturity (301 DAT)	Foliage	0.004	Not extracted [b]	
		Sugarcane	0.002	Not extracted[b]	
Pyridine	42 DAT	Foliage	0.888	88.5	11.5
	Maturity (301 DAT)	Foliage	0.003	Not extracted[b]	
		Sugarcane	0.004	Not extracted[b]	

[a] Extractable radioactivity prior to aqueous extraction and hydrolysis

[b] The maturity samples were not extracted or analysed since the TRR was < 0.01 mg/kg

Fractions containing the majority of the extracted radioactivity were analysed by HPLC, TLC and by LC-MS. Bicyclopyrone was not detected in immature foliage. The most significant metabolite detected was the desmethyl monohydroxy metabolite CSCD677693 which was present as both the free form (17.4 to 18.4% TRR, 0.136 to 0.163 mg eq/kg) and as a glycoside conjugate (5.6 to 7.1% TRR, 0.050–0.055 mg eq/kg). Two other demethylated metabolites of bicyclopyrone were present, the desmethyl monohydroxy metabolite CSCD675162 (9.9 to 12.6% TRR, 0.088 to 0.098 mg eq/kg) and the desmethyl dihydroxy metabolite CSCD677692 (5.5 to 6.5% TRR, 0.043 to 0.058 mg eq/kg). CSCD677306, the monohydroxy metabolite of bicyclopyrone, was present in both the free form and conjugated as the glycoside (4.6 to 5.7% TRR, 0.036 to 0.051 mg eq/kg and 10.7 to 13.5% TRR, 0.095 to 0.105 mg eq/kg respectively). Two other glycosides of monohydroxylated bicyclopyrone; including the glycoside of CSCD675164, were detected (2.0 to 4.2% TRR, 0.018 to 0.033 mg eq/kg and 2.3 to 3.5% TRR, 0.020 to 0.027 mg eq/kg). The dihydroxy metabolite CSCD677694 (8.1 to 9.3% TRR, 0.072 mg eq/kg) was also observed. Detected metabolites that contained only the pyridine ring of bicyclopyrone were identified as CSCD686480, which was present in both the free form (2.7% TRR, 0.024 mg eq/kg) and as a glycoside (17.0% TRR, 0.151 mg eq/kg) and CSCD686481 (6.4% TRR, 0.057 mg eq/kg). The unextracted residues remaining after the initial solvent extraction were

further investigated by sequential extraction with 0.1 M and 1M HCl at 40 ºC and 90 ºC respectively after rehydration with water. The water released 0.5–0.7% TRR (0.004 to 0.0005 mg eq/kg), the mild acid 0.6% TRR (0.005 mg eq/kg) and the stronger acid conditions 2.6 to 4.3% TRR (0.023 to 0.03 mg eq/kg). A further 7.8 to 8.9%TRR, corresponding to 0.069 mg eq/kg in each debris fraction, remained unextracted.

Table 5 Distribution of extracted ^{14}C residue in the sugar cane matrices following foliar application of [^{14}C] bicyclopyrone

Sugarcane Sample	Component	Bicyclooctenone-^{14}C		Pyridine -^{14}C	
		% of TRR	Residue (mg eq/kg)	% of TRR	Residue (mg eq/kg)
42 DAT Foliage	CSCD686480	ND	ND	17.0	0.151
	CSCD686480 glycoside	ND	ND	2.7	0.024
	CSCD686481	ND	ND	6.4	0.057
	CSCD677692	5.5	0.043	6.5	0.058
	CSCD675162	12.6	0.098	9.9	0.088
	CSCD677693	17.4	0.136	18.4	0.163
	CSCD677693 glycoside	7.1	0.055	5.6	0.050
	CSCD677306	4.6	0.036	5.7	0.051
	CSCD677306 glycoside	13.5	0.105	10.7	0.095
	Monohydroxylated bicyclopyrone glycoside[a]	4.2	0.033	2.0	0.018
	Monohydroxylated bicyclopyrone glycoside[a]	3.5	0.027	2.3	0.020
	Water extract	0.7	0.005	0.5	0.004
	Debris extract-HCl	4.9	0.038	3.2	0.028
	Unextracted	8.9	0.069	7.8	0.069
	Losses/gains on fractionation	5.0 (Gain)	0.038 (Gain)	9.6 (Gain)	0.085 (Gain)

ND = not detected

[a] Two components were characterised as glycosides of monohydroxylated bicyclopyrone, one of these was the glycoside of CSCD675164

Bicyclopyrone metabolites represent a minor residue (≤ 0.004 mg eq/kg) in the mature sugar cane commodity and in mature foliage. The metabolic pathways of bicyclopyrone in sugar cane foliage were in general consistent with that of other plants and animals, primarily involves demethylation and hydroxylation with some glycoside conjugation. Cleavage between the rings was also observed.

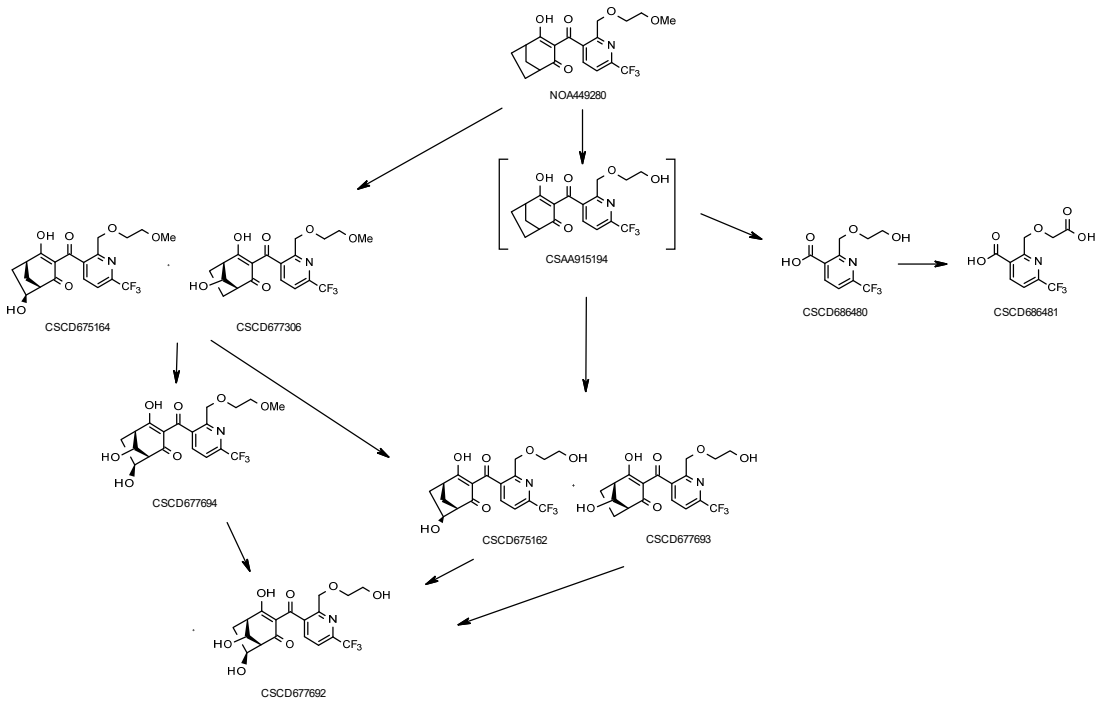


Figure 2 Proposed metabolic pathways for bicyclopyrone in sugar cane

Soya bean

A metabolism study was conducted with [bicyclooctenone-6,7-$^{14}C_2$]- or [pyridine-3-^{14}C]-bicyclopyrone in soya bean variety CLO81215 (Dobson, 2010, NOA449280_11111). Each radiochemical was formulated as an emulsifiable concentrate (EC) and applied once to the soil before emergence of the plants with a track sprayer. The nominal application rate was 200 g ai/ha. The soybean plants were maintained in containers under glasshouse conditions. Forage was harvested 35–36 days after application (DAT) at BBCH 16–21, hay 62–63 DAT at BBCH 65–74 and mature beans 113–114 DAT at BBCH 89. Each harvested commodity was homogenised in dry ice and a sub-sample analysed by oxidation followed by liquid scintillation counting (LSC) to determine the initial total radioactive residue (TRR) values. Commodities with a TRR exceeding 0.01 mg eq/kg were extracted with combinations of solvents and water and the appropriate extracts analysed by HPLC, TLC and HPLC-MS, as required, to determine the nature of the residue.

The total radioactive residues (TRRs) in the beans were 0.190 mg eq/kg and 0.206 mg eq/kg for the [bicyclooctenone-6,7-$^{14}C_2$] and [pyridine-3-^{14}C] labelled experiments, respectively, while the residue in the corresponding hay samples reached 0.149 mg eq/kg and 0.193 mg eq/kg. The TRR in the forage samples were significantly lower, reaching only 0.020 mg eq/kg and 0.031 mg eq/kg for the bicyclooctenone-6,7-$^{14}C_2$] and [pyridine-3-^{14}C] labelled experiments, respectively.

Table 6 Extractability of residues from soya bean matrices and Total Radioactive Residues

Radiolabelled experiment	Sample/ Commodity	Extractable radioactivity		%TRR Unextractable radioactivity	TRR
		Acetonitrile: water (80:20 v/v)	Acetonitrile: 0.2M HCl (50:50 v/v)		
		%TRR (mg eq/kg)	%TRR (mg eq/kg)	%TRR (mg eq/kg)	(mg eq/kg)
Bicyclooctenone	Forage[a, b]	70.1 (0.015)	NP	29.9 (0.006)	0.020
	Hay	74.5 (0.112)	NP	25.6 (0.038)	0.149
	Beans	76.6 (0.146)	4.4 (0.008)	19.0 (0.036)	0.190
Pyridine	Forage	84.1	NP	15.9	0.031

Radiolabelled experiment	Sample/ Commodity	Extractable radioactivity		%TRR Unextractable radioactivity	TRR
		Acetonitrile: water (80:20 v/v)	Acetonitrile: 0.2M HCl (50:50 v/v)		
		%TRR (mg eq/kg)	%TRR (mg eq/kg)	%TRR (mg eq/kg)	(mg eq/kg)
		(0.026)		(0.005)	
	Hay	89.2 (0.171)	NP	10.8 (0.021)	0.193
	Beans	79.3 (0.163)	9.0 (0.019)	11.6 (0.024)	0.206

NP – Not performed

[a] The value given for the extractability of the bicyclooctenone-label forage is based on the activity measured in the concentrated pooled extract after concentration to a volume of 18.7 mL as the low levels of activity in the unconcentrated extracts made measurements of the activity levels contained in them unreliable

[b] The forage samples were initially extracted with hexane, but no radioactivity was extracted

Further, more exhaustive extraction was performed in order to release residues that could not be extracted by the initial solvent extraction regime. This involved acid hydrolysis in 0.1M HCl at *approximately* 40 °C for 4 hours, followed by further hydrolysis with 1.0M HCl for 4 hours at 90 °C.

Table 7 Extractability of residues from soya bean matrices and Total Radioactive Residues following acid hydrolysis

Radiolabelled experiment	Sample/ Commodity	Unextractable radioactivity	Further extractions		Remaining Unextractable radioactivity
			0.1 M HCl 40 °C, 4h	1M HCl 90 °C, 4h	
		%TRR (mg eq/kg)	%TRR (mg eq/kg)	%TRR (mg eq/kg)	(mg eq/kg)
Bicyclooctenone	Forage	29.9 (0.006)	NP	NP	29.9 (0.006)
	Hay	25.6 (0.038)	4.6 (0.007)	0.3 (< 0.001)	20.7 (0.031)
	Beans	19.0 (0.036)	4.5 (0.009)	5.0 (0.009)	9.5 (0.018)
Pyridine	Forage	15.9 (0.005)	NP	NP	15.9 (0.005)
	Hay	10.8 (0.021)	2.3 (0.004)	0.6 (0.002)	7.9 (0.015)
	Beans	11.6 (0.024)	4.7 (0.010)	0.2 (< 0.001)	6.7 (0.014)

NP – Not Performed

Table 8 Total radioactive residues in soya bean forage sampled 35–36 days after treatment

		[Bicyclooctenone-$^{14}C_2$]		[Pyridine-^{14}C]	
TRR by summation (mg eq/kg)		0.020		0.031	
TRR by quantification (mg eq/kg)		0.020		0.031	
% TRR analysed		41.4		78.4	
Origin of component	Component	TRR (%)	mg eq/kg	TRR (%)	mg eq/kg
Analysed	Bicyclopyrone	10.2	0.002	9.2	0.003
	Total unassigned	9.1	0.002	32.6	0.010
	Baseline	4.7	< 0.001	2.6	< 0.001
	Remainder	17.3	0.004	33.9	0.010
Not analysed	Unextracted	29.9	0.006	15.9	0.005
	Loss/gain on fractionation	28.7 (loss)	0.006 (loss)	5.7 (loss)	0.002 (loss)

Table 9 Total radioactive residues in soya bean hay sampled 62–63 days after treatment

		[Bicyclooctenone-$^{14}C_2$]		[Pyridine-^{14}C]	
TRR by summation (mg eq/kg)		0.149		0.193	
TRR by quantification (mg eq/kg)		0.156		0.186	
% TRR analysed		53.6		67.5	
Origin of	Component	TRR (%)	mg eq/kg	TRR (%)	mg eq/kg
Analysed	Bicyclopyrone	3.9	0.006	3.3	0.006
	CSCD686480	ND	ND	14.2	0.027
	CSCD656832	ND	ND	1.2	0.002
	CSCD677694	3.1	0.005	2.1	0.004
	CSCD675162	15.5	0.023	14.0	0.027
	CSCD677693	6.7	0.010	5.6	0.011
	CSAA915194 glycoside	ND	ND	1.9	0.004
	CSCD675164	9.2	0.014	7.2	0.014
	CSCD677306	1.7	0.003	2.1	0.004
	CSAA915194	6.2	0.009	4.7	0.009
	Total unassigned	7.3	0.011	11.1	0.021
Not analysed	Unanalysed Fractions	18.4	0.028	19.3	0.037
	Radioactivity extracted	4.9	0.006	2.9	0.006
	Unextracted	20.7	0.031	7.9	0.015
	Loss/gain on	2.5 (loss)	0.004 (loss)	2.4 (loss)	0.004 (loss)

Table 10 Total radioactive residues in soya bean sampled 113–114 days after treatment

		[Bicyclooctenone-$^{14}C_2$]		[Pyridine-^{14}C]	
TRR by summation (mg eq/kg)		0.190		0.206	
TRR by quantification (mg eq/kg)		0.174		0.216	
% TRR analysed		66.7		64.8	
Origin of	Component	TRR(%)	mg eq/kg	TRR(%)	mg eq/kg
Analysed	Bicyclopyrone	15.0	0.029	12.7	0.026
	CSCC163768	ND	ND	0.7	0.001
	CSCD686480	ND	ND	5.6	0.011
	CSCD656832	ND	ND	1.7	0.003
	CSCD677694	0.9	0.002	0.9	0.002
	CSCD675162	4.7	0.009	5.2	0.011
	CSCD677693	3.1	0.006	2.8	0.006
	CSAA915194 glycoside	4.9	0.009	3.9	0.008
	CSCD675164	18.1	0.034	13.7	0.028
	CSCD677306	3.8	0.007	2.7	0.006
	CSAA915194	7.6	0.015	8.5	0.018
	CSCD642512	2.7	0.005	1.4	0.003
	Total unassigned	5.9	0.011	5.1	0.010
Not analysed	Radioactivity extracted	9.5	0.018	4.9	0.010
	Unextracted	9.5	0.018	6.7	0.014
	Loss/gain on	14.3 (loss)	0.027 (loss)	23.5 (loss)	0.048 (loss)

In mature beans, bicyclopyrone was detected at 15.0% TRR (0.029 mg/kg) and 12.7% TRR (0.026 mg/kg) in the [bicyclooctenone-6,7-$^{14}C_2$] and [pyridine-3-^{14}C] experiments respectively. The most significant metabolite detected was the monohydroxy metabolite CSCD675164 (13.7–18.1% TRR; 0.028–0.034 mg eq/kg). A second monohydroxy metabolite CSCD677306 and the dihydroxy metabolite CSCD677694 were also present but at very low levels (2.7–3.8% TRR; 0.006–0.007 mg eq/kg and 0.9 %TRR; 0.002 mg eq/kg for CSCD677306 and CSCD677694 respectively). The demethylated metabolite of NOA449280, CSAA915194 was detected at 7.6–8.5 %TRR (0.015–0.018 mg eq/kg) along with the two desmethyl monohydroxy metabolites CSCD675162 (4.7–5.2% TRR; 0.009–0.011 mg eq/kg) and CSCD677693 (2.8–3.1 %TRR; 0.006 mg eq/kg). A metabolite tentatively identified as a glycoside of CSAA915194 was detected at 3.9–4.9 %TRR (0.008–0.009 mg eq/kg). The carboxylic acid metabolite CSCD642512 (1.4–2.7 %TRR; 0.003–0.005 mg eq/kg) was also observed. Metabolites that contained only the pyridine ring of

bicyclopyrone were identified as CSCD686480 (5.6% TRR; 0.011 mg eq/kg), CSCD656832 (1.7% TRR; 0.003 mg eq/kg) and CSCC163768 (0.7% TRR; 0.001 mg eq/kg). No bicyclooctenone-specific metabolites were observed.

In hay, bicyclopyrone was detected at low levels of 3.3 and 3.9% TRR for the [pyridine-3-^{14}C] and [bicyclooctenone-6,7-$^{14}C_2$] experiments respectively with both corresponding to a residue of 0.006 mg/kg. The most significant metabolite detected was the desmethyl monohydroxy metabolite CSCD675162 (14.0–15.5 %TRR; 0.023–0.027 mg eq/kg). A second desmethyl monohydroxy metabolite CSCD677693 was also present (5.6–6.7% TRR; 0.010–0.011 mg eq/kg) along with the desmethyl metabolite CSAA915194 (4.7–6.2% TRR; 0.009 mg eq/kg). Two monohydroxy metabolites were also observed, CSCD675164 (7.2–9.2% TRR; 0.0014 mg eq/kg) and CSCD677306 (1.7–2.1% TRR; 0.003–0.004 mg eq/kg) A metabolite tentatively identified as a glycoside of CSAA915194 was detected in the pyridine-labelled experiment and represented 1.9% TRR (0.004 mg eq/kg). The dihydroxy metabolite CSCD677694 (2.1–3.1% TRR; 0.004–0.005 mg eq/kg) was also present. Metabolites that contained only the pyridine ring of bicyclopyrone were identified as CSCD686480 (14.2% TRR; 0.027 mg eq/kg) and CSCD656832 (1.2% TRR; 0.002 mg eq/kg). There were no bicyclooctenone-specific metabolites

In forage, residues was detected at low levels from both the radiolabelled experiments (0.020 and 0.031 mg eq/kg for the [bicyclooctenone-6,7-$^{14}C_2$] and [pyridine-3-^{14}C] experiments respectively). In the forage treated with [bicyclooctenone-6,7-$^{14}C_2$]-bicyclopyrone, bicyclopyrone was detected at levels of 10.2% TRR (0.002 mg/kg). The remaining residue consisted of at least 4 distinct radioactive components none of which exceeded 6.8% TRR (0.001 mg eq/kg). In the [pyridine-3-^{14}C] experiment, NOA449280 was also detected at very low levels (9.2% TRR; 0.003 mg eq/kg) and the remainder of the radioactive residue was shown to consist of at least 10 distinct radioactive components none exceeding 11.3% (0.003 mg eq/kg).

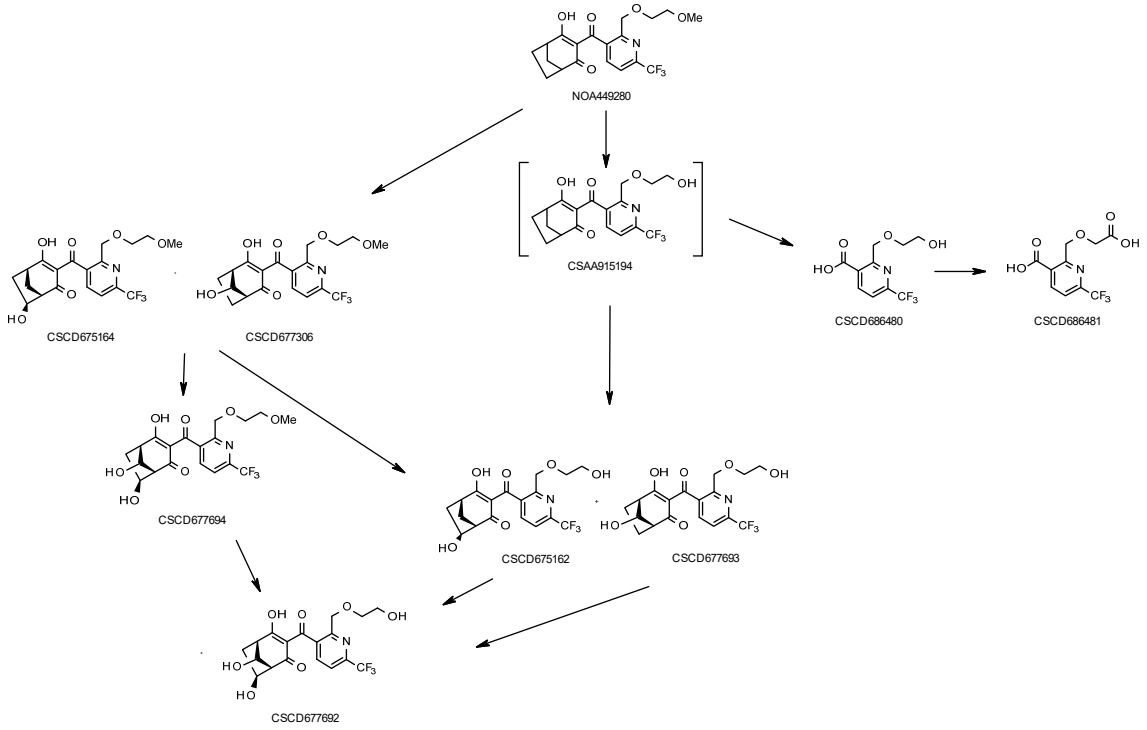


Figure 3 Proposed metabolic pathways of bicyclopyrone in soya bean

Summary of plant metabolism

In summary, when bicyclopyrone was applied in corn, sugarcane and soya bean, the metabolic pathways are similar but residues in soya bean samples were low and some of the metabolic products

may not have been detectable. Unchanged bicyclopyrone was found in corn forage, soya bean seed and hay and was absent in all other samples extracted. The majority of the metabolites were formed by hydroxylation on one or more sites on the bicyclic ring or demethylation of the methoxyethoxymethyl side chain followed by hydroxylation. Some glycoside conjugation of the hydroxyl derivatives and some cleavage between the two ring systems was observed.

Animal metabolism

The Meeting received information on the results of studies on lactating goats and laying hens which were fed isotope-labelled bicyclopyrone.

Rats

Metabolism studies on laboratory animals including rats were reviewed in the framework of toxicological evaluation by the WHO panel of the current JMPR.

Lactating goats

Radiolabelled [Pyridine-3-^{14}C]- and [Bicyclooctenone-6,7-^{14}C]- bicyclopyrone was administered orally by capsule to two lactating goats (Toggenburg Cross and British Alpine) once daily for 7 consecutive days at a nominal dose of 30 ppm in the feed assuming a daily intake of 1.8 kg dry matter [Goodwin, 2010, Ref: NOA449280_11099].

Animals were dosed in the morning prior to feeding and after milk and excreta collections. The actual mean concentrations were 33.78 (pyridinyl label) or 34.34 (bicyclooctenone label) ppm in the diet for goat 101F and 202F, respectively. Goats were less than 8 years of age. Body weights were 46 and 47 kg on arrival. It is noted that the animals lost weight during the acclimatisation. Average daily feed consumption during application was 1.0 kg of hay and 0.750 kg of concentrate twice /animal/day. Average daily milk production during application was 2.034 and 2.045 kg for goat 101F and 202F, respectively, and was not affected by the administration of bicyclopyrone. There were no adverse clinical findings during dosing.

Goats were sacrificed ca. 11 hours after the seventh and final doses. Blood and edible tissues (liver, kidneys, leg muscle, loin muscle and omental fat) were collected. The bile was removed from the gall bladder at the time of termination and quantified. Urine remaining in the bladder was added to the final urine sample for quantification.

Milk, urine, faeces, cage wash and tissues were weighed and representative sub-samples, were removed for radioactivity content analysis prior to storage at <-10 °C (nominally -20 °C). Tissue homogenates were sub-sampled prior to storage at <-10 °C (nominally-20 °C). Analysis of milk and tissues was performed on sequential sub-samples, thus leaving the bulk of the material continuously frozen. After selected sub-samples were thawed, aliquots of urine, bile, milk, plasma and cage washings were added directly to LSC. Sufficient sample was analysed to afford a limit of quantification of 0.001 mg/kg.

The total radioactive residue (TRR) was assessed by LSC or combustion/LSC. The total radioactive recovery was 87% and 82% for the pyridinyl and bicyclooctenone labels respectively. The majority of the administered radioactivity was excreted in the urine (pyridinyl label: 60%, bicyclooctenone label: 62%). Lower levels, amounting to approximately 6% of dose, where present in faeces from both radiolabels. The highest residues were found in the liver (2.726 mg eq/kg and 2.965 mg eq/kg for pyridinyl and bicyclooctenone labels respectively) and accounted for only ca 0.7% of the administered dose. Residue levels in other commodities such as kidney, muscle and fat were low and in total accounted for < 0.1% of the administered dose for both radiolabels. Radioactive residues in milk (mean for a 24-hour period) reached a plateau of about 0.008 mg eq/kg for both radiolabels at approximately 2 to 3 days.

Storage stability for study samples of milk, liver, kidney, composite muscle and fat was demonstrated by comparison of the quantitative metabolite patterns of freshly extracted material to original study extracts that had undergone periods of frozen (ca -20 °C) storage. There were no

qualitative or quantitative variations in the metabolite patterns found following frozen storage for 6 months in all analysed samples, with the exception of fat. There was some evidence of a change in the profile of subcutaneous fat extracts, but as the radioactive residue levels were so low, this was inconclusive. Since the analysis of all samples took place within these time periods, stability has been demonstrated. A summary of the TRR in milk and tissues from a goat dosed with either [Pyridinyl-^{14}C]- or [Bicyclooctenone-^{14}C]- bicyclopyrone is given below in Table 11.

Table 11 Total radioactive residue (TRR) in goat milk and tissues

Sample	Radioactive Residue (mg/kg)	
	Pyridinyl label	Bicyclooctenone label
Milk	0.017	0.017
Liver	2.736	2.976
Kidney	1.329	1.422
Muscle (forequarter)	0.025	0.028
Muscle (loin)	0.029	0.035
Muscle (hind)	0.025	0.023
Subcutaneous Fat	0.029	0.026
Renal Fat	0.011	0.018
Omental Fat	0.008	0.008

Identification of metabolites was accomplished by HPLC and TLC followed by MS and by co-chromatography with authentic reference standards. Profiling of the analysed samples showed unchanged parent to be the most significant residue in tissues and milk. The hydroxylated metabolite CSAA915194, resulting from O-demethylation of the parent compound was a major metabolite detected in all commodities. Hydroxylation of the bicyclooctenone ring occurred in two or more positions. Only trace levels of the pyridine-specific metabolite CSCD686480 were found, showing that cleavage between the rings was a very minor pathway. Little conjugation occurred, as only trace levels of the glucuronide of CSAA915194 were found in bile and urine. Two desmethyl monohydroxy metabolites, identified as CSCD675162 and CSCD677693,were present as minor metabolites in liver (maximum 2.5% TRR, 0.073 mg/kg). Trace levels of CSCD675162 were also detected by TLC in subcutaneous fat. A third metabolite with the same molecular weight was also characterised in liver. This was assumed to be a further isomer in which there was an alternative stereochemistry or position of substitution of the hydroxyl group. The same metabolite was detected at trace levels in urine. Three additional metabolites, which were not evident in tissues or milk, were detected in urine at trace levels. These included the monohydroxylated metabolites, CSCD675164 and CSCD677306, with positions of hydroxylation equivalent to CSCD675162 and CSCD677693 respectively and the desmethyl dihydroxy metabolite CSCD677692.

Table 12 Identification and characterisation of radioactive residues in goat milk and tissues

Component	Milk	Liver	Kidney	Composite Muscle	Subcutaneous Fat	Renal Fat
	%TRR (mg eq/kg)	%TRR (mg eq/kg)	%TRR (mg eq/kg)	%TRR (mg eq/kg)	%TRR (mg eq/kg)	%TRR (mg eq/kg)
[^{14}C]- pyridinyl bicyclopyrone						
Bicyclopyrone	22.9 (0.004)	16.0 (0.436)	43.5 (0.572)	41.0 (0.010)	41.4 (0.013)	29.4 (0.004)
CSAA915194	57.2 (0.010)	70.4 (1.920)	50.2 (0.660)	46.0 (0.012)	41.9 (0.013)	27.6 (0.004)
CSCD675162	ND	1.4 (0.038)	ND	ND	ND	ND
CSCD677693	ND	1.6 (0.044)	ND	ND	ND	ND
CSCD686480	ND	1.1 (0.030)	ND	ND	ND	ND
Desmethyl monohydroxy	ND	0.8 (0.022)	ND	ND	ND	ND

Component	Milk	Liver	Kidney	Composite Muscle	Subcutaneous Fat	Renal Fat
	%TRR (mg eq/kg)	%TRR (mg eq/kg)	%TRR (mg eq/kg)	%TRR (mg eq/kg)	%TRR (mg eq/kg)	%TRR (mg eq/kg)
bicyclopyrone						
TRR Extracted	96.9 (0.016)	91.2 (2.489)	97.9 (1.289)	94.5 (0.024)	87.9 (0.027)	63.3* (0.009)
Unextracted	3.1 (0.001)	8.7 (0.237)	2.2 (0.029)	5.1 (0.001)	1.2 (< 0.001)	0.8* (< 0.001)
Total (by Summation)	100.0 (0.017)	99.9 (2.726)	100.1 (1.318)	100.0 (0.025)	100.1 (0.029)	100.1 (0.014)
[^{14}C]- bicyclooctenone bicyclopyrone						
Bicyclopyrone	27.0 (0.005)	22.4 (0.664)	50.1 (0.641)	39.2 (0.009)	43.6 (0.012)	27.9 (0.006)
CSAA915194	59.5 (0.010)	59.6 (1.763)	47.4 (0.606)	43.0 (0.011)	40.4 (0.011)	31.7 (0.007)
CSCD675162	ND	1.6 (0.047)	ND	ND	ND	ND
CSCD677693	ND	2.5 (0.073)	ND	ND	ND	ND
CSCD686480	ND	ND	ND	ND	ND	ND
Desmethyl monohydroxy bicyclopyrone	ND	1.7 (0.050)	ND	ND	ND	ND
Extracted	95.5 (0.016)	91.3 (2.702)	97.1 (1.242)	94.1 (0.023)	86.4 (0.023)	70.5* (0.016)
Unextracted	4.4 (0.001)	8.9 (0.263)	2.9 (0.037)	5.6 (0.001)	2.4 (0.001)	1.2* (< 0.001)
Total (by summation)	99.9 (0.017)	100.2 (2.965)	100.0 (1.279)	100.0 (0.024)	100.0 (0.026)	100.0 (0.022)

ND = not detected

* Only low levels of radioactive components were present in renal fat

In summary, the majority of the dose was excreted in urine (pyridinyl 60%; bicyclooctenone 62%) indicating that bicyclopyrone was extensively absorbed. Much lower levels, amounting to approximately 6% of dose, were present in faeces. There was no significant difference in excretion profiles between the two radiolabels.

Radioactive residues in milk were very low and a plateau level of about 0.008 mg/kg was reached after approximately 2 to 3 days.

Results were essentially the same for both radiolabelled treatments. The highest tissue residues were found in liver (pyridinyl label 2.7 mg eq/kg, bicyclooctenone label 3.0 mg eq/kg) and kidney (pyridinyl label 1.3 mg eq/kg, bicyclooctenone label 1.4 mg eq/kg). The remaining muscle and fat commodities contained radioactive residues < 0.035 mg eq/kg. These residues were readily extracted with solvents (e.g. acetonitrile, acetonitrile:water (4:1, v/v), acetonitrile:water (3:7, v/v) and water) and all unextracted residues were either < 10% TRR or < 0.05 mg eq/kg.

A major component identified in all samples was unchanged bicyclopyrone. The lowest levels of bicyclopyrone were found in the liver (pyridinyl label 16.0% TRR, 0.436 mg/kg), and the highest in kidney ((bicyclooctenone label 50.1% TRR, 0.641 mg/kg). The most abundant metabolite detected in all commodities was CSAA915194, a primary alcohol which results from demethylation of the methoxy group. This compound was the principal component of the residue in liver and milk (maximum 70% TRR, 1.920 mg eq/kg (pyridinyl label) and 59.5% TRR, 0.01 mg eq/kg (bicyclooctenone label) respectively for the two commodities) and was present at similar levels to parent in kidney, muscle and fat. Trace levels of this metabolite were detected as a glucuronide in

urine and bile, but it was observed only in its free form in edible commodities. All other detected metabolites were below 3%TRR in all commodities.

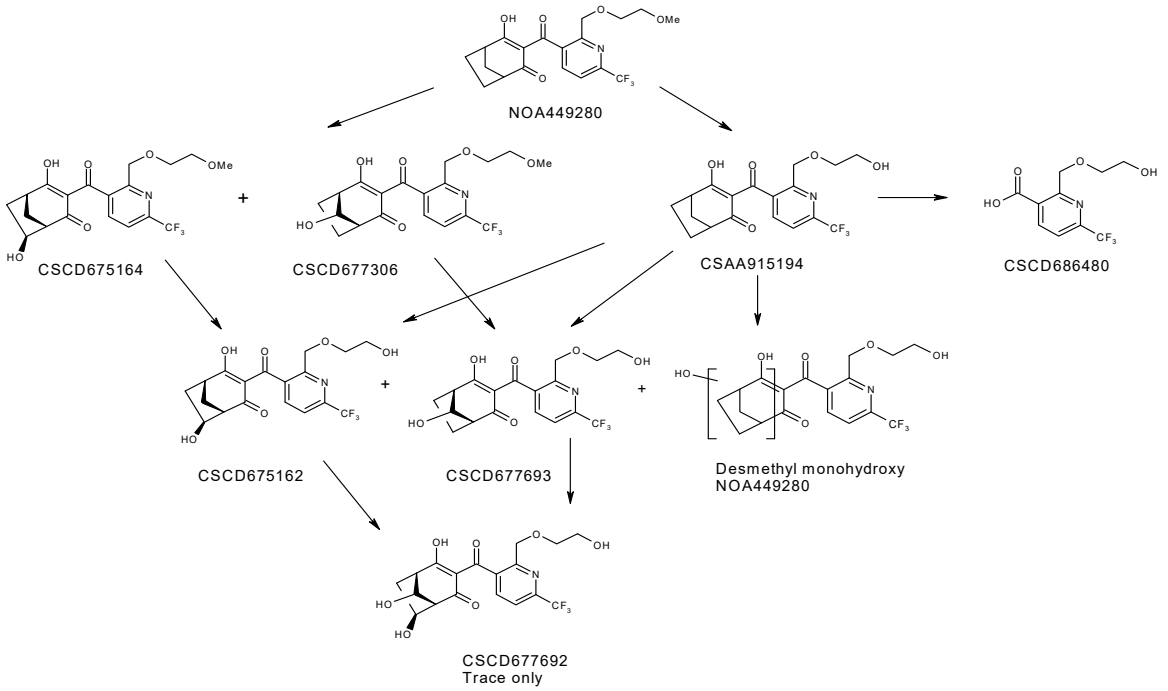


Figure 4 Proposed metabolic pathways of bicyclopyrone in lactating goat

Laying hens

The elimination, distribution and metabolic fate of [Pyridinyl-^{14}C]- bicyclopyrone and [Bicyclooctenone-^{14}C]-bicyclopyrone were investigated following repeated oral administration to the laying hen (Cotton *et al*. 2010, NOA449280_11100). Two groups consisting of five laying hens (ISA Brown), each hen weighing approximately 2.0 kg were used as test animals in this metabolism study. The two groups of hens were dosed orally by capsule for ten consecutive days with a nominal dose level of 20 ppm [^{14}C]- bicyclopyrone in dry diet. The eggs were collected twice daily and excreta in 24 hr intervals. Eggs were kept refrigerated and separated into egg yolks and egg whites prior to radio analysis. Approximately 11 hours after the last dose, the hens were sacrificed and the tissues (fat, muscle and skin) and organs (kidney and liver) were removed. Samples were stored at -20 °C.

The TRR in the daily egg samples were determined by LSC. The TRR in the blood, tissues and excreta were determined by combustion followed by LSC. Radioactivity in the extracts of excreta and in liquid chromatographic fractions was determined by combustion and by LSC; radioactivity in the post extraction solids of excreta was determined by combustion followed by LSC. The metabolite profile of bicyclopyrone was defined by analysing acetone extracts of the excreta using high performance liquid chromatography. The identity of the main residue component bicyclopyrone was determined by HPLC-MS/MS.

The total radioactive recovery was 81% and 79% for the pyridinyl and bicyclooctenone labels respectively. More than 84% of radioactivity in tissue samples was extracted by solvents (e.g. acetonitrile, acetonitrile:water (4:1, v/v), acetonitrile:water (3:7, v/v) and water). The majority of the administered radioactivity was recovered in the excreta (pyridinyl label: 76%, bicyclooctenone label: 76%). The highest residues were found in liver (1.752 mg eq/kg and 1.776 mg eq/kg for pyridinyl and bicyclooctenone labels respectively) and accounted for only ca 0.3% of the administered dose. Residue levels in other commodities such as egg yolk, egg white, muscle, peritoneal fat and skin and subcutaneous fat were low and in total accounted for < 0.25% of the administered dose for both

radiolabels. Radioactive residues in eggs (mean for a 24 hour period) reached a plateau of 0.10 mg eq/kg in both labels at approximately 6 to 8 days.

Table 13 Total radioactive residues (TRR) in egg and tissues of hens

Sample	Radioactive Residue (mg eq/kg)	
	Pyridinyl label	Bicyclooctenone label
Egg Yolk	0.104	0.101
Egg White	0.127	0.086
Liver	1.752	1.776
Composite Muscle	0.136	0.084
Peritoneal Fat	0.160	0.178
Skin and Subcutaneous Fat	0.536	0.416

The extent of metabolism was limited for both radiolabels with radioactive residues in edible tissues predominantly consisting of bicyclopyrone at greater than 73% TRR. CSAA915194, a primary alcohol which results from demethylation of the methoxy group, was detected at up to 3% total radioactivity in egg yolk, egg white, liver, muscle and peritoneal fat by HPLC and TLC.

LC/MS confirmed the presence of the monohydroxylated metabolites, CSCD675164 and CSCD677306 at very low levels in bicyclooctenone label liver (1.6% TRR, 0.029 mg eq/kg and 2.0% TRR, 0.035 mg eq/kg respectively). The presence of these metabolites was also confirmed by HPLC and TLC but levels were too low to be detected in liver from the pyridinyl label. In addition the desmethyl dihydroxy metabolite CSCD677692 was detected at levels too low to quantify. This metabolite was also detected in excreta.

The desmethyl monohydroxy metabolite CSCD675162 was detected by TLC at low levels in peritoneal fat (5.4% TRR, 0.01 mg eq/kg) from the bicyclooctenone label and in egg yolk (2.2% TRR, 0.002 mg eq/kg) from the pyridinyl label. Another desmethyl monohydroxy metabolite CSCD677693 was detected in excreta only. All other metabolites detected for both labels were ≤ 0.009 mg eq/kg irrespective of detection method or label.

Table 14 Identification and characterisation of radioactive residues in hen egg and tissues

Component	Egg Yolk	Egg White	Liver	Composite Muscle	Peritoneal Fat	Subcutaneous Fat + Skin
	%TRR (mg eq/kg)	%TRR (mg eq/kg)	%TRR (mg eq/kg)	%TRR (mg eq/kg)	%TRR (mg eq/kg)	%TRR (mg eq/kg)
[^{14}C]- pyridinyl bicyclopyrone						
Bicyclopyrone	76.4 (0.080)	94.8 (0.119)	86.4 (1.514)	83.4 (0.112)	91.9 (0.147)	85.9 (0.461)
CSAA915194	1.0 (0.001)	2.0 (0.003)	ND	3.0 (0.004)	ND	ND
CSCD675162	2.2 (0.002)	ND	ND	ND	ND	ND
CSCD675164	ND	ND	ND	ND	ND	ND
CSCD677306	ND	ND	ND	ND	ND	ND
Extracted	91.1 (0.094)	99.6 (0.126)	91.5 (1.604)	99.2 (0.134)	94.8 (0.152)	92.3 (0.495)
Unextracted	9.0 (0.009)	0.5 (0.001)	8.4 (0.147)	0.7 (0.001)	5.1 (0.008)	7.7 (0.041)
Total (by Summation)	100.1 (0.104)	100.1 (0.127)	99.9 (1.752)	99.9 (1.752)	99.9 (0.160)	100 (0.536)
[^{14}C]- bicyclooctenone bicyclopyrone						
Bicyclopyrone	79.3 (0.080)	93.2 (0.080)	73.7 (1.310)	83.5 (0.070)	93.3 (0.166)	89.3 (0.371)
CSAA915194	ND	ND	ND	ND	2.4	ND

Component	Egg Yolk	Egg White	Liver	Composite Muscle	Peritoneal Fat	Subcutaneous Fat + Skin
	%TRR (mg eq/kg)	%TRR (mg eq/kg)	%TRR (mg eq/kg)	%TRR (mg eq/kg)	%TRR (mg eq/kg)	%TRR (mg eq/kg)
					(0.004	
CSCD675162	ND	ND	ND	ND	5.4 (0.01)	ND
CSCD675164	ND	ND	1.6 (0.029)	ND	ND	ND
CSCD677306	ND	ND	2.0 (0.035)	ND	ND	ND
Extracted	90.0 (0.091)	99.9 (0.085)	84.5 (1.500)	97.3 (0.082)	98.1 (0.174)	90.9 (0.378)
Unextracted	10.1 (0.010)	0.2 (< 0.001)	15.6 (0.277)	2.8 (0.002)	1.9 (0.003)	9.1 (0.038)
Total (by Summation)	100.0 (0.101)	100.1 (0.086)	100.3 (1.776)	100.1 (0.084)	100 (0.178)	100 (0.416)

ND = not detected

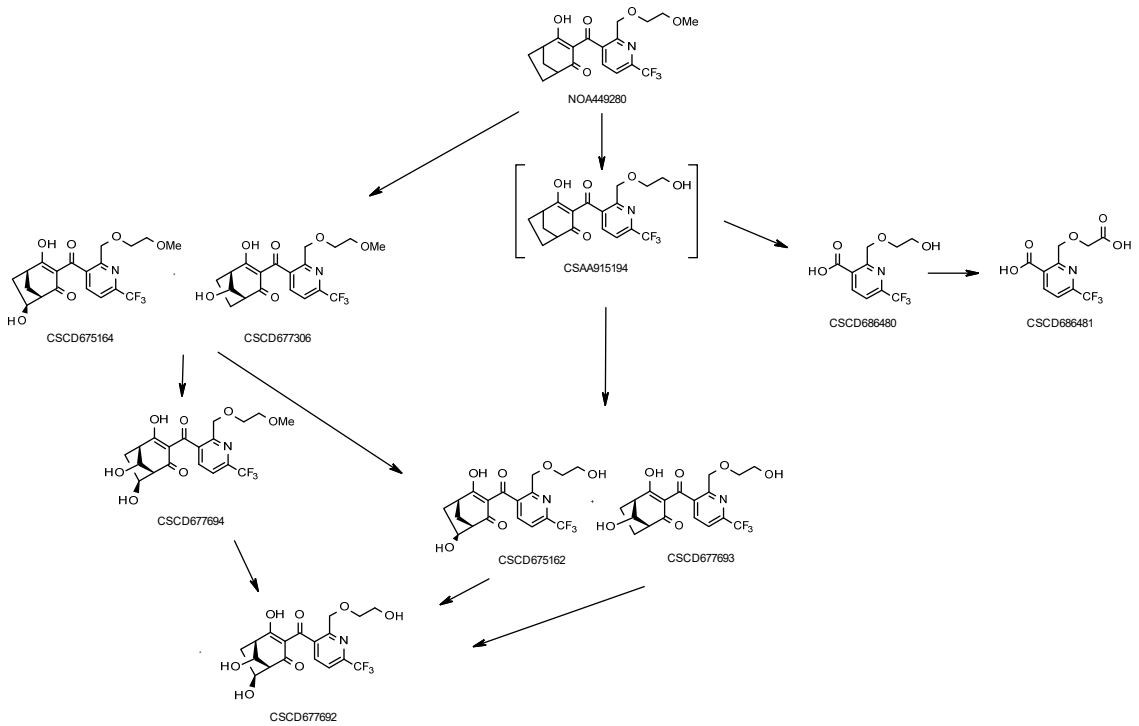


Fig 5 Proposed metabolic pathways of bicyclopyrone in laying hen

Summary of animal metabolism

Metabolism studies conducted in laying hens and lactating goats have provided a detailed understanding of the biotransformation of bicyclopyrone in livestock. The metabolic pathways in these species are similar.

Tissue residues in both animals consisted primarily of parent bicyclopyrone and CSAA915194 (desmethyl parent) and several very minor metabolites found in the liver for the goat and several samples for the laying hen. Analysis of the excreta and urine provided a more detailed understanding of the biotransformation of bicyclopyrone in these animals and allowed for a comparison of the metabolic pathways with that found in the rat. All three animals, goat, hen and rat show similar biotransformation pathways for bicyclopyrone.

The primary metabolic processes observed include O-demethylation, oxidation on one or more sites of the bicyclooctenone ring, a minor amount of bridge cleavage between the rings, and conjugation to some extent. Eggs and milk were minor routes of excretion for bicyclopyrone.

In the hen metabolism study, bicyclopyrone was not extensively metabolised and was the largest component of the total radioactive residue (TRR) in all hen commodities. Residues of bicyclopyrone ranged from 1.514 mg/kg (86.4% TRR) in liver to 0.07 mg/kg (83.5% TRR) in muscle. Minor metabolites CSCD677306 and CSCD675164 were found in liver at levels of 0.035 mg eq/kg (2.0% TRR) and 0.029 mg eq/kg (1.6% TRR) respectively. Only trace levels of CSAA915194 and CSCD675162 were found in other commodity samples.

In the goat metabolism study, the principle metabolites were CSAA915194 and unchanged bicyclopyrone which were found in all goat commodities. The highest levels of each from both label experiments occurred in liver and kidney; 1.920 mg/kg (70.4% TRR) and 0.660 mg/kg (50.2% TRR) respectively for CSAA915194, and 0.664 mg/kg (22.4% TRR) and 0.641 mg/kg (50.1% TRR) respectively for bicyclopyrone. Other metabolites were found only in liver at levels ≤ 2.5% TRR and 0.073 mg eq/kg.

Environmental fate in soil

The Meeting received information on the environmental fate and behaviour of bicyclopyrone, including aerobic metabolism studies, hydrolytic stability and photochemical degradation in soils. The fate and behaviour of bicyclopyrone in soils were investigated using [^{14}C- bicyclooctenone] and [^{14}C-pyridine] labelled compounds.

Aerobic degradation in soil-laboratory studies

Study 1

The rate of aerobic degradation of bicyclopyrone in a loamy sand soil at a temperature of 20 °C was investigated [Lewis and Gilbert,2009b, 1983/071-D2149]. Soil samples were mixed with [Bicyclo-^{14}C] bicyclopyrone at rate of 0.267 mg/kg dry weight of soil, equivalent to a single field application rate of 200 g ai/ha and incubated for 365 days in darkness at 20 ± 2°C. Samples were taken at DAT = 0, 7, 14, 21, 35, 50, 80, 120, 181, 268 and 365. All samples generated during the study were analysed as soon as possible, within a few days (maximum of 10 days) after generation. Soil samples were extracted sequentially with calcium chloride, ammonium hydroxide, ammonium hydroxide: acetone (50:50 v/v) and acetone. They were finally extracted under reflux conditions with acetonitrile: acidified water (70:30 v/v). The extracts were combined to form three fractions-calcium chloride extracts, basic extracts (including acetone extracts) and reflux extracts. Calcium chloride and basic extracts and the reflux extracts were separately analysed by LSC and HPLC. Any unextracted radioactivity present in the soil residue was quantified by sample oxidation and LSC.

Bicyclopyrone was extensively mineralised to carbon dioxide, with no other metabolites present at > 5% of applied radioactivity. Many of the basic extracts contained two unidentified polar compounds that were not present in calcium chloride extracts. These were therefore considered to be transient minor products that are tightly bound to the soil. Calcium chloride extracts were analysed directly by HPLC and contained predominantly parent compound. Radioactivity in calcium chloride extracts decreased steadily from 65.6% of applied radioactivity, initially, to ≤ 1% of applied radioactivity at 80 DAT. Levels of bicyclopyrone decreased from 65.3% of applied radioactivity, initially, to 0.2% at 365 DAT. Total other compounds present comprised a maximum of ≤ 1.3% of applied radioactivity at any sampling interval.

Basic extracts contained parent compound and minor unknowns. Total radioactivity decreased steadily from 33.8% of applied radioactivity, initially, to 3.0% at 365 DAT. Parent compound decreased from 33.6% of applied radioactivity, initially, to 0.3% at 365 DAT. Total other compounds present comprised a maximum of 4.5% of applied radioactivity at 80 DAT decreasing to 2.6% at 365 DAT. Most samples contained two unidentified compounds with short retention times, which were considered to be transient minor products, as detailed previously. Bound residues were at their

highest (approximately 23% of applied radioactivity) at 80 DAT then decreased. It is proposed that the bicyclopyrone and/or its metabolites became incorporated into soil organic matter and that the bicyclo ring system was then relatively quickly mineralised to carbon dioxide. The single first-order DT_{50} value for the degradation of bicyclopyrone in Gartenacker soil was 19.8 days.

Significant levels of volatile radioactivity were formed during the incubation period increasing to approximately 76% of applied radioactivity at 365 DAT. The volatile material was proven to be carbon dioxide by barium precipitation of the radioactivity from a pooled sample of all the traps associated with the 365 DAT sample. All of the radioactivity in the solution precipitated on addition of barium chloride solution.

Table 15 Distribution of radioactivity in ^{14}C-bicyclopyrone-treated soil at 20 °C (aerobic conditions) following application of [bicyclo-^{14}C] bicyclopyrone

Incubation Time [d]	Mean Percent Applied Radioactivity						
	CO_2	Extractables				Non-extractables	Recovery
		$CaCl_2$ Extract	Basic Extract	Reflux Extract	Sum		
0	-	65.6	33.8	0.8	100.2	0.7	100.9
7	9.4	45.5	33.5	1.9	80.8	5.9	96.1
14	18.4	35.1	29.9	2.6	67.5	10.4	96.2
21	31.0	22.2	25.5	2.1	49.7	13.7	94.4
35	45.4	10.1	15.8	3.2	29.0	19.4	93.7
50	55.8	8.1	13.5	2.3	23.8	20.9	100.5
80	67.1	1.0	7.6	2.0	10.5	22.6	100.1
120	68.2	0.6	5.4	1.7	7.7	21.5	97.4
181	73.1	0.4	4.0	1.5	5.8	20.8	9.7
268	74.9	0.3	3.6	1.1	5.0	19.7	99.5
365	75.8	0.2	3.0	0.8	4.0	18.3	98.0

Table 16 Characterization and identification of mean residues in soil at 20 °C (aerobic conditions) following application of [bicyclo-^{14}C] bicyclopyrone

Time	Mean Percent Applied Radioactivity		
	Bicyclopyrone	Minor Unknowns	Unresolved Background
0	99.6	-	0.5
7	79.0	1.3	0.5
14	64.9	2.1	0.5
21	46.0	3.2	0.4
35	25.7	3.1	0.2
50	20.3	3.2	0.3
80	6.0	4.5	0.1
120	3.3	4.3	0.1
181	2.4	3.4	<0.1
268	1.9	3.0	<0.1
365	1.3	2.6	<0.1

Table 17 Route and rate of degradation in soil at 20 °C (aerobic conditions) following application of [bicyclo-^{14}C] bicyclopyrone

Soil	SFO			
	DT_{50} (days)	Chi^2 (%)	R^2	Prob > t
Gartenacker	19.8	5.60	0.9958	$5.5\ 10^{-19}$

Degradation of [bicyclo-^{14}C] bicyclopyrone was rapid and extensive, as indicated by the evolution of CO_2 and formation of bound residues. Carbon dioxide increased to 68.2% at 120 DAT and 75.8% at 365 DAT. No other extractable metabolite was observed at a significant level (maximum individual level 3.9%).

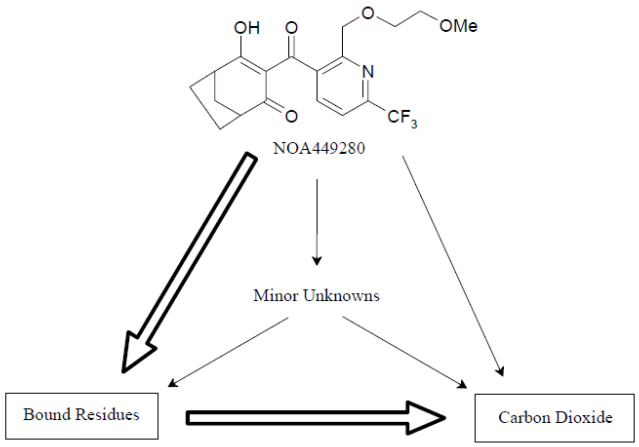


Figure 6 Proposed metabolic pathway of bicyclopyrone in aerobic soil

Study 2

The rate of aerobic degradation of bicyclopyrone in five different soils: Gartenacker (loam), Iowa (sandy clay loam), 18 Acres (sandy clay loam), Marsillargues (silty clay) and Nebraska (silt loam) at a temperature of 20 °C was investigated [Lewis, 2009c, NOA449280_11045]. [Pyridine-^{14}C] bicyclopyrone was applied at a nominal rate of 0.267 mg/kg dry weight of soil, equivalent to a field application rate of 200 g ai/ha. The soils were incubated under aerobic conditions in the laboratory and maintained under moist, dark conditions at 20 ± 2 °C for up to 365 days. Samples were taken at DAT=0, 7, 14, 21, 35, 50, 79, 120, 180, 271 and 365.

The soils were extracted sequentially with 0.01M calcium chloride, 0.5M ammonium hydroxide, 0.5M ammonium hydroxide:acetone (50:50 v/v) and acetone. Samples were finally extracted under reflux conditions with acetonitrile:formic acid acidified water (70:30 v/v). The extracts were pooled to form three fractions. Calcium chloride, basic and reflux extracts were separately analysed by LSC and HPLC except where the amount of radioactivity was < 4%. Any unextracted radioactivity present in the soil residue was quantified by sample oxidation and LSC. Bound residue extraction was performed where necessary. Radioactivity was measured by LSC. TLC and LC/MS were used to provide qualitative confirmation of the identification of bicyclopyrone and the metabolites SYN503780, CSCC163768 and CSCD656832.

There were two metabolites present at ≥ 5% of applied radioactivity in one or more soils, namely CSCD656832 in four soils (up to 14.4% in Iowa soil) and CSCD642512, present in 18 Acres soil up to 6.0%. The three minor metabolites were SYN503780 (in all soils and to a maximum 4.2% of applied radioactivity in Nebraska soil), CSCD163768 (in 2 soils and to a maximum ≤ 1.2% of applied radioactivity in Gartenacker soil) and CSAA757083 (a maximum of approximately 1% of applied radioactivity in Gartenacker soil only). A number of minor unknown metabolites were also observed, each of which individually comprised < 5% of applied radioactivity.

Carbon dioxide was a major product of metabolism in all soils, reaching a maximum 65.8, 10.7, 30.1 and 27.3% of the applied radioactivity by the end of the incubation (120 DAT) for Gartenacker, 18 Acres, Marsillargues and Nebraska soils respectively. The level of carbon dioxide for Iowa soil at 365 DAT reached 44.3%.

Unextracted residues were low at 0 DAT (maximum 1.3%), increasing slowly throughout the incubation to reach a maximum of 22.3, 10.6, 23.6 and 17.2% of applied radioactivity by the end of incubation (120 DAT) for Gartenacker, 18 Acres, Marsillargues and Nebraska soils respectively. The unextracted residue in Iowa soil at 365 DAT was 27.9%.

Table 18 Distribution of radioactivity in bicyclopyrone-treated soil at 20 °C (aerobic conditions) following application of [pyridine -^{14}C] bicyclopyrone-Gartenacker Soil

Incubation Time [d]	Mean Percent Applied Radioactivity						
	CO_2	Extractables				Non-extractables	Recovery
		$CaCl_2$ Extract	Basic Extract	Reflux Extract	Sum		
0	-	64.5	32.7	2.0	99.2	-	99.2
7	5.1	49.1	37.2	3.8	90.0	4.5	99.5
14	13.0	36.7	34.5	5.1	76.2	8.5	97.7
21	20.0	28.5	19.6	13.1	61.2	13.8	95.0
35	31.8	17.1	22.1	6.5	45.6	17.3	94.7
50	50.2	4.7	10.1	7.8	22.5	23.0	95.7
79	58.9	1.8	6.6	4.1	12.4	22.9	94.2
120	65.8	0.4	3.9	2.4	6.7	22.3	94.7

Table 19 Distribution of radioactivity in bicyclopyrone-treated soil at 20 °C (aerobic conditions) following application of [pyridine -^{14}C] bicyclopyrone-Iowa Soil

Incubation Time [d]	Mean Percent Applied Radioactivity						
	CO_2	Extractables				Non-extractables	Recovery
		$CaCl_2$ Extract	Basic Extract	Reflux Extract	Sum		
0	-	68.8	24.1	4.2	97.1	1.1	98.2
7	0.8	57.0	29.7	7.1	93.7	3.4	97.8
14	2.3	45.7	34.5	9.1	89.2	5.3	96.7
21	4.9	36.3	30.4	14.4	81.1	9.6	95.5
35	8.8	29.4	29.6	14.9	73.9	13.4	96.0
50	13.2	21.3	22.0	18.8	62.0	19.0	94.1
79	18.6	14.9	19.6	18.7	53.2	22.0	93.8
120	25.3	10.2	22.5	14.5	47.1	22.2	94.6
180	35.2	5.8	11.7	13.8	31.3	26.1	92.6
271	39.2	3.5	8.4	12.8	24.6	29.4	93.2
365	44.3	2.1	9.2	11.1	22.3	27.9	94.4

Table 20: Distribution of radioactivity in bicyclopyrone-treated soil at 20 °C (aerobic conditions) following application of [pyridine -14C] bicyclopyrone-18 Acres Soil

Incubation Time [d]	Mean Percent Applied Radioactivity						
	CO_2	Extractables				Non-extractables	Recovery
		$CaCl_2$ Extract	Basic Extract	Reflux Extract	Sum		
0	-	42.8	53.0	1.5	97.2	1.0	98.2
7	2.4	28.0	58.6	6.4	93.0	4.2	99.5
14	4.5	20.2	59.1	7.9	87.1	5.9	97.5
21*	4.4	17.2	8.4	44.1	69.7	21.7	95.8
29	5.9	12.6	62.2	8.3	83.1	7.9	96.9
35	6.8	11.6	50.2	17.5	79.2	11.2	97.2
50	7.0	10.1	50.5	19.3	79.8	10.6	97.4
79	7.2	9.6	46.9	20.5	77.0	12.5	96.7
120	10.7	6.5	55.7	13.2	75.4	10.6	96.7

* The distribution of radioactivity between basic and reflux extracts is incorrect because of a laboratory error. Values replaced by 29 DAT time point.

Table 21 Distribution of radioactivity in bicyclopyrone-treated soil at 20 °C (aerobic conditions) following application of [pyridine -^{14}C] bicyclopyrone-Marsillargues Soil

Incubation Time [d]	Mean Percent Applied Radioactivity						
	CO_2	Extractables				Non-extractables	Recovery
		$CaCl_2$ Extract	Basic Extract	Reflux Extract	Sum		
0	-	70.9	22.4	4.0	97.2	1.3	98.5
7	0.7	66.1	24.0	4.9	97.4	3.1	98.7
14	2.6	59.7	22.5	6.4	88.6	6.8	98.0
21*	4.3	56.7	5.6	19.7	82.0	10.9	97.1
29	7.5	49.7	24.7	4.7	79.1	10.5	97.1
35	9.0	49.9	13.7	11.2	74.8	14.2	97.9
50	12.6	41.1	10.0	13.7	64.7	17.4	94.7
79	20.8	33.9	8.6	10.8	53.3	20.5	94.6
120	30.1	22.1	12.9	5.3	40.2	23.6	93.9

* The distribution of radioactivity between basic and reflux extracts is incorrect because of a laboratory error. Values replaced by 29 DAT time point.

Table 22 Distribution of radioactivity in bicyclopyrone-treated soil at 20 °C (aerobic conditions) following application of [pyridine -^{14}C] bicyclopyrone-Nebraska Soil

Incubation Time [d]	Mean Percent Applied Radioactivity						
	CO_2	Extractables				Non-extractables	Recovery
		$CaCl_2$ Extract	Basic Extract	Reflux Extract	Sum		
0	-	71.9	27.1	2.0	100.9	-	100.9
7	0.3	61.9	32.7	4.1	98.7	1.3	100.2
14	0.8	49.1	36.9	8.0	94.0	3.0	97.8
21	2.4	44.3	35.8	10.2	90.3	4.6	97.2
35	7.5	35.2	34.4	10.3	79.9	8.8	96.1
50	11.2	26.7	31.5	16.6	74.7	11.5	97.3
79	18.5	18.7	32.4	13.6	64.7	13.4	96.5
120	27.3	11.6	25.1	14.1	50.7	17.2	95.1

Half-lives of bicyclopyrone in the five soils were calculated using linear regression analysis. The results are summarized in the following table.

Table 23 Route and rate of degradation of bicyclopyrone in soil at 20 °C (aerobic conditions) following application of ^{14}C – [pyridine -^{14}C] bicyclopyrone

Soil	First order kinetics			
	DT_{50}	Chi^2	R^2	Prob > t
Gartenacker	20.5	4.88	0.9923	$2.5x10^{-13}$
Iowa	59.3	4.15	0.9950	$6.1x10^{-18}$
Nebraska	68.4	1.60	0.9935	$1.1x10^{-15}$
Marsillargues	89.0	1.39	0.9936	$4.2x10^{-16}$
18 Acres	153.2	5.53	0.8277	$1.0x10^{-6}$

Study 3

The rate of aerobic degradation of bicyclopyrone in seven different US soils, Georgia (sandy loam), Illinois (silty clay loam), North Carolina (loamy sand), Minnesota (clay loam), Iowa (sandy loam), Michigan (loamy sand) and Ohio (loam) at a temperature of 20 °C was investigated [Lewis, Gilbert,

and Kendrick, 2015, NOA449280_11068]. [Pyridine-^{14}C] bicyclopyrone was applied at a nominal rate of 0.267 mg/kg dry weight of soil, equivalent to a single field application rate of 200 g ai/ha. The soils were incubated under aerobic conditions in the laboratory and maintained under moist dark conditions at 20 ± 2 °C for up to 365 days. Samples were taken at DAT=0, 7, 14, 22, 35, 50, 79, 120, 181, 272 and 365. Samples were extracted using GM030.02A Residue analytical method and radioactivity quantified by LSC. Parent and metabolites were confirmed by HPLC and TLC co-chromatography with reference standards and by LC/MS.

The amount of extractable radioactivity decreased with time for all seven soils. The extractability at 0 DAT was high for all soils (range 97.3—100.1%) and decreased to 74.0% (Illinois soil), 93.6% (North Carolina soil), 56.5% (Minnesota soil), 82.0% (Iowa soil), 77.4% (Michigan soil) and 34.8% (Ohio soil) at 120 DAT. The extractable radioactivity for Georgia soil at 365 DAT was 58.0%. High recovery of parent compound was obtained at zero time (93.6–99.5%) showing that the extraction method was efficient and did not degrade the compound. In addition to parent bicyclopyrone, five metabolites were identified.

Three metabolites were present at ≥ 5% of applied radioactivity. CSCD656832 was present at up to 10% in Ohio soil and CSCD642512 was present at up to 6% in Michigan soil. SYN503780 was present at a maximum 6% of applied radioactivity in four of the seven soils. CSCD163768 and CSAA757083 were minor metabolites in the soils tested (maximum levels 0.9% and approximately 2% of applied radioactivity respectively). No other extractable metabolite was observed at a significant level (maximum levels of 4%). Mineralisation to carbon dioxide was a major end point of metabolism in the seven soils investigated (range 4.8–44.1% by end of incubation period).

Table 24 Distribution of radioactivity in bicyclopyrone-treated soil at 20 °C (aerobic conditions) following application of [pyridine -^{14}C] bicyclopyrone-Georgia Soil

Incubation Time [d]	Mean Percent Applied Radioactivity						
	CO_2	Extractables				Non-extractables	Recovery
		$CaCl_2$ Extract	Basic Extract	Reflux Extract	Sum		
0	-	80.5	19.3	-	99.8	-	99.8
8	0.6	51.3	41.0	5.4	97.6	1.2	99.4
14	1.4	41.3	47.3	6.1	94.6	1.7	97.7
22	1.9	31.4	52.6	8.0	92.0	2.0	95.9
35	2.8	26.4	57.4	7.7	91.5	2.5	96.8
50	3.6	23.0	59.3	6.5	88.7	1.5	93.8
79	7.4	20.4	50.6	13.2	84.1	4.0	95.5
120	13.4	17.8	46.8	14.5	79.0	4.6	96.9
181	17.0	14.6	43.7	16.0	74.3	5.8	97.0
272	24.0	12.4	45.6	11.7	69.7	5.0	98.6
365	33.6	9.5	35.1	13.4	58.0	6.9	98.4

Table 25 Distribution of radioactivity in bicyclopyrone-treated soil at 20 °C (aerobic conditions) following application of [pyridine -^{14}C] bicyclopyrone-Illinois Soil

Incubation Time [d]	Mean Percent Applied Radioactivity						
	CO_2	Extractables				Non-extractables	Recovery
		$CaCl_2$ Extract	Basic Extract	Reflux Extract	Sum		
0	-	55.3	40.1	2.0	97.3	0.4	97.7
8	1.3	36.6	45.2	8.5	90.3	3.5	95.0
14	3.0	29.8	51.8	7.7	89.2	4.2	96.3
22	3.6	26.8	51.4	9.5	87.6	4.6	95.8
35	4.6	19.4	53.7	12.5	85.5	7.0	97.1
50	5.1	17.6	54.1	12.7	84.3	6.9	96.3
79	6.5	14.9	52.6	14.2	81.7	8.8	96.9
120	7.1	12.4	43.8	17.8	74.0	12.3	93.3

Table 26 Distribution of radioactivity in ^{14}C-bicyclopyrone-treated soil at 20 °C (aerobic conditions) following application of [pyridine -^{14}C] bicyclopyrone-North Carolina Soil

Incubation Time [d]	Mean Percent Applied Radioactivity						
	CO_2	Extractables				Non-extractables	Recovery
		$CaCl_2$ Extract	Basic Extract	Reflux Extract	Sum		
0	-	73.3	25.2	-	98.5	-	98.5
8	0.2	41.6	54.0	1.6	97.2	0.5	97.9
14	0.3	34.6	60.0	1.6	96.1	0.5	96.9
22	0.5	31.2	62.1	1.8	95.1	0.7	96.3
35	0.8	29.0	64.8	2.2	96.0	0.9	97.7
50	0.8	21.4	73.0	2.2	96.6	0.9	98.2
79	2.1	19.9	71.6	3.4	94.9	1.6	98.5
120	4.8	19.3	69.9	4.5	93.6	2.2	100.5

Table 27 Distribution of radioactivity in ^{14}C-bicyclopyrone-treated soil at 20 °C (aerobic conditions) following application of [pyridine -^{14}C] bicyclopyrone-Minnesota Soil

Incubation Time [d]	Mean Percent Applied Radioactivity						
	CO_2	Extractables				Non-extractables	Recovery
		$CaCl_2$ Extract	Basic Extract	Reflux Extract	Sum		
0	-	60.5	37.5	2.1	100.1	0.4	100.5
8	0.9	50.2	37.7	8.3	96.1	2.6	99.6
14	1.9	47.0	36.6	10.2	93.8	3.9	99.5
22	4.1	41.9	34.9	11.1	87.9	6.1	98.0
35	6.5	40.0	30.8	13.2	83.9	8.5	98.9
50	12.1	33.5	29.6	13.3	76.3	9.8	98.2
79	22.4	24.8	25.9	12.4	63.0	12.0	97.3
120	23.4	22.2	19.8	14.5	56.5	15.2	95.0

Table 28 Distribution of radioactivity in ^{14}C-bicyclopyrone-treated soil at 20 °C (aerobic conditions) following application of [pyridine -^{14}C] bicyclopyrone-Iowa Soil

Incubation Time [d]	Mean Percent Applied Radioactivity						
	CO_2	Extractables				Non-extractables	Recovery
		$CaCl_2$ Extract	Basic Extract	Reflux Extract	Sum		
0	-	40.1	54.5	2.8	97.3	0.7	98.0
8	0.4	26.0	67.5	4.0	97.4	1.4	99.2
14	0.8	20.5	68.9	4.7	94.0	2.1	96.9
22	1.2	16.3	69.2	8.2	93.6	3.3	98.1
35	1.3	13.6	68.3	8.2	90.0	4.5	95.7
50	2.2	12.8	66.7	11.5	90.9	5.6	98.7
79	3.0	12.0	59.2	16.3	87.5	7.1	97.5
120	5.1	10.3	58.8	13.0	82.0	6.9	93.9

Table 29 Distribution of radioactivity in ^{14}C-bicyclopyrone-treated soil at 20 °C (aerobic conditions) following application of [pyridine -^{14}C] bicyclopyrone-Michigan Soil

Incubation Time [d]	Mean Percent Applied Radioactivity						
	CO_2	Extractables				Non-extractables	Recovery
		$CaCl_2$ Extract	Basic Extract	Reflux Extract	Sum		
0	-	76.2	23.7	0.1	100.0	-	100.0
8	0.6	57.2	37.0	3.3	97.4	1.2	99.2
14	1.8	41.7	47.4	4.9	94.0	2.1	97.8
22	2.9	29.5	57.7	5.5	92.6	3.8	99.2
35	3.5	23.1	60.4	5.7	89.2	3.2	95.8

Incubation Time [d]	Mean Percent Applied Radioactivity						
	CO_2	Extractables				Non-extractables	Recovery
		$CaCl_2$ Extract	Basic Extract	Reflux Extract	Sum		
50	4.5	19.7	61.1	8.3	89.0	3.8	97.3
79	6.0	17.5	61.2	8.9	87.6	4.0	97.5
120	10.4	14.3	54.0	9.1	77.4	4.9	92.6

Table 30 Distribution of radioactivity in ^{14}C-bicyclopyrone-treated soil at 20 °C (aerobic conditions) following application of [pyridine -^{14}C] bicyclopyrone-Ohio Soil

Incubation Time [d]	Mean Percent Applied Radioactivity						
	CO_2	Extractables				Non-extractables	Recovery
		$CaCl_2$ Extract	Basic Extract	Reflux Extract	Sum		
0	-	63.4	35.1	0.7	99.1	0.2	99.2
8	1.4	48.4	44.3	2.9	95.5	1.6	98.5
14	2.6	43.9	45.5	3.8	93.2	2.5	98.3
22	6.6	38.0	41.3	6.1	85.3	3.9	95.8
35	10.9	32.1	37.9	7.7	77.7	7.1	95.7
50	19.2	22.7	34.6	10.1	67.3	11.3	97.8
79	33.0	12.5	28.1	9.3	49.9	13.5	96.3
120	44.1	7.5	17.9	9.4	34.8	17.0	95.9

Half-lives of bicyclopyrone in the seven soils were calculated using linear regression analysis. The DT_{50} values were 59, 108, 141, 159, 331, 335 and 357 days for Ohio, Minnesota, Michigan, Illinois, North Carolina, Iowa and Georgia soils, respectively. The results are summarized in the following table.

Table 31 Route and rate of degradation in soil at 20 °C (aerobic conditions) following application of ^{14}C – [pyridine -^{14}C] bicyclopyrone

Soil	First order kinetics			
	DT_{50}	Chi^2	R^2	Prob > t
Ohio	59	1.72	0.9887	8.9×10^{-14}
Minnesota	108	2.07	0.9825	3.2×10^{-13}
Michigan	141*	5.26	0.8526	4.0×10^{-7}
Illinois	159*	1.88	0.9743	2.5×10^{-12}
North Carolina	331*	1.52	0.8747	8.5×10^{-8}
Iowa	335*	1.59	0.8812	5.7×10^{-8}
Georgia	357*	4.72	0.8876	3.3×10^{-10}

* Extrapolated beyond the end of the study

Study 4

The rate of aerobic degradation of bicyclopyrone in representative Brazilian soils, i.e. Argissolo, Latossolo, Neossolo and Gleissolo treated with [^{14}C-pyridinyl-3]- bicyclopyrone at a rate of approximately 300 g ai/ha at a temperature of 20 °C was investigated [Tasso de Souza, 2011, NOA449280_11122]. Samples were taken at DAT=0, 3, 6, 14, 28, 64, 93 and 120.

Soil samples were extracted with 0.05M ammonium hydroxide. The samples were extracted under reflux with acetonitrile:0.05M ammonium hydroxide (50:50 v/v). Extracts were radioassayed by LSC and analysed by HPLC and 2D-TLC to quantify levels of bicyclopyrone and any transformation products that co-chromatographed with reference standards. The post-extraction soils (PES) were combusted in a sample oxidizer and subsequently radioassayed by LSC.

After the 120-day incubation, [^{14}C]-CO_2 comprised 11.0% to 26.2% AR across the four test systems, and the non-extractable radioactivity reached levels of 4.7% to 17.2% AR. Depending on the soil analysed, bicyclopyrone comprised 41.1% to 75.1% AR at the end of the study. Although the rate of transformation of bicyclopyrone differed between soils, the same transformation products were observed in each soil indicating a similar route of transformation. In addition to bicyclopyrone, a total of 8 discrete HPLC peaks were observed in the extracts of the four soils. One peak reached levels above 10% AR and was identified by co-elution with a reference standard as CSCD642512. SYN503780, CSCD656832 and CSCC163768, which were observed at 2.1% AR or less, were also identified by co-elution with reference substances.

Table 32 Distribution of radioactivity in bicyclopyrone-treated soil at 20 °C (aerobic conditions) following application of [pyridinyl-3 -^{14}C] bicyclopyrone – Argissolo Soil

Incubation Time [d]	Mean Percent Applied Radioactivity					
	CO_2	Extractables			Non-extractables	Recovery
		Cold Extract	Reflux Extract	Sum		
0	-	98.5	0.7	99.2	0.4	99.6
3	0.4	91.3	6.1	97.4	2.1	99.9
6	0.6	85.2	10.0	95.1	4.5	100.2
14	3.2	79.6	10.9	90.5	6.1	99.8
28	5.0	73.8	15.3	89.1	10.7	104.7
64	9.0	65.7	13.7	79.4	10.7	99.1
93	10.0	62.4	16.7	79.1	11.3	100.5
120	11.4	57.9	19.0	77.0	13.9	102.3

Table 33 Distribution of radioactivity in bicyclopyrone-treated soil at 20 °C (aerobic conditions) following application of [pyridinyl-3 -^{14}C] bicyclopyrone – Latossolo Soil

Incubation Time [d]	Mean Percent Applied Radioactivity					
	CO_2	Extractables			Non-extractables	Recovery
		Cold Extract	Reflux Extract	Sum		
0	-	95.2	-	95.2	-	95.2
3	0.4	96.2	1.8	98.0	1.2	99.5
6	1.0	90.9	3.5	94.4	3.2	98.6
14	4.5	87.0	4.5	91.5	6.9	102.9
28	11.0	72.0	5.2	77.2	10.0	98.1
64	20.7	62.9	6.4	69.2	12.1	102.0
93	22.7	51.5	7.2	58.7	13.3	94.7
120	26.0	52.0	8.3	60.3	17.2	103.4

Table 34 Distribution of radioactivity in bicyclopyrone-treated soil at 20 °C (aerobic conditions) following application of [pyridinyl-3 -^{14}C] bicyclopyrone – Neossolo Soil

Incubation Time [d]	Mean Percent Applied Radioactivity					
	CO_2	Extractables			Non-extractables	Recovery
		Cold Extract	Reflux Extract	Sum		
0	-	106.7	-	106.7	-	106.7
3	-	103.3	1.2	104.5	0.3	104.7
6	0.2	99.0	2.1	101.0	0.5	101.7
14	0.3	96.1	3.2	99.3	1.0	100.5
28	2.0	92.2	6.1	98.4	1.9	102.2
64	9.0	77.9	10.3	88.2	3.1	100.3
93	9.7	86.1	7.0	93.2	4.1	107.0
120	11.0	77.1	9.3	86.4	4.7	102.0

Table 35 Distribution of radioactivity in bicyclopyrone-treated soil at 20 °C (aerobic conditions) following application of [pyridinyl-3 -^{14}C] bicyclopyrone – Gleissolo Soil

Incubation Time [d]	Mean Percent Applied Radioactivity					
	CO_2	Extractables			Non-extractables	Recovery
		Cold Extract	Reflux Extract	Sum		
0	-	88.4	2.1	90.5	2.4	93.0
3	0.7	88.2	5.3	93.6	2.7	97.0
6	1.0	86.7	5.7	92.4	1.4	94.8
14	5.2	80.6	6.4	87.0	1.5	93.6
28	11.3	75.2	6.3	81.5	7.4	100.2
64	19.2	70.4	10.5	81.0	6.3	106.5
93	22.0	65.1	11.1	76.3	8.9	107.1
120	26.2	54.0	11.7	65.7	14.5	106.4

Kinetic calculations were performed assuming first-order kinetics, using single and two-compartmental models. The DT_{50} and DT_{90} values obtained are shown in Table 35 and 36. The rate of bicyclopyrone transformation in soil varied with half-life values (using the single, first-order model) of 230, 90, 264, and 147 days for Argissolo, Latossolo, Neossolo and Gleissolo soils. Employing a first-order model with two-compartments, half-lives of 308, 82, 433 and 152 days were calculated for Argissolo, Latossolo, Neossolo and Gleissolo soils.

Table 35 Best fit values of half-lives and DT_{90} of bicyclopyrone in soil using a single-compartment model

Soil	Single First-Order (SFO) Model		
	DT_{50} (days)	DT_{90} (days)	R^2
Argissolo	230	732	0.915
Latossolo	90	301	0.943
Neossolo	264	876	0.893
Gleissolo	147	490	0.952

Table 36 Best fit values of half-lives and DT_{90} of bicyclopyrone in soil using a two-compartment model

Soil	First-Order, Two-Compartment Model		
	DT_{50}	DT_{90}	R^2
Argissolo	308	1238	0.995
Latossolo	82	510	0.993
Neossolo	433	1774	0.990
Gleissolo	152	566	0.969

Study 5

The rate of aerobic degradation of bicyclopyrone in sandy loam soils from Borstel and Lorsch, both locations in Germany, treated with bicyclopyrone (non-radiolabelled) at target rates of 0.267 mg/kg, equivalent to a field rate of 200 g as/ha at a temperature of 20 °C was investigated [Fitzmaurice, and Mackenzie, 2008, NOA449280_11011]. The treated soil samples were incubated in the dark at a moisture content equivalent to pF2 (water holding capacity at 0.1 bar, g/100g dry soil) for up to 120 days.

Samples were extracted using suitable solvents (calcium chloride solution, ammonium hydroxide solution, ammonium hydroxide: acetone, and finally acetone). The bicyclopyrone present in the extracts was quantified by LC-MS/MS using methodology based upon a validated soil residue method (GRM030.02A). Bicyclopyrone was steadily degraded, with DT_{50} values of 66.3 and 59.2 days in the Borstel and Lorsch soils, respectively.

Table 37 Rate of degradation in soil at 20 °C (aerobic conditions) following application of [non-radiolabelled] bicyclopyrone

Soil	DT_{50} (days)	Chi^2 (%)	R^2	Prob > t
Borstel	66.3	6.94	0.927	3.0×10^{-8}
Lorsch	59.2	5.31	0.961	5.0×10^{-10}

Study 6

The rate of aerobic degradation of bicyclopyrone in five European soils at a temperature of 20 °C was investigated [Brice and Heslop, 2009, NOA449280_11066]. Bicyclopyrone (non-radiolabelled) was applied to the surface of individual soil samples at a target application rate of 0.267 mg/kg, equivalent to a field rate of 200 g as/ha. Bicyclopyrone was steadily degraded, with DT_{50} values of 92.0, 135, 212, 300 and 372 days in the Terrassa Padovana, Aba, Osthouse, Orzinuovi and Buzet-sur-Tarn soils, respectively.

Table 38 Rate of degradation in soil at 20 °C (aerobic conditions) following application of non-radiolabelled] bicyclopyrone

Soil	SFO			
	DT_{50} (days)	Chi^2 (%)	R^2	Prob > t
Aba	135	8.44	0.756	4.1×10^{-6}
Buzet-sur-Tarn	372	3.30	0.749	9.5×10^{-5}
Orzinuovi	300	5.92	0.603	9.4×10^{-5}
Osthouse	212	7.89	0.618	7.8×10^{-5}
Terrassa Padovana	92.0	5.68	0.945	1.1×10^{-10}

Aerobic degradation of metabolite

Aerobic degradation of SYN503780, major metabolite of bicyclopyrone, was investigated in three European soils by Lewis and Gilbert (2010a, SYN503780_10000). [Pyridine-^{14}C]SYN503780 was applied at a rate of 0.222 mg/kg dry weight of soil, which is equivalent to a single field application rate of 237 g ai/ha of parent (assuming 100% conversion to SYN503780), incorporated into the soil to a depth of 5 cm and assuming a soil bulk density of 1.5 g/cm^3.

The soils were incubated under aerobic conditions in the laboratory and maintained under moist (approximately pF2), dark conditions at 20 ± 2 °C for up to 95 days. Samples were analysed for extractable parent compound, degradation products and unextracted residues. Any volatile radioactivity was continuously flushed from the vessels and collected in liquid traps. A mass balance was determined for each sample. Parent and metabolites were confirmed by HPLC and TLC co-chromatography with reference standards and by LC/MS.

A number of minor unknown metabolites were also observed, each of which individually comprised a maximum of 4.9% of applied radioactivity. Carbon dioxide was a major product of metabolism in all soils, reaching a maximum 68.0, 51.2 and 50.1% of the applied radioactivity by the end of the incubation for Gartenacker, 18 Acres and Marsillargues soils respectively. Unextracted residues were low at 0 DAT (maximum 2.3%), then increased slowly throughout the incubation, reaching a maximum of 20.3 and 16.2% of applied radioactivity at 45 DAT for Gartenacker and 18 Acres soils respectively. The unextracted residue in Marsillargues soil reached a maximum of 36.2% of applied radioactivity at 61 DAT. Bound residue fractionation results from selected samples showed that radioactivity was recovered from all three fractions indicating progressive assimilation and metabolism of the test compound within the soil organic matter fractions.

Table 39 SYN503780: Single First Order (SFO) half-lives in each test soil

Soil	SFO statistics		
	DT_{50} (days)	Chi^2	R2
Gartenacker	4.1	4.9	0.993
18 Acres	5.0	7.1	0.992
Marsillargues	9.1	5.8	0.992
Mean	6.1		

Photochemical degradation in soil

Two soil photo-degradation studies were conducted, incorporating two tests with the pyridinyl label and one with the bicyclo label.

The photolysis of bicyclopyrone was investigated on both dry and moist soil surfaces by Lewis and Gilbert (2010b, NOA449280_11113). The pyridinyl and bicyclo-labelled forms of bicyclopyrone were applied at rates equivalent to approximately 200 g as/ha, to thin layers of either dry or moist soil in individual photolysis vessels. The treated soils were maintained at approximately 20 °C and continuously irradiated for periods of up to the equivalent of approximately 30 days summer sunlight using light from a xenon arc lamp that had been filtered to give a spectral intensity and wavelength distribution close to that of natural sunlight. Degradation rates were determined using single first-order kinetics. The mean mass balance from the irradiated samples was 96.6% (range 87.5–102.2%) and from the dark controls was 96.8% (range 87.9–102.1%).

There was no degradation in samples incubated in the dark in the dry layer tests. In dry-layer tests incubated in the light there was only one degradate present at ≥ 5% of applied radioactivity, namely SYN503780 (maximum 17.2% at 12 DAT). The two minor degradates were CSAA589691 (bicyclo label) and CSCC163768 (pyridinyl label).

There was degradation in samples irradiated and incubated in the dark in the moist layer tests. In addition to parent NOA449280, four known degradates were identified from the pyridinyl label, one of which was present at ≥ 10% of applied radioactivity, namely SYN503780 (maximum 25.3%); CSCC163768, CSCD656832 and CSCD642512 were minor degradates. For the test with [bicyclo-^{14}C] bicyclopyrone, other degradates were detected but all individually comprised ≤ 1% of applied radioactivity.

Table 40 Maximum degradates residues in each test system

Test moisture/ item	% applied radioactivity				
	SYN503780	CSCD656832	CSCC163768	CSCD642512	CSAA589691
Dry/bicyclo	NA	NA	NA	-	4.6
Wet/bicyclo	NA	NA	NA	6.2	1.4
Dry/pyridinyl	17.2	-	1.1	-	NA
Wet/pyridinyl	25.3	4.8	9.6	5.1	NA

NA – not applicable because of label position

Degradation involved cleavage between the two ring systems, yielding pyridinyl and bicyclo ring degradates. Photolytic DT_{50} values were approximately 58 and 25 days in dry soil and in moist soil respectively. Maximum residues of SYN503780 were much higher (25.3% vs 6.3% AR) than those measured in the aerobic metabolism studies conducted in the dark. Elevated SYN503780 residues are thus diagnostic of photolytic breakdown of bicyclopyrone.

Table 41 DT50 Values and kinetic fitting statistics

Test System	Label	$DegT_{50}$	Chi^2	R^2
Dry Soil, Light	Pyridinyl	65.6*	7.28	0.5151
Dry Soil, Light	Bicyclo	50.5*	4.90	0.8033
Moist Soil, Light	Pyridinyl	25.4	3.91	0.9535
Moist Soil, Light	Bicyclo	24.1	1.44	0.9824

* Extrapolated value since study duration was 30 days

In addition to the study presented, the photolysis of bicyclopyrone was investigated in moist soil taken from three sites in the US by Lewis C, Gilbert J, (2011, NOA449280_11118). [Pyridinyl-3-^{14}C] bicyclopyrone was applied to thin layers of moist soil at a rate equivalent to approximately 200 g as/ha. The samples were maintained at approximately 20 °C and were irradiated continuously for periods up to the equivalent of approximately 30 days summer sunlight (15 study days). The mean mass balance from the irradiated samples was 98.1% (range 95.2–100.9%) and from the dark controls was 97.9% (range 94.1–100.4%).

SYN503780 was the major degradation product in light irradiated samples at up to 62.5% AR but only traces (4.7% AR) were measured in the dark control samples. CSCC163768, the degradation product of SYN503780, reached a maximum of 17.8% in the light and 3.1% in the dark.

Table 42 Maximum degradate residues in each test system

Soil	% applied radioactivity			
	SYN503780	CSCD656832	CSCC163768	CSCD642512
Georgia	62.2	8.0	11.7	2.9
Iowa	62.5	7.0	11.9	2.2
Nebraska	35.8	7.6	17.8	4.1

Under continuous irradiation, photolytic DT_{50} values for bicyclopyrone in the three moist soils were in the range 2.0–5.7 days. When adjusted to equivalent summer days at latitudes 30–50°N, the DT_{50} values ranged from 3.9 to 11.0 days. The adjusted values are also applicable to summer days at a latitude of 20°S. Degradation involved cleavage of the bridge between the two ring systems and the main photodegradation product was SYN503780.

Table 43 DT_{50} Values and kinetic-fitting statistics

Soil	DT_{50} (days)		Chi^2	R^2	DT_{50} corrected for rate in microbial degradation study	
	Study days	Summer sunlight days			Study days	Summer sunlight days
Nebraska	5.7	11.0	5.00	0.945	6.2	12.0
Iowa	2.4	4.6	27.9	0.799	2.5	4.8
Georgia	2.0	3.9	27.1	0.808	2.0	3.9

Furthermore, research investigations were conducted by Hand, Nichols, and Kuet (2012, NOA449280_11167), to further elucidate the fate and behaviour of bicyclopyrone when exposed to light. The investigations involved the application of [^{14}C]-labelled bicyclopyrone at a nominal rate equivalent to 200g as/ha and were designed to address the following aspects to assist in the assessment of the relevance of soil photolysis under field conditions:

- Effect of varying the light intensity on the photo-degradation rate in thin soil layers
- Effect of incorporation of bicyclopyrone into 2-5 cm depth soil prior to irradiation
- Validation of the soil core experimental design using water soluble dye

- Movement of bicyclopyrone in intact soil cores after simulated rainfall

Light Intensity

In the study, degradation occurred more rapidly in the soil samples exposed to higher intensity irradiation even after correction to account for variations in the light intensity and hours of incubation. This indicates that there may be additional processes or factors dependent on the incident energy contributing to the susceptibility of bicyclopyrone to photo-degradation and the process is not solely direct photolysis. Furthermore, examination of the results of the guideline studies shows that dry soil yields slower degradation rates than moist soil; it is therefore evident that the presence of water is an important contributor for rapid photo-degradation to occur.

Soil incorporation

This incorporation test was designed to investigate the potential for incorporated bicyclopyrone to migrate up to the surface of a soil layer as a consequence of evaporation of water from the surface, thereby exposing the compound to photolytic processes. The test was conducted with soil from two of the US terrestrial field dissipation study locations: Georgia and Nebraska. In the test using the Georgia soil, bicyclopyrone was mixed by spatula into the top 2 cm of a 5 cm deep layer in a photolysis vessel. In test using the Nebraska soil, the chemical was evenly distributed throughout the 5 cm deep sample. The irradiation intensity was ca 50 W/m2 and the soil moisture was maintained throughout the experiment by daily watering from below and, if required, from above to avoid surface cracking.

The degradation rates of bicyclopyrone found in these tests were significantly faster and the formation of SYN503780 was significantly higher than in the soil degradation studies. This indicated that the test compound had undergone photolytic degradation despite being incorporated into the soil to depths between 2 and 5 cm. As it is known that photolytic degradation can only occur if the test compound is within the top layer of the soil (approximately 1 mm depth), it was hypothesised that bicyclopyrone had been transported by the evaporative flux of water to the surface of the soil thus returning it to the photolytic zone.

Movement of bicyclopyrone in intact soil cores after simulated rainfall

The first test was designed to assess the distribution of bicyclopyrone through the entire soil core following localised application and simulated rainfall. A single core of each soil type was treated with [^{14}C]-bicyclopyrone and the chemical watered in over a period of 60–80 minutes using a volume of water equivalent to 15 mm rainfall. After three hours equilibration, the cores were sectioned and analysed.

A second test was designed to measure the rate of dissipation of bicyclopyrone in soil cores and formation of degradates under simulated field conditions that included sunlight and sub-surface moisture supply. Seven cores of each soil type were treated with [^{14}C]-bicyclopyrone. Simulated rainfall was applied immediately after application and the cores exposed to a day/night cycle of 14 hours irradiation followed by 10 hours rest. To replicate morning dew, a spray of approximately 1 mL water was applied almost daily, the volume of water spray was increased to 2—3 mL for Nebraska and Iowa soils if the cores were visibly dry on the surface.

Following application and simulated rainfall, the radioactivity was widely distributed throughout the core with > 80% of total radioactivity found below the 1 cm horizon, thus demonstrating that the chemical could be rapidly moved away from the soil surface by a single rainfall event.

The results of the tests with the intact soil cores demonstrated that bicyclopyrone could be transported downwards through the soil with rainfall but was available to be returned to the soil surface from at least 5 cm depth. Once returned to the surface bicyclopyrone was rapidly degraded in high yield to the photodegradate SYN503780. The occurrence of the diagnostic degradate in high concentrations demonstrated that bicyclopyrone was predominantly degraded by a photolytic route.

In summary The route of degradation of bicyclopyrone has been studied in numerous aerobic soils using material radiolabelled in two possible positions and is well characterised. A proposed pathway for the degradation of bicyclopyrone from these studies is given in Figure 7. The pathway is essentially derived from the pyridinyl label, since the only components derived from the study with the bicyclo label were minor unidentified components, bound residues and carbon dioxide.

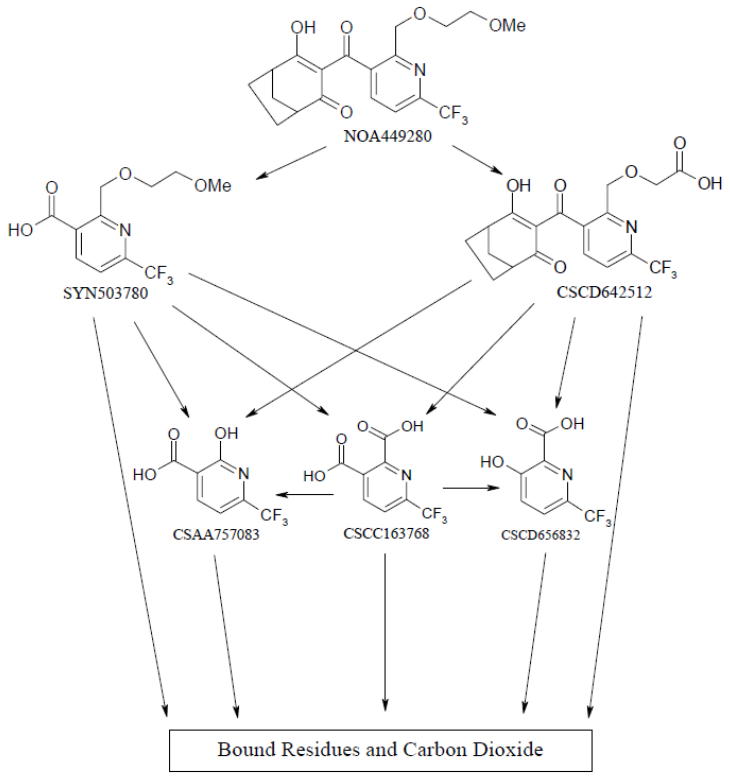


Figure 7 Metabolic pathway of bicyclopyrone in aerobic soil

Hydrolysis

The hydrolytic degradation of bicyclopyrone was investigated at pH ranging from 4 to 9 using [Pyridinyl-^{14}C]-bicyclopyrone and reported by Adam, D. (2008, NOA449280_10121). Bicyclopyrone is stable to hydrolysis at pH values ranging from 4 to 9. After five days of incubation at 50 °C, the test item represented 97.7%, 96.0%, 98.0% and 96.4% of the applied radioactivity for pH 4, 5, 7 and 9, respectively. Based on these results, the DT_{50} was extrapolated to be > 1 year at 25 °C. A second test at 25 °C confirmed these results. After 31 days of incubation, the test item still represented 99.0%, 97.6% and 97.6% of the applied radioactivity for pH 5, 7 and 9, respectively.

Aqueous photolysis

Lewis and Gilbert (2009d, NOA449280_11044) studied the photolysis of bicyclopyrone in sterile aqueous citrate (pH 5), phosphate (pH 7) and borate (pH 9) buffers and in sterilised natural pond water at pH 7.33. Solutions containing 2.5µg [^{14}C] bicyclopyrone /mL were continuously irradiated using light from a xenon arc lamp filtered to give a spectral distribution close to that of natural sunlight. The mean light intensity achieved was 25.1 W/m^2, which was approximately equivalent to 1 day of UK/US summer sunlight for 24 hours continuous irradiation. In addition, quantum yield was determined at pH 5 and pH 7 using an adjustable chemical actinometer irradiated in vessels alongside those in the aqueous photolysis tests.

Preliminary tests were performed using pH 5, pH 7, pH 9 buffers and with natural pond water. The results indicated that while degradation occurred at pH 5 and 7, < 20% degradation of bicyclopyrone would occur at pH 9 after 30 days of light irradiation, therefore no further testing was

conducted at pH 9. Definitive tests were only performed using pH 5, pH 7 buffers and in natural water. In the definitive tests all tests had high mass balance with overall recoveries > 96% applied radioactivity (AR). Three major and two minor degradates were formed.

Degradation occurred by cleavage of the two ring systems then by separate degradation of the two parts of the molecule. The two main photo-degradation products at pH 5 were CSAA589691 from the bicyclo ring system and CSCC163768 from the pyridine ring system. At pH 7 the major photo-degradation product from the pyridine ring system was a compound for which no reference standard was available only an elemental formula could be assigned following LC-MS analysis (Unknown C). This compound was unstable to storage at this pH and is therefore unlikely to persist in the environment.

Table 44 Half-lives and kinetic fitting statistics

Test system	Single first-order kinetics		
	DT_{50} (days)	Chi^2	R^2
pH 5 Buffer	10.2	6.3	0.9565
pH 7 Buffer	50.1	3.1	0.8111
Natural Water	49.7	2.2	0.7833

The proposed degradation pathway from aqueous photolysis is shown in Figure 8. It is clear from the data that bicyclopyrone was extensively degraded under simulated sunlight. The degradation rate was pH-dependent in the order pH 5 > pH 7/natural water > pH 9.

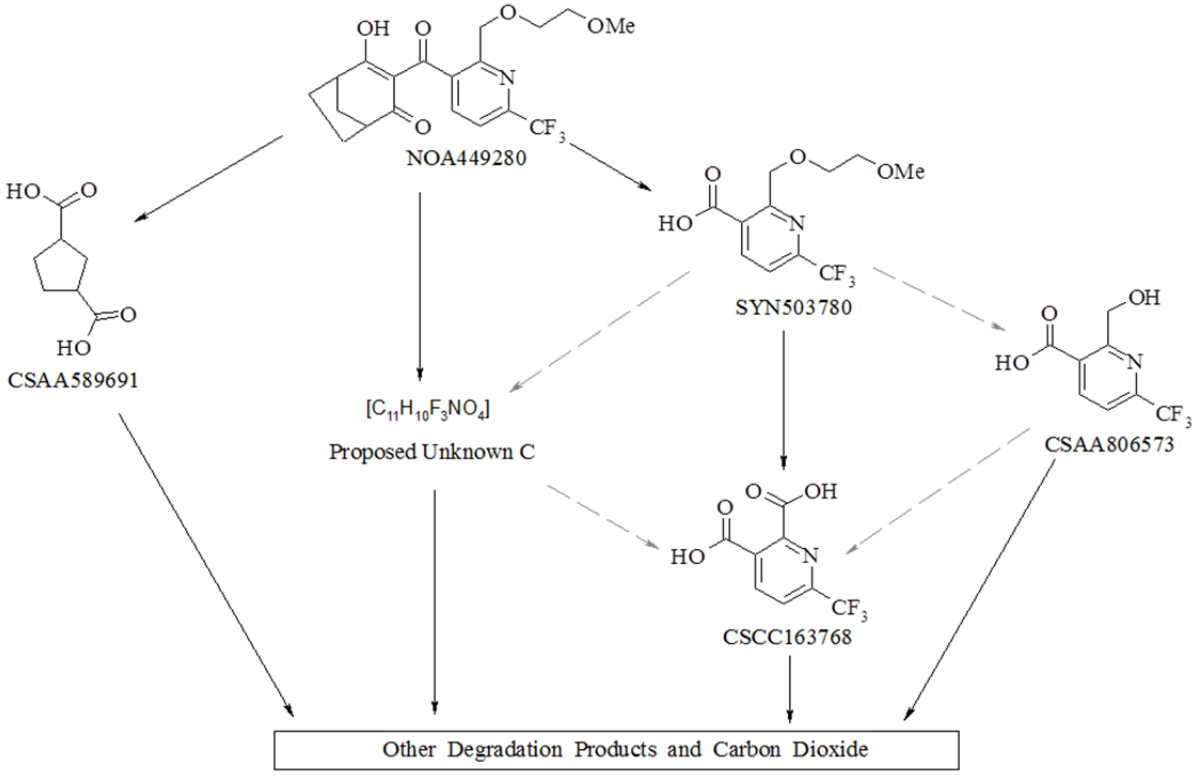


Figure 8 Bicyclopyrone degradation pathway during aqueous hydrolysis

Residues in rotational crops

Confined rotational crop studies

The metabolism of [^{14}C]-bicyclopyrone was investigated by Chapleo, 2010b in the rotational crops wheat, spinach and turnips from three consecutive rotations. The test substance was applied uniformly to the soil of a planting container by spray application (day 0) at nominal rates of 200 g ai/ha and 350 g ai/ha. Crops were sown at day 30, day 120 and day 270. Due to phytotoxicity of the test item to spinach and turnip, further sowings of both were made at 60 DAA and of spinach only at 180 DAA. Harvested crops were separated into commodities of representative food and feed items (wheat forage, hay, straw and grain; spinach immature and mature foliage; turnip foliage and tuberous roots). In addition, soil samples were taken at the time of each sowing ad at final harvest for wheat sown 270 DAA.

Samples of the individual crop commodities with the initial TRR exceeding 0.01 mg/kg were extracted with acetonitrile/water 80:20 v/v; acetonitrile/water 30:70 v/v and acetonitrile. Liquid extracts were analysed directly by LSC and the post extraction solids (PES) combusted and the levels of radioactivity measured by LSC. In order to hydrolyse conjugated metabolites, selected extracts were subjected to acid hydrolysis (1M HCl, approximately 100 °C for 5 hours, followed by liquid-liquid partition).

Residue levels in 30 and 120 DAA hay and straw debris remaining after aqueous acetonitrile and acetonitrile extraction exceeded 10% TRR and 0.05 mg/kg. Subsamples of hay debris fractions, from plants sown 120 DAA (both labels, 350 g ai/ha), which contained the highest unextracted residues and were considered as representative samples were subjected to further extraction under acidic conditions. Each was left to soak overnight in water to hydrate and then subjected to acid hydrolysis in 1M HCl under ambient conditions, at approximately 60 °C and at approximately 90 °C (each approximately 4h). The solid and liquid phases were separated by centrifugation and aspiration allowing radio-assay of the solid and liquid phases to be carried out by combustion analysis and LSC respectively.

Solid debris from the 30 and 120 DAA grain samples and initial acetonitrile:water (70:30 v/v) extracts (containing > 10% TRR & > 0.01 mg/kg) were both characterised for possible starch incorporation. Liquid phases were evaporated to incipient dryness and reconstituted in ethanol to precipitate starch. Debris fractions were extracted with dimethyl sulfoxide/water (DMSO, 9:1 v/v) and ethanol added again to precipitate any starch, solid phases were then incubated with α-amylase (approximately 50 °C, approximately 48h) and ethanol added to precipitate. The α-amylase hydrolysate was investigated for non-polar radioactivity following partitioning with diethyl ether.

Unextracted residues remaining after aqueous acetonitrile, acetonitrile and DMSO/water were subjected to further extraction under various conditions. Each was subjected to sequential hydrolysis in 1M HCl at approximately 60°C and at approximately 90 °C (each approximately 2h) and Driselase (2% Driselase in sodium acetate buffer, approximately pH 4.5, approximately 37 °C, approximately 18h).

The total radioactivity was determined by LSC. Major metabolites were identified and characterized by HPLC and TLC co-chromatography. Confirmation and identification of the radioactive components was carried out by LC-MS and co-chromatography with reference standards. In the following table the TRR found in plant samples are summarized.

Table 45 Total radioactive residues (TRR) in confined rotational crop after treatment at 200 g ai/ha or 350 g ai/ha of ^{14}C bicyclooctenone or ^{14}C-pyridine bicyclopyrone expressed in mg/kg

Crop	Sample	Days after application (DAA)	Bicyclooctenone-^{14}C		Pyridine-^{14}C	
			200 g ai/ha	350 g ai/ha	200 g ai/ha	350 g ai/ha
			mg eq/kg			
Wheat	Forage	30	0.057	0.068	0.066	0.088
	Hay	30	0.240	0.348	0.354	0.516

Crop	Sample	Days after application (DAA)	Bicyclooctenone-^{14}C		Pyridine-^{14}C	
			200 g ai/ha	350 g ai/ha	200 g ai/ha	350 g ai/ha
			mg eq/kg			
	Straw	30	0.275	0.445	0.356	0.497
	Grain	30	0.138	0.181	0.171	0.196
Spinach	Mature leaves	60	0.015	NA	0.014	NA
Turnip	Leaves	60	0.015	0.021	0.019	0.016
	Tubers	60	0.010	0.012	0.009	0.009
Wheat	Forage	120	0.022	0.046	0.051	0.074
	Hay	120	0.109	0.097	0.197	0.248
	Straw	120	0.092	0.108	0.141	0.299
	Grain	120	0.091	0.061	0.098	0.175
Spinach	Immature leaves	120	0.010	NA	0.011	NA
	Mature leaves	120	0.008	NA	0.032	0.016
Turnip	Leaves	120	0.011	0.010	0.018	0.018
	Tubers	120	0.005	0.008	0.008	0.010
Spinach	Mature leaves	180	0.008	0.004	0.005	0.007
Wheat	Forage	270	0.007	0.010	0.037	0.048
	Hay	270	0.040	0.044	0.094	0.160
	Straw	270	0.027	0.048	0.087	0.183
	Grain	270	0.026	0.029	0.038	0.061
Spinach	Immature leaves	270	0.006	0.006	0.008	0.010
	Mature leaves	270	0.007	0.006	0.010	0.009
Turnip	Leaves	270	0.006	0.011	0.009	0.016
	Tubers	270	0.003	0.007	0.005	0.006

NA = not applicable, no samples were available at 350 g ai/ha for analysis

Radioactive residues from crops grown in soil treated at the 350 g ha^{-1} rate were higher than those at the 200 g ha^{-1} rate. Values were generally highest in wheat forage, hay, straw and grain with residues declining between the sowing intervals; values from the [pyridine-3-^{14}C]- labelled experiment generally exceeded those from the [bicyclooctenone-6,7-$^{14}C_2$]-labelled experiment.

Grain at all three plant-back intervals had a significant part of the residue in the form of unextracted radioactivity. The highest levels of discreet metabolites were found in the wheat foliage commodities (forage, hay and straw) which provided an overview of the biotransformation of bicyclopyrone in rotational crops.

The residues in the turnip and spinach indicator crops were much lower at all plant-back intervals though some analysis was possible. In the following tables the extracted and identified radioactivity are presented.

Table 46 Identification and characterization of radioactive residues from confined rotational wheat planted 30 days after a single bare soil application (350 g ai/ha) with ^{14}C-bicyclooctenone and ^{14}C-pyridine bicyclopyrone

Rotational Crop Sample	Component	Bicyclooctenone-^{14}C		Pyridine -^{14}C	
		% of TRR	Residue (mg eq/kg)	% of TRR	Residue (mg eq/kg)
30d Wheat Forage	Bicyclopyrone	3.7	0.002	ND	ND
	CSAA860573	NA	NA	5.5	0.005
	CSCD686480[a]	NA	NA	16.6	0.016
	CSCD675162	13.3	0.009	19.1	0.018
	CSCD677693	9.8	0.006	8.1	0.008

Rotational Crop Sample	Component	Bicyclooctenone-^{14}C		Pyridine -^{14}C	
		% of TRR	Residue (mg eq/kg)	% of TRR	Residue (mg eq/kg)
	Total desmethyl monohydroxy bicyclopyrone isomers[b]	23.1	0.015	27.2	0.026
	CSCD675164	2.4	0.002	4.3	0.004
	CSCD675164 glycoside	9.1	0.006	7.7	0.007
	CSCD677306	10.1	0.007	7.0	0.007
	CSCD677306 glycoside	2.3	0.001	1.9	0.002
	Total monohydroxy bicyclopyrone isomers[a]	23.9	0.016	20.9	0.020
	CSCD677692	2.3	0.001	1.0	0.001
	CSCD677694	5.2	0.003	7.5	0.007
30d Wheat Hay	CSAA860573 glycoside	NA	NA	5.5	0.005
	CSCD686480[a]	NA	NA	21.5	0.105
	CSCD686481	NA	NA	4.4	0.022
	CSCD675162	11.3	0.036	10.9	0.053
	CSCD677693	9.9	0.031	5.3	0.026
	Total desmethyl monohydroxy bicyclopyrone isomers[b]	21.2	0.067	16.2	0.079
	CSCD675164	5.6	0.018	2.4	0.012
	CSCD677306	11.7	0.037	3.4	0.017
	Monohydroxy bicyclopyrone glycoside	12.2	0.038	5.4	0.026
	Total monohydroxy bicyclopyrone isomers[b]	29.5	0.093	11.2	0.055
	CSCD677694	8.6	0.027	4.5	0.022
	CSCD642512	2.6	0.008	1.1	0.005
30d Wheat Straw	Bicyclopyrone	5.8	0.026	1.4	0.007
	CSAA860573[a]	NA	NA	6.5	0.032
	CSCD686480[a]	NA	NA	15.0	0.071
	CSCD686481	NA	NA	4.2	0.020
	CSCD675162	11.4	0.051	7.7	0.037
	CSCD677693/CSCD677694	≤ 12.7	≤0 .057	≤ 8.2	≤ 0.039
	Total desmethyl monohydroxy bicyclopyrone isomers[2]	≤ 24.1	≤ 0.108	≤ 15.9	≤ 0.076
	CSCD675164/CSCD677306	≤ 6.9	≤ 0.031	≤ 12.5	≤0.060
	Monohydroxy bicyclopyrone glycoside	7.9	0.035	4.5	0.022
	Total monohydroxy bicyclopyrone isomers[b]	≤ 14.8	≤ 0.066	≤ 17.0	≤ 0.082
	CSCD642512	3.6	0.016	1.8	0.009
30d Wheat Grain	CSAA860573 glycoside	NA	NA	4.1	0.007
	CSCD686480[1]	NA	NA	9.8	0.018
	CSCD675162	3.8	0.005	2.9	0.005
	CSCD675162 glycoside	0.7	0.001	ND	ND
	CSCD677693	1.8	0.003	2.5	0.005
	Total desmethyl monohydroxy bicyclopyrone isomers[2]	6.3	0.009	5.4	0.010
	CSCD675164	2.2	0.003	2.2	0.004
	CSCD675164 glycoside	1.6	0.002	5.0	0.009
	CSCD677306	3.3	0.005	2.6	0.005
	CSCD677306 glycoside	4.9	0.007	ND	ND
	Total monohydroxy bicyclopyrone isomers[b]	12.0	0.017	9.8	0.018
	CSCD677692	1.1	0.002	ND	ND
	CSCD677694	4.2	0.006	2.9	0.005

ND = not detected

NA = not applicable

[a]Total for metabolite includes glycosides

[b]Total of all isomers with these structural characteristics including specific metabolites, metabolites of undefined substitution specificity, and conjugates

Table 47 identification and characterization of radioactive residues from confined rotational wheat planted 120 days after a single bare soil application (350 g ai/ha) with ^{14}C-bicyclooctenone and ^{14}C-pyridine bicyclopyrone

Rotational Crop Sample	Component	Bicyclooctenone-^{14}C		Pyridine -^{14}C	
		% of TRR	Residue (mg/kg)	% of TRR	Residue (mg/kg)
120d Wheat Forage	Bicyclopyrone	4.3	0.002	1.4	0.001
	CSCD656832[1]	NA	NA	10.0	0.006
	CSAA860573[1]	NA	NA	6.2	0.003
	CSCD686480[1]	NA	NA	9.5	0.006
	CSCD675162	11.0	0.004	5.8	0.004
	CSCD677693	7.4	0.003	5.1	0.003
	Total desmethyl monohydroxy bicyclopyrone isomers[2]	18.4	0.007	10.9	0.007
	CSCD675164	6.7	0.002	4.0	0.003
	CSCD675164 glycoside	5.0	0.002	1.3	0.001
	CSCD677306	14.7	0.005	7.7	0.005
	CSCD677306 glycoside	ND	ND	2.2	0.001
	Total monohydroxy bicyclopyrone isomers[2]	26.4	0.009	15.2	0.010
	CSCD677694	5.6	0.002	3.1	0.002
	CSCD642512	1.7	0.001	ND	ND
120d Wheat Hay	Bicyclopyrone	1.1	0.001	2.4	0.005
	CSCD656832[a]	NA	NA	10.1	0.020
	CSAA757083	NA	NA	2.0	0.004
	CSAA860573[a]	NA	NA	5.3	0.011
	CSCD675162	6.8	0.007	5.5	0.011
	CSCD677693	4.2	0.004	5.8	0.012
	Total desmethyl monohydroxy bicyclopyrone isomers[b]	11.0	0.011	11.3	0.023
	CSCD675164	6.6	0.006	4.7	0.010
	CSCD675164 glycoside	ND	ND	2.0	0.004
	CSCD677306	12.3	0.012	8.4	0.017
	Total monohydroxy bicyclopyrone isomers[b]	18.9	0.018	15.1	0.031
	CSCD686480[1]	NA	NA	13.9	0.029
	CSCD677694	2.2	0.002	2.8	0.006
120d Wheat Straw	Bicyclopyrone	2.1	0.002	1.5	0.004
	CSCD656832[a]	NA	NA	9.2	0.027
	CSCC163768	NA	NA	2.1	0.006
	CSAA860573[a]	NA	NA	6.2	0.017
	CSCD686480[a]	NA	NA	7.3	0.020
	CSCD686481	NA	NA	4.9	0.014
	CSCD675162	9.2	0.009	3.6	0.010
	CSCD677693	4.3	0.004	4.0	0.011
	Total desmethyl monohydroxy bicyclopyrone isomers[b]	13.5	0.013	7.6	0.021
	CSCD675164	5.3	0.005	2.4	0.007
	CSCD675164 glycoside	3.1	0.003	ND	ND
	CSCD677306	7.7	0.008	3.2	0.009
	CSCD677306 glycoside	2.8	0.003	ND	ND
	Total monohydroxy bicyclopyrone isomers[b]	18.9	0.019	5.6	0.016
	CSCD677692	1.1	0.001	1.1	0.003
	CSCD677694	5.3	0.005	2.4	0.007
	CSCD642512	5.9	0.006	3.5	0.010
120d Wheat Grain	CSCD656832[a]	NA	NA	5.9	0.010
	CSAA860573[a]	NA	NA	3.2	0.006
	CSCD686480[a]	NA	NA	8.1	0.014
	CSCD686481	NA	NA	1.0	0.002

Rotational Crop Sample	Component	Bicyclooctenone-^{14}C		Pyridine -^{14}C	
		% of TRR	Residue (mg/kg)	% of TRR	Residue (mg/kg)
	CSCD677694	1.2	0.001	0.5	0.001
	CSCD675162	1.3	0.001	0.6	0.001
	CSCD677693	0.4	< 0.001	ND	ND
	Total desmethyl monohydroxy bicyclopyrone isomers[b]	1.7	0.001	0.6	0.001
	CSCD675164	1.8	0.001	0.8	0.001
	CSCD675164 glycoside	0.6	< 0.001	0.4	0.001
	CSCD677306	2.7	0.002	1.0	0.002
	CSCD677306 glycoside	ND	ND	0.5	0.001
	Total monohydroxy bicyclopyrone isomers[b]	5.1	0.003	2.7	0.005

ND = not detected

NA = not applicable

[a]Total for metabolite includes glycosides

[b]Total of all isomers with these structural characteristics including specific metabolites, metabolites of undefined substitution specificity, and conjugates

Table 48 Identification and characterization of radioactive residues from confined rotational wheat planted 270 days after a single bare soil application (350 g ai/ha) with ^{14}C-bicyclooctenone and ^{14}C-pyridine bicyclopyrone

Rotational Crop Sample	Component	Bicyclooctenone-^{14}C		Pyridine -^{14}C	
		% of TRR	Residue (mg eq/kg)	% of TRR	Residue (mg eq/kg)
270d Wheat Forage	Bicyclopyrone	NC	NC	1.7	0.001
	CSCD656832[a]	NC	NC	39.3	0.018
	CSCC163768	NC	NC	5.0	0.002
	CSCD686480 glycoside	NC	NC	14.8	0.007
	CSCD677694	NC	ND	2.7	0.001
	CSCD675162	NC	ND	5.9	0.003
	Total monohydroxy bicyclopyrone isomers[b]	NC	ND	7.6	0.004
270d Wheat Hay	Bicyclopyrone	2.0	0.001	ND	ND
	CSCD656832[a]	NA	NA	41.2	0.064
	CSAA860573[a]	NA	NA	8.6	0.013
	CSCD686480[a]	NA	NA	18.7	0.029
	CSCD677694	6.4	0.003	2.4	0.004
	CSCD675162	3.3	0.001	3.4	0.005
	CSCD677693	ND	ND	1.8	0.003
	Total desmethyl monohydroxy bicyclopyrone isomers[b]	3.3	0.001	5.2	0.008
	CSCD675164	6.3	0.003	2.2	0.003
	CSCD677306	10.8	0.004	3.1	0.005
	CSCD677306 glycoside	3.5	0.001	ND	ND
	Total monohydroxy bicyclopyrone isomers[b]	20.6	0.008	5.3	0.008
270d Wheat Straw	CSCD656832[a]	NA	NA	35.3	0.056
	CSAA860573 glucoside	NA	NA	7.9	0.013
	CSCD686480[l]	NA	NA	11.8	0.019
	CSCD677692	ND	ND	0.5	0.001
	CSCD675162	ND	ND	2.3	0.004
	CSCD642512	ND	ND	1.2	0.002
	CSCD675164/CSCD677306	≤17.7	≤0.008	1.5	0.002
	Mono bicyclopyrone glycoside	≤7.4	≤0.003	ND	ND
	Total monohydroxy bicyclopyrone isomers[b]	≤25.1	≤0.011	4.4	0.007

Rotational Crop Sample	Component	Bicyclooctenone-^{14}C		Pyridine -^{14}C	
		% of TRR	Residue (mg eq/kg)	% of TRR	Residue (mg eq/kg)
270d Wheat Grain	CSCD656832[a]	NC	NC	15.9	0.009
	CSAA860573 glycoside	NC	NC	2.2	0.001
	CSCD686480[a]	NC	NC	14.0	0.008
	CSCD677306	NC	NC	3.2	0.002

NC = not chromatographed

NA = not applicable

ND = not detected

[a] Total for metabolite includes glycosides

[b] Total of all isomers with these structural characteristics including specific metabolites, metabolites of undefined substitution specificity, and conjugates

Table 49: Identification and characterization of radioactive residues from confined rotational turnips planted 60 days or 270 days after a single bare soil application (350 g ai/ha) with ^{14}C-bicyclooctenone

Rotational Crop Sample	Component	Bicyclooctenone-^{14}C		Pyridine -^{14}C	
		% of TRR	Residue (mg eq/kg)	% of TRR	Residue (mg eq/kg)
60d Turnip Foliage	Bicyclopyrone	3.8	0.001	ND	ND
	CSCD675162	3.5	0.001	ND	ND
	CSCD677693	2.8	0.001	ND	ND
	Total desmethyl monohydroxy bicyclopyrone isomers [a]	6.3	0.002	ND	ND
	CSCD675164	33.7	0.007	ND	ND
	CSCD677306	10.6	0.002	ND	ND
	Total monohydroxy bicyclopyrone isomers [a]	44.3	0.009	ND	ND
60d Turnip Tubers	CSCD675164	32.8	0.005	ND	ND
270d Turnip Foliage	CSCD656832[a]	ND	ND	70.6	0.012

[a] Total of all isomers with these structural characteristics including specific metabolites, metabolites of undefined substitution specificity, and conjugates

Table 50 Identification and characterization of radioactive residues from confined rotational spinach planted 120 days after a single bare soil application (350 g ai/ha) with ^{14}C-pyridine bicyclopyrone, and confined rotational spinach planted 180 days after a single bare soil application (350 g ai/ha) with ^{14}C-bicyclooctenone and ^{14}C- pyridine bicyclopyrone

Rotational Crop Sample	Component	Bicyclooctenone-^{14}C		Pyridine -^{14}C	
		% of TRR	Residue (mg eq/kg)	% of TRR	Residue (mg eq/kg)
120d Spinach	Bicyclopyrone	ND-	ND-	69.7	0.030
180d Spinach	Bicyclopyrone	19.1	0.002	12.4	0.001
	CSAA915194[a]	5.9	< 0.001	2.4	< 0.001

[a] Tentative identification, detected in one chromatographic system

The key observations from identification work were as follows (unless otherwise stated, the percent TRRs and mg/kg quoted were the highest observed for all rotational interval and radiolabelled experiments):

- Low levels of bicyclopyrone were detectable in wheat (up to 5.8% TRR and 0.026 mg/kg) and turnip foliage (up to 3.8% TRR and 0.001 mg/kg). Higher residues were determined in spinach exhibiting phytotoxicity (up to 69.7% TRR and 0.030 mg/kg).
- Two monohydroxy bicyclopyrone isomers, shown to be present in wheat in both the free and glycoside conjugated metabolite forms, collectively accounted for up to 29.5% TRR and 0.093 mg eq/kg. Individually these isomers accounted for up to 23.9% TRR and 0.082 mg eq/kg (CSCD677306) and up to 25.1% TRR and 0.082 mg eq/kg (CSCD675164). The free metabolites were also found to be present in early rotation turnip foliage but at much lower absolute residue levels, accounted for up to 10.6% TRR and 0.002 mg eq/kg (CSCD677306) and up to 33.7% TRR and 0.007 mg eq/kg (CSCD675164).
- Two desmethyl monohydroxy-bicyclopyrone isomers, shown to be present in wheat in only the free metabolite form, collectively accounted up to 27.2% TRR and 0.108 mg eq/kg. Individually these metabolites accounted for up to 12.7% TRR and 0.057 mg eq/kg (CSCD677693) and up to 19.1% TRR and 0.053 mg eq/kg (CSCD675162).
- Two metabolites present in wheat with structures that retained only the pyridine ring of bicyclopyrone, both of which were found in the free and glycoside conjugated metabolite forms, accounted for up to 21.5% TRR and 0.105 mg eq/kg (CSCD686480) and up to 41.2% TRR and 0.064 mg eq/kg (CSCD656832). CSCD656832 was also present in turnip foliage but at much lower absolute residue levels, accounted for up to 70.6% TRR and 0.012 mg eq/kg.
- A dihydroxy-bicyclopyrone metabolite (CSCD677694), shown to be present in wheat in the free form, accounted for up to 12.7% TRR and 0.057 mg eq/kg.
- Significant proportions of the residue in wheat grain (up to 37.5%TRR) were shown to be attributable to naturally incorporated radioactivity.

The principal metabolism transformations of bicyclopyrone observed in rotational crops involve:

- Hydroxylation of the bicyclooctenone ring to produce monohydroxylated and dihydroxylated bicyclopyrone.
- Cleavage between the bicyclooctenone and pyridine ring systems of bicyclopyrone.
- O-demethylation, and successive oxidation of the methoxyethoxymethyl side-chain of bicyclopyrone to produce desmethyl, carboxyl and alcohol metabolites.
- Conjugation of some of the metabolites to from their O-glycosides.

In summary, the metabolic pathway of bicyclopyrone residues after uptake into succeeding crops is very similar to the pathways observed in primary crops of maize, sugar cane and soya. Qualitatively, the biotransformation pathways for bicyclopyrone in rotational crops and primary crops (corn, sugarcane and soya bean) were similar. CSAA757083, a known soil metabolite was found at very low levels (2.0% TRR, 0.004 mg eq/kg) in wheat hay from the 120-day plant-back interval. Otherwise the identified metabolites in rotational crops of wheat, turnips and spinach were identical to the metabolites identified in primary crops.

Quantitatively, metabolites resulting from bridge cleavage were more prevalent in the rotational crops than the primary crops and were formed to a larger extent in the later plant-back intervals compared with the crops at the 30 day interval.

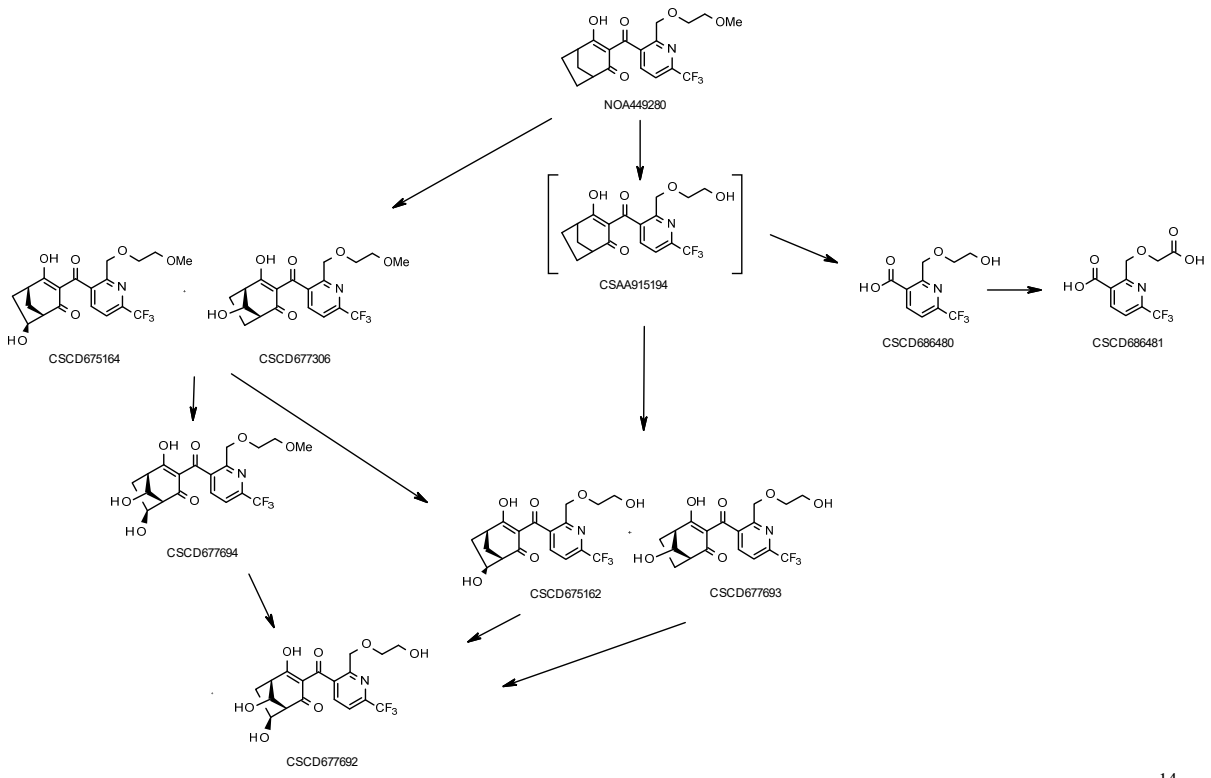


Figure 9 Proposed metabolic pathway of bicyclopyrone in rotational crops after application of ^{14}C-bicyclooctenone and ^{14}C- pyridine bicyclopyrone

Field Rotational Crop Studies

The Meeting received information on the metabolism of bicyclopyrone in wheat, spinach and radish grown as field rotational crops and in a range of representative field crops grown in bicyclopyrone-treated soil.

The metabolic profile of bicyclopyrone in rotational radish (leaves and roots), spinach (leaves) and wheat (forage, hay, straw, and grain) was investigated (Oakes T (2012a, EC_50011). In this study, bare ground was treated with bicyclopyrone formulated as an emulsifiable concentrate (EC) at a rate of 200 g ai/ha. The rotational crops were planted into the treated plots at plant-back intervals of 90, 150, 187, and 270 days after treatment.

Samples were harvested at normal maturity and homogenized in the presence of dry ice. Due to difficulties in obtaining spinach samples caused by poor germination and weather, an additional spinach trial was added in Texas (trial number W07TX091450) that provided 90 and 187 day plant back data for spinach. Homogenized samples were extracted with acetonitrile; water (80:20 v/v), centrifuged and filtered prior to analysis. Residues of bicyclopyrone and metabolites in rotational crops were determined using Syngenta Methods GRM030.03A and GRM030.05A, respectively. The LOQ for bicyclopyrone, SYN503780, bicyclopyrone as SYN503780, CSAA915194 as CSCD686480 and CSAA806573 in all matrices was 0.01 mg/kg. The mean concurrent recoveries were all between 70 and 120 for all analytes in all matrices using both analytical methods. The percent relative standard deviations were all ≤ 20%. These data indicate acceptable performance of the methods during the conduct of this study.

No residues of bicyclopyrone or SYN503780 (Method GRM030.03A) were found for any sample at any time interval. The only detectable residues found were either SYN503780 or CSCS686480 (Common Moiety Method – GRM030.05A)

In spinach, samples were analysed from trials in Georgia (E13GA081441, E13GA081442) and Texas (W07TX091450). Samples from other locations and intervals were not available as the

results of weather conditions and poor germination. A detectable residue of 0.01 mg/kg SYN503780 was found in the Georgia site at 90 days but no residues were found in the Georgia site at 150 plant back or at either of the Texas 90 or 187 day plant back intervals.

Table 51 Residues of bicyclopyrone in rotational spinach

Field Test No./ Location	Nominal Plant Back Interval	Total Trt. Rate (g ai/ha)	Method (GRM030.03A)		Method (GRM030.05A)	
			Bicyclopy-rone (mg/kg)	SYN 503780 (mg/kg)	SYN 503780 (mg/kg)	CSCD 686480 (mg/kg)
E13GA081441/ Georgia	90	Control	< 0.01	< 0.01	< 0.01	< 0.01
	90	200	< 0.01	< 0.01	0.011	< 0.01
	90	200	< 0.01	< 0.01	0.013	< 0.01
E13GA081442/ Georgia	150	Control	< 0.01	< 0.01	< 0.01	< 0.01
	150	200	< 0.01	< 0.01	< 0.01	< 0.01
	150	200	< 0.01	< 0.01	< 0.01	< 0.01
W07TX091450/ Texas	90	Control	< 0.01	< 0.01	< 0.01	< 0.01
	90	200	< 0.01	< 0.01	< 0.01	< 0.01
	90	200	< 0.01	< 0.01	< 0.01	< 0.01
W07TX091450/ Texas	187	Control	< 0.01	< 0.01	< 0.01	< 0.01
	187	200	< 0.01	< 0.01	< 0.01	< 0.01
	187	200	< 0.01	< 0.01	< 0.01	< 0.01

In Radish, samples were analysed from trials in Georgia (E13GA081441, E13GA081442) and Missouri (C23MO081444, C23MO081447, C23MO081446 and C23MO081449). No residues of any of the analytes above the limit of quantification were found in the radish root samples from all the plant back intervals.

In radish tops, residues of CSCD686480 were found in the 90-day plant back trials in Georgia and in Missouri (C23MO081444), and in the 150-day plant back trial in Missouri (C23MO081445). All other locations had no residues above the LOQ.

Table 52 Residues of bicyclopyrone in rotational radish tops

Field Test No./ Location	Nominal Plant Back Interval	Total Trt. Rate (g ai/ha)	Method (GRM030.03A)		Method (GRM030.05A)	
			Bicyclopyrone (mg/kg)	SYN 503780 (mg/kg)	SYN 503780 (mg/kg)	CSCD 686480 (mg/kg)
E13GA081441 Georgia	90	Control	< 0.01	< 0.01	< 0.01	< 0.01
	90	200	< 0.01	< 0.01	< 0.01	0.016
	90	200	< 0.01	< 0.01	< 0.01	0.025
C23MO081444 Missouri	90	Control	< 0.01	< 0.01	< 0.01	< 0.01
	90	200	< 0.01	< 0.01	< 0.01	0.011
	90	200	< 0.01	< 0.01	< 0.01	< 0.01
C23MO081447 Missouri	90	Control	< 0.01	< 0.01	< 0.01	< 0.01
	90	200	< 0.01	< 0.01	< 0.01	< 0.01
	90	200	< 0.01	< 0.01	< 0.01	< 0.01
E13GA081442 Georgia	150	Control	< 0.01	< 0.01	< 0.01	< 0.01
	150	200	< 0.01	< 0.01	< 0.01	< 0.01
	150	200	< 0.01	< 0.01	< 0.01	< 0.01
C23MO081445 Missouri	150	Control	< 0.01	< 0.01	< 0.01	< 0.01
	150	200	< 0.01	< 0.01	< 0.01	0.013
	150	200	< 0.01	< 0.01	< 0.01	0.016
E13GA081443 Georgia	270	Control	< 0.01	< 0.01	< 0.01	< 0.01
	270	200	< 0.01	< 0.01	< 0.01	< 0.01
	270	200	< 0.01	< 0.01	< 0.01	< 0.01

Field Test No./ Location	Nominal Plant Back Interval	Total Trt. Rate (g ai/ha)	Method (GRM030.03A)		Method (GRM030.05A)	
			Bicyclopyrone (mg/kg)	SYN 503780 (mg/kg)	SYN 503780 (mg/kg)	CSCD 686480 (mg/kg)
C23MO081446 Missouri	270	Control	< 0.01	< 0.01	< 0.01	< 0.01
	270	200	< 0.01	< 0.01	< 0.01	< 0.01
	270	200	< 0.01	< 0.01	< 0.01	< 0.01
C23MO081449 Missouri	270	Control	< 0.01	< 0.01	< 0.01	< 0.01
	270	200	< 0.01	< 0.01	< 0.01	< 0.01
	270	200	< 0.01	< 0.01	< 0.01	< 0.01

In wheat, no residues above the LOQ (0.01 mg/kg) of any analyte were found in any samples (forage, hay, straw, or grain) at any location or interval (90, 150 or 270 day). This study supports a 270-day plant back interval for all crops following application of bicyclopyrone at 200 g ai/ha or less.

A further study with twenty field trials was conducted at an application rate of 200 g ai/ha to generate residue data for wheat planted 90-days after application of bicyclopyrone to bare ground for winter wheat or 270 days after application for spring wheat (Oakes, (2012b, EC_10003).

For winter wheat trials only, autumn forage was collected 45 days after planting (DAP). For all wheat trials forage was collected at 150–200 mm (6 to 8 inch) stage to stem elongation. Hay was sampled at early flower to soft dough and straw and grain samples were collected at maturity.

For the winter wheat residue decline trial, fall forage samples were collected at 31, 38, 45, and 52 DAP. For both the winter wheat and spring wheat residue decline trials, spring forage samples were collected at 14 days prior, 7 days prior, at 6 to 8 inch stage to stem elongation, and 7 days after. Hay was collected at 7 and 14 days prior to early flower (boot) to soft dough stage, early flower (boot) to soft dough stage (target harvest) and 7 days after target harvest. Straw and grain samples were collected at 14 days prior, 7 days prior, at maturity, and 7 days after maturity.

For the processing trials, bulk grain (~90 kg) was collected at maturity for processing into bran, flour, middlings, shorts, and germ.

Residues of bicyclopyrone and metabolites in wheat grain, forage, straw, and hay and in wheat processed fractions were determined using Syngenta Methods GRM030.03A and GRM030.05A. The limit of quantification (LOQ) for bicyclopyrone, SYN503780, CSAA915194 as CSCD686480 and CSAA806573 in wheat grain, forage, straw, and hay and in wheat processed fractions was 0.01 mg/kg.

In autumn forage (winter wheat), the only residues quantified included bicyclopyrone analysed directly via Method GRM030.03A and common moiety residue of SYN503780 analysed via method GRM030.05A. All other analytes in all other wheat matrices were <LOQ (0.01 mg/kg).

In the decline trials, these residues did decrease with longer intervals to harvest. All other residues were <LOQ in all matrices, including processed fractions. No residues were detected in any untreated wheat RAC or processed fraction samples. For field trial E19IA081776 (winter wheat), residues in autumn forage decreased with time. No residues were found in spring forage or hay, straw, and grain. No residues were found in any wheat matrix sample for field trial C13ND081781 (spring wheat).

Two field trials in this study were conducted on winter (C18IA081775) and spring (C13ND081782) wheat to generate bulk grain samples for processing. Wheat grain was processed into bran, flour, gluten feed meal, starch, shorts, whole meal flour, whole grain bread, milled by-products, middlings, gluten, and germ. No residues above LOQ were detected in any grain or processed commodity samples thus no residue concentration was observed. The residue results are presented in the following table:

Table 53 Residue data for bicyclopyrone and metabolites on rotational wheat

GLP and Trial Details	Crop (Variety)	Country (Region)	Form'n Type and Content (g/L)	Bare ground Application			Crop Part2	DAP[a] (days)	Residues1 (mg/kg)			
				Rate (g ai/ha)	Volume (L/ha)	Growth Stage			Method GRM030.03A		Common Moiety Method GRM030.05A	
									Bicyclop-yrone	SYN 503780	SYN 503780	CSCD 686480
Report: T000764-08 Study: T000764-08 Trial: E19NC081771 - Study to GLP - Carried out in 2008/09	Wheat (Coker 9663)	United States (NAFTA/ Region 2)	250 EC	197.4	138.1	BBCH 00	F Forage	45	< 0.01	< 0.01	< 0.01	< 0.01
									< 0.01	< 0.01	< 0.01	< 0.01
							S Forage	196	< 0.01	< 0.01	< 0.01	< 0.01
									< 0.01	< 0.01	< 0.01	< 0.01
							Hay	221	< 0.01	< 0.01	< 0.01	< 0.01
									< 0.01	< 0.01	< 0.01	< 0.01
							Grain	272	< 0.01	< 0.01	< 0.01	< 0.01
									< 0.01	< 0.01	< 0.01	< 0.01
							Straw	272	< 0.01	< 0.01	< 0.01	< 0.01
									< 0.01	< 0.01	< 0.01	< 0.01
Report: T000764-08 Study: T000764-08 Trial: E17LA081772 - Study to GLP - Carried out in 2008/09	Wheat (Terral LA841)	United States (NAFTA/ Region 4)	250 EC	201.0	142.7	BBCH 00	F Forage	45	< 0.01	< 0.01	< 0.01	< 0.01
									< 0.01	< 0.01	< 0.01	< 0.01
							S Forage	104	< 0.01	< 0.01	< 0.01	< 0.01
									< 0.01	< 0.01	< 0.01	< 0.01
							Hay	126	< 0.01	< 0.01	< 0.01	< 0.01
									< 0.01	< 0.01	< 0.01	< 0.01
							Grain	183	< 0.01	< 0.01	< 0.01	< 0.01
									< 0.01	< 0.01	< 0.01	< 0.01
							Straw	183	< 0.01	< 0.01	< 0.01	< 0.01
									< 0.01	< 0.01	< 0.01	< 0.01
Report: T000764-08 Study: T000764-08 Trial: C19MO081773 - Study to GLP - Carried out in 2008/09	Wheat (Arlin)	United States (NAFTA/ Region 5)	250 EC	196.5	149.4	BBCH 00	F Forage	46	< 0.01	< 0.01	< 0.01	< 0.01
									< 0.01	< 0.01	< 0.01	< 0.01
							S Forage	211	< 0.01	< 0.01	< 0.01	< 0.01
									< 0.01	< 0.01	< 0.01	< 0.01
							Hay	255	< 0.01	< 0.01	< 0.01	< 0.01
									< 0.01	< 0.01	< 0.01	< 0.01
							Grain	278	< 0.01	< 0.01	< 0.01	< 0.01
									< 0.01	< 0.01	< 0.01	< 0.01
							Straw	278	< 0.01	< 0.01	< 0.01	< 0.01
									< 0.01	< 0.01	< 0.01	< 0.01
Report: T000764-08 Study: T000764-08 Trial: C19KS081774 - Study to GLP - Carried out in 2008/09	Wheat (Santa Fe)	United States (NAFTA/ Region 5)	250 EC	205.1	149.0	BBCH 00	F Forage	48	< 0.01	< 0.01	< 0.01	< 0.01
									< 0.01	< 0.01	< 0.01	< 0.01
							S Forage	201	< 0.01	< 0.01	< 0.01	< 0.01
									< 0.01	< 0.01	< 0.01	< 0.01
							Hay	238	< 0.01	< 0.01	< 0.01	< 0.01
									< 0.01	< 0.01	< 0.01	< 0.01
							Grain	272	< 0.01	< 0.01	< 0.01	< 0.01
									< 0.01	< 0.01	< 0.01	< 0.01
							Straw	272	< 0.01	< 0.01	< 0.01	< 0.01
									< 0.01	< 0.01	< 0.01	< 0.01
Report: T000764-08 Study: T000764-08 Trial: C18IA1775 - Study to GLP - Carried out in 2008/09	Wheat (733)	United States (NAFTA/ Region 5)	250 EC	200.9	106.0	BBCH 00	F Forage	45	< 0.01	< 0.01	< 0.01	< 0.01
									< 0.01	< 0.01	< 0.01	< 0.01
							S Forage	202	< 0.01	< 0.01	< 0.01	< 0.01
									< 0.01	< 0.01	< 0.01	< 0.01
							Hay	245	< 0.01	< 0.01	< 0.01	< 0.01
									< 0.01	< 0.01	< 0.01	< 0.01
							Grain	291	< 0.01	< 0.01	< 0.01	< 0.01
									< 0.01	< 0.01	< 0.01	< 0.01
							Straw	291	< 0.01	< 0.01	< 0.01	< 0.01
									< 0.01	< 0.01	< 0.01	< 0.01

GLP and Trial Details	Crop (Variety)	Country (Region)	Form'n Type and Content (g/L)	Bare ground Application			Crop Part2	DAP[a] (days)	Residues1 (mg/kg)			
				Rate (g ai/ha)	Volume (L/ha)	Growth Stage			Method GRM030.03A		Common Moiety Method GRM030.05A	
									Bicyclop-yrone	SYN 503780	SYN 503780	CSCD 686480
Report: T000764-08 Study: T000764-08 Trial: E19IA081776 - Study to GLP - Carried out in 2008/09	Wheat (Briggs)	United States (NAFTA/ Region5)	250 EC	203.0	159.8	BBCH 00	F Forage	31	0.01	< 0.01	0.019	< 0.01
								38	< 0.01	< 0.01	0.016	< 0.01
								45	0.020	< 0.01	0.028	< 0.01
								45	0.013	< 0.01	0.021	< 0.01
								52	< 0.01	< 0.01	< 0.01	< 0.01
							S Forage	236	< 0.01	< 0.01	< 0.01	< 0.01
								243	< 0.01	< 0.01	< 0.01	< 0.01
								250	< 0.01	< 0.01	< 0.01	< 0.01
								250	< 0.01	< 0.01	< 0.01	< 0.01
								257	< 0.01	< 0.01	< 0.01	< 0.01
							Hay	264	< 0.01	< 0.01	< 0.01	< 0.01
								271	< 0.01	< 0.01	< 0.01	< 0.01
								278	< 0.01	< 0.01	< 0.01	< 0.01
								278	< 0.01	< 0.01	< 0.01	< 0.01
								287	< 0.01	< 0.01	< 0.01	< 0.01
							Grain	296	< 0.01	< 0.01	< 0.01	< 0.01
								302	< 0.01	< 0.01	< 0.01	< 0.01
								309	< 0.01	< 0.01	< 0.01	< 0.01
								309	< 0.01	< 0.01	< 0.01	< 0.01
								315	< 0.01	< 0.01	< 0.01	< 0.01
							Straw	296	< 0.01	< 0.01	< 0.01	< 0.01
								302	< 0.01	< 0.01	< 0.01	< 0.01
								309	< 0.01	< 0.01	< 0.01	< 0.01
								309	< 0.01	< 0.01	< 0.01	< 0.01
								315	< 0.01	< 0.01	< 0.01	< 0.01
Report: T000764-08 Study: T000764-08 Trial: E19IA081777 - Study to GLP - Carried out in 2008/09	Wheat (Briggs)	United States (NAFTA/ Region 5)	250 EC	203.6	160.0	BBCH 00	F Forage	45	< 0.01	< 0.01	0.018	< 0.01
									< 0.01	< 0.01	0.016	< 0.01
							S Forage	247	< 0.01	< 0.01	< 0.01	< 0.01
									< 0.01	< 0.01	< 0.01	< 0.01
							Hay	264	< 0.01	< 0.01	< 0.01	< 0.01
									< 0.01	< 0.01	< 0.01	< 0.01
							Grain	310	< 0.01	< 0.01	< 0.01	< 0.01
									< 0.01	< 0.01	< 0.01	< 0.01
							Straw	310	< 0.01	< 0.01	< 0.01	< 0.01
									< 0.01	< 0.01	< 0.01	< 0.01
Report: T000764-08 Study: T000764-08 Trial: W07TX081778 - Study to GLP - Carried out in 2008/09	Wheat (Mit)	United States (NAFTA/ Region 6)	250 EC	199.9	138.1	BBCH 00	F Forage	44	< 0.01	< 0.01	< 0.01	< 0.01
									< 0.01	< 0.01	< 0.01	< 0.01
							S Forage	99	< 0.01	< 0.01	< 0.01	< 0.01
									< 0.01	< 0.01	< 0.01	< 0.01
							Hay	129	< 0.01	< 0.01	< 0.01	< 0.01
									< 0.01	< 0.01	< 0.01	< 0.01
							Grain	173	< 0.01	< 0.01	< 0.01	< 0.01
									< 0.01	< 0.01	< 0.01	< 0.01
							Straw	173	< 0.01	< 0.01	< 0.01	< 0.01
									< 0.01	< 0.01	< 0.01	< 0.01
Report: T000764-08 Study: T000764-08 Trial: C12ND081779 - Study to GLP - Carried out in 2009	Wheat (CA907-816W)	United States (NAFTA/ Region 7)	250 EC	202.5	189.5	BBCH 00	S Forage	42	< 0.01	< 0.01	< 0.01	< 0.01
									< 0.01	< 0.01	< 0.01	< 0.01
							Hay	64	< 0.01	< 0.01	< 0.01	< 0.01
									< 0.01	< 0.01	< 0.01	< 0.01
							Grain	99	< 0.01	< 0.01	< 0.01	< 0.01
									< 0.01	< 0.01	< 0.01	< 0.01
							Straw	99	< 0.01	< 0.01	< 0.01	< 0.01
									< 0.01	< 0.01	< 0.01	< 0.01

GLP and Trial Details	Crop (Variety)	Country (Region)	Form'n Type and Content (g/L)	Bare ground Application			Crop Part2	DAP[a] (days)	Residues1 (mg/kg)			
				Rate (g ai/ha)	Volume (L/ha)	Growth Stage			Method GRM030.03A		Common Moiety Method GRM030.05A	
									Bicyclop-yrone	SYN 503780	SYN 503780	CSCD 686480
Report: T000764-08 Study: T000764-08 Trial: C12ND081780 - Study to GLP - Carried out in 2009	Wheat (Agawam)	United States (NAFTA/ Region 7)	250 EC	202.0	189.0	BBCH 00	S Forage	42	< 0.01	< 0.01	< 0.01	< 0.01
									< 0.01	< 0.01	< 0.01	< 0.01
							Hay	64	< 0.01	< 0.01	< 0.01	< 0.01
									< 0.01	< 0.01	< 0.01	< 0.01
							Grain	99	< 0.01	< 0.01	< 0.01	< 0.01
									< 0.01	< 0.01	< 0.01	< 0.01
							Straw	99	< 0.01	< 0.01	< 0.01	< 0.01
									< 0.01	< 0.01	< 0.01	< 0.01
Report: T000764-08 Study: T000764-08 Trial: C13ND081781 - Study to GLP - Carried out in 2009	Wheat (WPB Nick)	United States (NAFTA/ Region 7)	250 EC	202.9	140.7	BBCH 00	S Forage	31	< 0.01	< 0.01	< 0.01	< 0.01
								38	< 0.01	< 0.01	< 0.01	< 0.01
								45	< 0.01	< 0.01	< 0.01	< 0.01
									< 0.01	< 0.01	< 0.01	< 0.01
								52	< 0.01	< 0.01	< 0.01	< 0.01
							Hay	45	< 0.01	< 0.01	< 0.01	< 0.01
								52	< 0.01	< 0.01	< 0.01	< 0.01
								59	< 0.01	< 0.01	< 0.01	< 0.01
									< 0.01	< 0.01	< 0.01	< 0.01
								66	< 0.01	< 0.01	< 0.01	< 0.01
							Grain	94	< 0.01	< 0.01	< 0.01	< 0.01
								101	< 0.01	< 0.01	< 0.01	< 0.01
								108	< 0.01	< 0.01	< 0.01	< 0.01
									< 0.01	< 0.01	< 0.01	< 0.01
								115	< 0.01	< 0.01	< 0.01	< 0.01
							Straw	94	< 0.01	< 0.01	< 0.01	< 0.01
								101	< 0.01	< 0.01	< 0.01	< 0.01
								108	< 0.01	< 0.01	< 0.01	< 0.01
									< 0.01	< 0.01	< 0.01	< 0.01
								115	< 0.01	< 0.01	< 0.01	< 0.01
Report: T000764-08 Study: T000764-08 Trial: C13ND081782 - Study to GLP - Carried out in 2009	Durum (Divide)	United States (NAFTA/ Region 7)	250 EC	202.3	140.7	BBCH 00	S Forage	45	< 0.01	< 0.01	< 0.01	< 0.01
									< 0.01	< 0.01	< 0.01	< 0.01
							Hay	59	< 0.01	< 0.01	< 0.01	< 0.01
									< 0.01	< 0.01	< 0.01	< 0.01
							Grain	108	< 0.01	< 0.01	< 0.01	< 0.01
									< 0.01	< 0.01	< 0.01	< 0.01
							Straw	108	< 0.01	< 0.01	< 0.01	< 0.01
									< 0.01	< 0.01	< 0.01	< 0.01
Report: T000764-08 Study: T000764-08 Trial: C12ND081783 - Study to GLP - Carried out in 2008/09	Wheat (Diamond)	United States (NAFTA/ Region 7)	250 EC	202.2	189.2	BBCH 00	S Forage	42	< 0.01	< 0.01	< 0.01	< 0.01
									< 0.01	< 0.01	< 0.01	< 0.01
							Hay	64	< 0.01	< 0.01	< 0.01	< 0.01
									< 0.01	< 0.01	< 0.01	< 0.01
							Grain	99	< 0.01	< 0.01	< 0.01	< 0.01
									< 0.01	< 0.01	< 0.01	< 0.01
							Straw	99	< 0.01	< 0.01	< 0.01	< 0.01
									< 0.01	< 0.01	< 0.01	< 0.01
Report: T000764-08 Study: T000764-08 Trial: W12CO081784 - Study to GLP - Carried out in 2008/09	Wheat (Bill Brown)	United States (NAFTA/ Region 8)	250 EC	200.3	140.6	BBCH 00	F Forage	46	< 0.01	< 0.01	< 0.01	< 0.01
									< 0.01	< 0.01	< 0.01	< 0.01
							S Forage	235	< 0.01	< 0.01	< 0.01	< 0.01
									< 0.01	< 0.01	< 0.01	< 0.01
							Hay	270	< 0.01	< 0.01	< 0.01	< 0.01
									< 0.01	< 0.01	< 0.01	< 0.01
							Grain	295	< 0.01	< 0.01	< 0.01	< 0.01
									< 0.01	< 0.01	< 0.01	< 0.01
							Straw	295	< 0.01	< 0.01	< 0.01	< 0.01

GLP and Trial Details	Crop (Variety)	Country (Region)	Form'n Type and Content (g/L)	Bare ground Application			Crop Part2	DAP[a] (days)	Residues1 (mg/kg)			
				Rate (g ai/ha)	Volume (L/ha)	Growth Stage			Method GRM030.03A		Common Moiety Method GRM030.05A	
									Bicyclop-yrone	SYN 503780	SYN 503780	CSCD 686480
									< 0.01	< 0.01	< 0.01	< 0.01
Report: T000764-08 Study: T000764-08 Trial: W12CO081785 - Study to GLP - Carried out in 2008/09	Wheat (Yuma)	United States (NAFTA/ Region)	250 EC	202.3	142.0	BBCH 00	F Forage	46	< 0.01	< 0.01	< 0.01	< 0.01
									< 0.01	< 0.01	< 0.01	< 0.01
							S Forage	235	< 0.01	< 0.01	< 0.01	< 0.01
									< 0.01	< 0.01	< 0.01	< 0.01
							Hay	270	< 0.01	< 0.01	< 0.01	< 0.01
									< 0.01	< 0.01	< 0.01	< 0.01
							Grain	295	< 0.01	< 0.01	< 0.01	< 0.01
									< 0.01	< 0.01	< 0.01	< 0.01
							Straw	295	< 0.01	< 0.01	< 0.01	< 0.01
									< 0.01	< 0.01	< 0.01	< 0.01
Report: T000764-08 Study: T000764-08 Trial: W12CO081786 - Study to GLP - Carried out in 2008/09	Wheat (Jagalene)	United States (NAFTA/ Region 8)	250 EC	205.1	143.9	BBCH 00	F Forage	46	< 0.01	< 0.01	< 0.01	< 0.01
									< 0.01	< 0.01	< 0.01	< 0.01
							S Forage	235	< 0.01	< 0.01	< 0.01	< 0.01
									< 0.01	< 0.01	< 0.01	< 0.01
							Hay	270	< 0.01	< 0.01	< 0.01	< 0.01
									< 0.01	< 0.01	< 0.01	< 0.01
							Grain	295	< 0.01	< 0.01	< 0.01	< 0.01
									< 0.01	< 0.01	< 0.01	< 0.01
							Straw	295	< 0.01	< 0.01	< 0.01	< 0.01
									< 0.01	< 0.01	< 0.01	< 0.01
Report: T000764-08 Study: T000764-08 Trial: W39TX081787 - Study to GLP - Carried out in 2008/09	Wheat (TAM 105)	United States (NAFTA/ Region 8)	250 EC	200.8	186.9	BBCH 00	F Forage	44	< 0.01	< 0.01	< 0.01	< 0.01
									< 0.01	< 0.01	< 0.01	< 0.01
							S Forage	148	< 0.01	< 0.01	< 0.01	< 0.01
									< 0.01	< 0.01	< 0.01	< 0.01
							Hay	206	< 0.01	< 0.01	< 0.01	< 0.01
									< 0.01	< 0.01	< 0.01	< 0.01
							Grain	240	< 0.01	< 0.01	< 0.01	< 0.01
									< 0.01	< 0.01	< 0.01	< 0.01
							Straw	240	< 0.01	< 0.01	< 0.01	< 0.01
									< 0.01	< 0.01	< 0.01	< 0.01
Report: T000764-08 Study: T000764-08 Trial: W07TX081791 - Study to GLP - Carried out in 2008/09	Wheat (Fannin)	United States (NAFTA/ Region 8)	250 EC	203.6	154.9	BBCH 00	F Forage	45	< 0.01	< 0.01	< 0.01	< 0.01
									< 0.01	< 0.01	< 0.01	< 0.01
							S Forage	85	< 0.01	< 0.01	< 0.01	< 0.01
									< 0.01	< 0.01	< 0.01	< 0.01
							Hay	141	< 0.01	< 0.01	< 0.01	< 0.01
									< 0.01	< 0.01	< 0.01	< 0.01
							Grain	177	< 0.01	< 0.01	< 0.01	< 0.01
									< 0.01	< 0.01	< 0.01	< 0.01
							Straw	177	< 0.01	< 0.01	< 0.01	< 0.01
									< 0.01	< 0.01	< 0.01	< 0.01
Report: T000764-08 Study: T000764-08 Trial: E13TX081792 - Study to GLP - Carried out in 2008/09	Wheat (Deliver)	United States (NAFTA/ Region 8)	250 EC	206.6	241.5	BBCH 00	F Forage	45	< 0.01	< 0.01	< 0.01	< 0.01
									< 0.01	< 0.01	< 0.01	< 0.01
							S Forage	129	< 0.01	< 0.01	< 0.01	< 0.01
									< 0.01	< 0.01	< 0.01	< 0.01
							Hay	155	< 0.01	< 0.01	< 0.01	< 0.01
									< 0.01	< 0.01	< 0.01	< 0.01
							Grain	216	< 0.01	< 0.01	< 0.01	< 0.01
									< 0.01	< 0.01	< 0.01	< 0.01
							Straw	216	< 0.01	< 0.01	< 0.01	< 0.01
									< 0.01	< 0.01	< 0.01	< 0.01

GLP and Trial Details	Crop (Variety)	Country (Region)	Form'n Type and Content (g/L)	Bare ground Application			Crop Part2	DAP[a] (days)	Residues1 (mg/kg)			
				Rate (g ai/ha)	Volume (L/ha)	Growth Stage			Method GRM030.03A		Common Moiety Method GRM030.05A	
									Bicyclop-yrone	SYN 503780	SYN 503780	CSCD 686480
Report: T000764-08 Study: T000764-08 Trial: W20OR081793 - Study to GLP - Carried out in 2008/09	Wheat (Stephens)	United States (NAFTA/ Region 11)	250 EC	201.9	151.3	BBCH 00	F Forage	45	< 0.01	< 0.01	< 0.01	< 0.01
									< 0.01	< 0.01	< 0.01	< 0.01
							S Forage	204	< 0.01	< 0.01	< 0.01	< 0.01
									< 0.01	< 0.01	< 0.01	< 0.01
							Hay	226	< 0.01	< 0.01	< 0.01	< 0.01
									< 0.01	< 0.01	< 0.01	< 0.01
							Grain	288	< 0.01	< 0.01	< 0.01	< 0.01
									< 0.01	< 0.01	< 0.01	< 0.01
							Straw	288	< 0.01	< 0.01	< 0.01	< 0.01
									< 0.01	< 0.01	< 0.01	< 0.01

[a] DAP = days after planting; F Forage = Autumn/Fall Forage, Nominally Harvested at 45 DAP; S Forage = Spring Forage, Nominally Harvested at 6-8"; Hay, Nominally Harvested at Boot Stage; Grain and Straw Nominally Harvested at Maturity

In summary, the confined rotational crop study showed total radioactive residues ≥ 0.01 mg/kg in some samples of succeeding crops. Limited field rotational crop studies were therefore conducted. In one study with nine trials, bare ground was treated with bicyclopyrone formulated as an emulsifiable concentrate (EC) at a rate of 200 g ai/ha. Radish (root and tuber vegetable), spinach (leafy vegetable) and wheat (cereals) were planted 90, 150, 187, and 270 days after the application of the test substance and harvested at typical agricultural intervals. Since it is common commercial practice to rotate winter wheat into a field after growing maize, a second study was conducted with twenty trials to determine possible residue levels in wheat commodities. Bicyclopyrone was applied to bare-ground at a rate of 200 g ai/ha. Winter wheat was planted 90 days after application and spring wheat 270 days after application. The rotational wheat was harvested at normal maturity to provide samples of forage (autumn and/or spring), hay, grain, and straw. The only residues found above the limit of quantification were of bicyclopyrone, analysed directly using method GRM030.03A, and of common moiety SYN503780, analysed via method GRM030.05A, in autumn forage (45 DAP). In the decline trials, these residues decreased with longer intervals to harvest. All other residues were <LOQ in all matrices, including processed fractions.

RESIDUE ANALYSIS

Analytical methods

The Meeting received analytical method descriptions and validation data for bicyclopyrone, SYN503780, CSCD686480, CSAA806573 and CSAA589691 in plant and animal matrices, and these are summarised below.

Table 54 Summary of analytical methods for bicyclopyrone and its metabolites, developed for plant and animal matrices

Matrix	Analyte	Method	Principle	LOQ (mg/kg)	Reference
Plant matrix-Maize	bicyclopyrone SYN503780	GRM030.03A	Acetonitrile/water water dilution reverse-phase LC-MS/MS	0.01 0.01	NOA449280_11154
Plant matrices -Maize	SYN503780 CSD686480	GRM030.05A	Acetonitrile/water H_2O_2/NaOH oxidation reverse-phase LC-MS/MS	0.01 0.01	NOA449280_11296
Plant matrices -Maize	SYN503780 CSD686480	GRM030.05B	Acetonitrile/water H_2O_2/NaOH oxidation reverse-phase LC-MS/MS	0.01 0.01	NOA449280_11563

Plant matrices	CSAA589691	GRM030.09A	Acetonitrile/water water dilution reverse-phase LC-MS/MS	0.01	NOA449280_10001
Plant matrices	SYN503780 CSCD686480	POPIT MET.117	Acetonitrile/water H_2O_2/NaOH oxidation Acetonitrile/water dilution reverse-phase LC-MS/MS	0.01 0.01	NOA449280_11475
Animal matrices	bicyclopyrone CSAA915194 SYN503780 CSCD686480	GRM030.08A	Acetonitrile/ water H_2O_2/NaOH oxidation Acidification SPE clean-up LC-MS/MS	0.01 0.01 0.007 0.007	NOA449280_11098

Data collection methods

Method GRM030.03A, GRM030.05A and GRM030.09A (bicyclopyrone and three metabolites-plant matrices)

This LC-MS/MS methods for measuring residues of bicyclopyrone and its SYN503780, CSD686480, CSAA589691 metabolites in crops was reported by Melville and Lowrie (2012, NOA449280_11357].

Method GRM030.03A

This LC-MS/MS methods for measuring residues of bicyclopyrone and its SYN503780 metabolite in crops was reported by Crook (2012a, NOA449280_11154).

In this method, residues were extracted from crop samples using acetonitrile: water 80:20 v/v. The extracts were diluted with water and analysed by high performance liquid chromatography with triple-quadrupole mass-spectrometric detection (LC-MS/MS). An aliquot of the diluted extract was transferred to an auto-sampler vial for analysis. SYN503780 and bicyclopyrone were separated from co-extracts by reversed phase liquid chromatography and detected by electrospray mass spectrometry/mass spectrometry. Quantitation was performed using the mass transition 278.4→202.3 m/z for SYN503780, 400.3→324.4 m/z for bicyclopyrone. Confirmation was performed using the mass transition 278.4→146.1 m/z for SYN503780, 400.3→228.4 m/z for bicyclopyrone. The reported LOQ for each analyte is 0.01 mg/kg.

Good linearity was observed in the range of 0.05 to 2.0 ng/mL for bicyclopyrone and metabolites. Analysis of control samples resulted in no apparent residues of bicyclopyrone and metabolite (the response in the area of the bicyclopyrone and metabolites peak always corresponded to less than 30% of the limit of determination). It can therefore be concluded that few, if any, apparent residues or false positive values would arise.

The method was successfully validated on the first attempt for each matrix evaluated. Relative standard deviations of less than 20% were obtained for fortifications made at the quantification limit for each matrix, as well as at higher levels. Therefore, the repeatability of this method is adequate for the purposes of residue data collection and enforcement of MRLs.

Residue field trial concurrent recovery rates where this method was used are summarised in the discussions on the individual crop field trials. These concurrent recoveries produced similar results to the fortification data obtained during method validation. The average recoveries ranged from 70–120%, with a standard deviation of ≤ 20%. Therefore, the recovery of this method is adequate for the purposes of residue data collection.

Table 55 Bicyclopyrone Recovery Results Obtained during Validation of Method GRM030.03A – primary transition m/z = 400 → 324

Crop Matrix	Fortification Level (mg/kg)	Recovery (%)**	n	Mean (%)	RSD (%)	Range (%)
Field Corn Grain	0.01*	86, 89, 90, 84, 87	5	87	3	84-90
	0.1	99, 99, 96, 94, 98	5	97	2	94-99
	Overall		10	92	6	84-99
Field Corn Mature (dry) Whole plant	0.01*	86, 87, 78, 82, 83	5	83	5	78-87
	0.1	101, 99, 93, 92, 94	5	96	4	92-101
	Overall		10	90	9	78-101
Field Corn Immature (green) Whole plant	0.01*	71, 72, 71, 71, 67	5	70	3	67-72
	0.1	78, 74, 74, 76, 73	5	75	2	73-78
	Overall		10	73	4	67-78
Tomato fruit	0.01*	100, 98, 97, 96, 100	5	98	2	96-100
	0.1	99, 97, 99, 99, 99	5	99	1	97-99
	Overall		10	98	1	96-100
Orange Fruit	0.01*	80, 74, 73, 80, 73	5	76	5	73 – 80
	0.1	79, 76, 77, 81, 78	5	78	3	76-81
	Overall		10	77	4	73-81
Sunflower Seed	0.01*	89, 94, 93, 95, 97	5	94	3	89-97
	0.1	98, 94, 95, 91, 95	5	95	3	91-98
	Overall		10	94	3	89-98

*Limit of quantification, defined by the lowest validated fortification level
**Residues in control samples and reagent blanks were less than 30% of the LOQ.

Table 56 Bicyclopyrone Recovery Results Obtained during Validation of Method GRM030.03A– confirmatory transition m/z = 400 → 228

Crop Matrix	Fortification Level (mg/kg)	Recovery (%)**	n	Mean (%)	RSD (%)	Range (%)
Field Corn Grain	0.01*	78, 82, 80, 80, 83	5	81	3	78-83
	0.1	96, 95, 94, 93, 95	5	95	1	93-96
	Overall		10	88	9	78-96
Field Corn Mature (dry) Whole plant	0.01*	91, 88, 84, 91, 93	5	90	4	84-93
	0.1	97, 98, 91, 90, 95	5	94	4	90-98
	Overall		10	92	5	84-98
Field Corn Immature (green) Whole plant	0.01*	73, 73, 70, 69, 68	5	71	3	68-73
	0.1	79, 76, 76, 75, 74	5	76	3	74-79
	Overall		10	73	5	68-79
Tomato fruit	0.01*	91, 103, 88, 100, 95	5	95	6	88-103
	0.1	99, 95, 96, 99, 97	5	97	2	95-99
	Overall		10	96	4	88-103
Orange Fruit	0.01*	84, 73, 88, 91, 83	5	84	8	73-91
	0.1	79, 74, 74, 82, 77	5	77	4	74-82
	Overall		10	81	8	73-91
Sunflower Seed	0.01*	90, 103, 99, 97, 102	5	98	5	90-103
	0.1	94, 93, 91, 89, 93	5	92	2	89-94
	Overall		10	95	5	89-103

*Limit of quantification, defined by the lowest validated fortification level
**Residues in control samples and reagent blanks were less than 30% of the LOQ.

Table 57 SYN503780 Recovery Results Obtained during Validation of Method GRM030.03A – primary transition *m/z* = 278 → 202

Crop Matrix	Fortification Level (mg/kg)	Recovery (%)**	n	Mean (%)	RSD (%)	Range (%)
Field Corn Grain	0.01*	96, 97, 83, 97, 92	5	93	7	83-97
	0.1	100, 96, 97, 95, 101	5	98	3	95-101
	Overall		10	95	5	83-101
Field Corn Mature (dry) Whole plant	0.01*	85, 89, 83, 90, 93	5	88	4	83-93
	0.1	101, 102, 101, 96, 99	5	100	2	96-102
	Overall		10	94	7	83-102
Field Corn Immature (green) Whole plant	0.01*	88, 91, 91, 87, 94	5	90	3	87-94
	0.1	108, 109, 107, 108, 103	5	107	2	103-109
	Overall		10	98	9	87-109
Tomato fruit	0.01*	95, 97, 95, 95, 96	5	95	1	95-97
	0.1	95, 96, 95, 95, 96	5	96	1	95-96
	Overall		10	96	1	95-97
Orange Fruit	0.01*	96, 91, 95, 100, 93	5	95	3	91-100
	0.1	91, 91, 91, 93, 92	5	92	1	91-93
	Overall		10	93	3	91-100
Sunflower Seed	0.01*	109, 106, 105, 104, 108	5	106	2	104-109
	0.1	102, 102, 97, 101, 98	5	100	2	97-102
	Overall		10	103	4	97-109

*Limit of quantification, defined by the lowest validated fortification level

**Residues in control samples and reagent blanks were less than 30% of the LOQ.

Table 58 SYN503780 Recovery Results Obtained During Validation of Method GRM030.03A– confirmatory transition *m/z* = 278 → 146

Crop Matrix	Fortification Level (mg/kg)	Recovery (%)**	n	Mean (%)	RSD (%)	Range (%)
Field Corn Grain	0.01*	104, 104, 101, 101, 110	5	104	4	101-110
	0.1	102, 100, 98, 97, 102	5	100	2	97-102
	Overall		10	102	4	97-110
Field Corn Mature (dry) Whole plant	0.01*	95, 87, 76, 79, 95	5	86	10	76-95
	0.1	103, 102, 102, 97, 100	5	101	3	97-103
	Overall		10	94	10	76-103
Field Corn Immature (green) Whole plant	0.01*	94, 87, 100, 97, 94	5	95	5	87-100
	0.1	104, 109, 105, 105, 103	5	105	2	103-109
	Overall		10	100	7	87-109
Tomato fruit	0.01*	104, 96, 90, 99, 97	5	97	5	90-104
	0.1	90, 93, 92, 95, 87	5	91	3	87-95
	Overall		10	94	5	87-104
Orange Fruit	0.01*	105, 98, 95, 101, 102	5	100	4	95-105
	0.1	92, 96, 92, 95, 87	5	92	4	87-96
	Overall		10	96	5	87-105
Sunflower Seed	0.01*	105, 105, 109, 113, 111	5	109	3	105-113
	0.1	102, 101, 98, 100, 99	5	104	2	98-102
	Overall		10	104	5	98-113

*Limit of quantification, defined by the lowest validated fortification level

**Residues in control samples and reagent blanks were less than 30% of the LOQ.

During an independent laboratory validation (ILV) of GRM030.03A samples of field corn forage, grain and stover and soya bean seed were fortified at the proposed limit of quantification (0.01 mg/kg) and at ten times LOQ (0.1 mg/kg). The recoveries obtained are detailed in Tables 59 to 62.

Table 59 Bicyclopyrone Recovery Results Obtained During Independent Validation of Method GRM030.03A – primary transition *m/z* = 400 → 324

Crop Matrix	Fortification Level (mg/kg)	Recovery (%)**	n	Mean (%)	RSD (%)	Range (%)
Field Corn Forage	0.01*	95, 98, 91, 96, 98	5	96	3	91-98
	0.1	102, 101, 105, 100, 99	5	101	2	99-105
	Overall		10	99	4	91-105
Field Corn Grain	0.01*	76, 93, 91, 70, 88	5	84	12	70-93
	0.1	109, 86, 107, 87, 111	5	100	12	86-111
	Overall		10	92	15	70-111
Field Corn Stover	0.01*	86, 88, 86, 90, 88	5	88	2	86-90
	0.1	100, 95, 100, 95, 96	5	97	3	95-100
	Overall		10	92	5	86-100
Soya bean Seed	0.01*	108, 112, 128, 118, 122	5	118	7	108-128
	0.1	112, 108, 110, 105, 118	5	111	5	105-118
	Overall		10	114	6	105-128

*Limit of quantification, defined by the lowest validated fortification level

**Residues in control samples and reagent blanks were less than 30% of the LOQ.

Table 60 Bicyclopyrone Recovery Results Obtained During Independent Validation of Method GRM030.03A – confirmatory transition *m/z* = 400 → 228

Crop Matrix	Fortification Level (mg/kg)	Recovery (%)**	n	Mean (%)	RSD (%)	Range (%)
Field Corn Forage	0.01*	96, 96, 88, 90, 99	5	94	5	88-99
	0.1	102, 103, 105, 101, 102	5	103	2	101-105
	Overall		10	98	6	88-105
Field Corn Grain	0.01*	78, 93, 92, 71, 88	5	84	12	71-92
	0.1	107, 87, 107, 86, 111	5	100	12	86-111
	Overall		10	92	14	71-111
Field Corn Stover	0.01*	79, 83, 82, 86, 82	5	82	4	79-86
	0.1	103, 98, 100, 96, 96	5	99	3	96-103
	Overall		10	91	10	79-103
Soya bean Seed	0.01*	110, 119, 129, 120, 119	5	119	6	110-129
	0.1	113, 112, 110, 104, 103	5	108	5	103-113
	Overall		10	114	7	103-129

*Limit of quantification, defined by the lowest validated fortification level

**Residues in control samples and reagent blanks were less than 30% of the LOQ.

Table 61 SYN503780 Recovery Results Obtained During Independent Validation of Method GRM030.03A – primary transition *m/z* = 278 → 202

Crop Matrix	Fortification Level (mg/kg)	Recovery (%)**	n	Mean (%)	RSD (%)	Range (%)
Field Corn Forage	0.01*	84, 82, 84, 83, 94	5	85	6	82-94
	0.1	85, 88, 88, 89, 85	5	87	2	85-89
	Overall		10	86	5	82-94
Field Corn Grain	0.01*	95, 79, 94, 95, 95	5	92	8	79-95
	0.1	93, 91, 96, 94, 94	5	94	2	91-96
	Overall		10	93	5	79-96
Field Corn Stover	0.01*	85, 93, 87, 91, 80	5	87	6	80-93
	0.1	92, 86, 91, 88, 87	5	89	3	86-92
	Overall		10	88	5	80-93
Soya bean Seed	0.01*	95, 95, 87, 90, 89	5	91	4	87-95
	0.1	98, 89, 90, 90, 90	5	91	4	89-98
	Overall		10	91	3	87-98

*Limit of quantification, defined by the lowest validated fortification level

**Residues in control samples and reagent blanks were less than 30% of the LOQ.

Table 62 SYN503780 Recovery Results Obtained During Independent Validation of Method GRM030.03A – confirmatory transition *m/z* = 278 → 146

Crop Matrix	Fortification Level (mg/kg)	Recovery (%)**	n	Mean (%)	RSD (%)	Range (%)
Field Corn Forage	0.01*	88, 87, 78, 86, 88	5	85	5	78-88
	0.1	87, 88, 90, 92, 88	5	89	2	87-92
	Overall		10	87	5	78-92
Field Corn Grain	0.01*	89, 88, 88, 89, 85	5	88	2	85-89
	0.1	95, 94, 98, 93, 96	5	95	2	93-98
	Overall		10	92	4	85-98
Field Corn Stover	0.01*	84, 87, 84, 87, 87	5	86	2	84-87
	0.1	89, 86, 89, 88, 88	5	88	1	86-89
	Overall		10	87	2	84-89
Soya bean Seed	0.01*	92, 92, 90, 92, 92	5	92	1	90-92
	0.1	101, 95, 95, 97, 96	5	97	2	95-101
	Overall		10	94	3	90-101

*Limit of quantification, defined by the lowest validated fortification level

**Residues in control samples and reagent blanks were less than 30% of the LOQ.

Method GRM030.05A/B

This LC-MS/MS methods for measuring residues of bicyclopyrone and its SYN503780 and CSCD686480 and CSAA806573 metabolite in crops was reported by Crook (2012b, NOA449280_11296).

In this method, residues were extracted from crop samples using acetonitrile:water 80:20 v/v. The extracts were centrifuged and an aliquot of the sample is evaporated to dryness. Hydrogen peroxide and 0.05M sodium hydroxide solution were added and the samples are left at room temperature for 3 hours to oxidise bicyclopyrone and structurally-related metabolites to SYN503780 or CSCD686480. After the basic oxidation step samples are cooled and diluted with water. Final determination is by high performance liquid chromatography with triple-quadrupole mass-

spectrometric detection (LC-MS/MS). The limit of quantification (LOQ) was 0.01 mg/kg (expressed as bicyclopyrone equivalents).

Good linearity was observed in the range of 0.02 to 1.0 ng/mL for SYN503780 and CSCD686480. Analysis of control samples resulted in no apparent residues of bicyclopyrone and metabolite (the response in the area of the bicyclopyrone and metabolites peak always corresponded to less than 30% of the limit of determination).

The method was successfully validated on the first attempt for each matrix evaluated. Relative standard deviations of less than 20% were obtained for fortifications made at the quantification limit for each matrix, as well as at higher levels. The average recoveries ranged from 70–120%, with a standard deviation of ≤ 20%. Therefore, the recovery of this method is adequate for the purposes of residue data collection.

A modification of method GRM030.05A was reported as Method GRM030.05B by Crook S (2014, NOA449280_11563). There are only two changes: mention of the additional analyte CSAA806573 was removed, and the recommended correction factors are modified so that both analytes determined by the method (SYN503780 and CSCD686480) are expressed as bicyclopyrone equivalents, whereas in the previous version (GRM0303.05A), CSCD686480 was expressed as CSAA915194.

The principle of the method is exactly the same as for method GRM030.05A; there is no alteration to the analytical procedures employed. Consequently, all of the validation data and independent validation data reported above for GRM030.05A are also applicable to method GRM030.05B.

Table 63 SYN503780 Recovery results obtained during validation of Method GRM030.05A – primary transition m/z = 278 → 202

Matrix	Fortification Level* (mg/kg)	Recovery (%)	n	Mean (%)	RSD (%)	Range (%)
Field Corn Forage	0.01**	118, 112, 109, 119, 120, 109, 111, 120, 108, 95, 84, 115, 109, 111, 99, 90, 101, 120, 85, 112	20	107	11	84-120
	0.1	120, 110, 114, 123, 120, 118, 115, 120, 120, 114, 100, 114, 96, 103, 114, 120, 106, 105, 99	19	112	7	96-123
	Overall		39	110	9	84-120
Field Corn Ears	0.01**	112, 115, 101, 117, 101, 88, 101, 119, 109	9	107	9	88-119
	0.1	106, 117, 120, 117, 115, 116, 108, 113, 113	9	113	4	108-120
	Overall		18	110	8	88-120
Field Corn Grain	0.01**	97, 115, 87, 102, 112, 117, 111, 117, 120, 112, 118, 109, 118, 89, 90, 75	16	105	13	75-120
	0.1	107, 120, 118, 120, 113, 118, 99, 106, 113, 120, 114, 118, 114, 115, 101, 92	16	112	8	92-120
	Overall		32	109	12	75-120
Field Corn Stover	0.01**	118, 106, 84, 102, 74, 105, 91, 106, 77, 103, 103, 102, 87, 112, 76, 94, 85, 91, 102	19	96	13	74-118
	0.1	106, 126, 102, 96, 109, 91, 120, 105, 119, 100, 112, 116, 117, 115, 110, 117, 112, 95	18	109	10	91-126
	Overall		37	102	13	74-126
Wheat Forage	0.01**	113, 114, 97, 104	4	107	8	97-114
	0.1	107, 108, 106, 119	4	110	6	106-119
	Overall		8	108	6	97-119
Wheat Hay	0.01**	106, 107, 117	3	110	6	106-117
	0.1	111, 105, 110	3	109	3	105-111
	Overall		6	109	4	105-117
Wheat Straw	0.01**	115, 80, 102	3	99	18	80-115
	0.1	84, 81, 115	3	93	19	81-115
	Overall		6	96	18	80-115

Matrix	Fortification Level* (mg/kg)	Recovery (%)	n	Mean (%)	RSD (%)	Range (%)
Wheat Grain	0.01**	110, 108	2	109	N/A	108-110
	0.1	111, 119	2	115	N/A	111 – 119
	Overall		4	112	4	108-119
Radish Roots	0.01**	93, 104, 104	3	100	6	93-104
	0.1	119, 107, 117	3	114	6	107 – 119
	Overall		6	107	9	93-119
Radish Tops	0.01**	113, 89, 119, 86	4	102	16	86-119
	0.1	105, 119, 103, 118	4	111	8	103-119
	Overall		8	107	12	86-119
Spinach Leaves	0.01**	119, 112, 98	3	110	10	98-119
	0.1	116, 116, 113	3	115	2	113-116
	Overall		6	112	7	98-119

N/A = Not applicable

*Expressed as bicyclopyrone

**Limit of quantification, defined by the lowest validated fortification level

***Residues in duplicate control samples and reagent blanks were less than 30% of the LOQ.

Table 64 CSCD686480 Recovery Results Obtained During Validation of Method GRM030.05A – primary transition *m/z* = 264 → 175

Matrix	Fortification Level* (mg/kg)	Recovery (%)	n	Mean (%)	RSD (%)	Range (%)
Field Corn Forage	0.01**	91, 81, 73, 90, 77, 107, 107, 82, 79, 80, 83, 83, 78, 84, 88, 97, 79, 90, 74, 79	20	85	11	73-107
	0.1	82, 82, 79, 90, 80, 80, 80, 80, 89, 82, 70, 73, 70, 72, 76, 79, 87, 105, 92	19	81	10	70-105
	Overall		39	83	11	70-107
Field Corn Ears	0.01**	99, 91, 74, 104, 93, 79, 79, 99, 97	9	91	12	74-104
	0.1	73, 78, 80, 78, 77, 73, 92, 103, 111	9	85	16	73-111
	Overall		18	88	14	73-111
Field Corn Grain	0.01**	99, 81, 77, 103, 75, 101, 71, 93, 75, 110, 96, 90, 77, 109, 93, 115	16	92	15	71-110
	0.1	71, 83, 110, 89, 103, 93, 94, 77, 76, 77, 78, 82, 101, 118, 107, 107	16	92	16	71-118
	Overall		32	92	15	71-118
Field Corn Stover	0.01**	87, 72, 84, 71, 86, 80, 72, 75, 75, 92, 81, 94, 78, 72, 75, 101, 119, 87, 99	19	84	15	71-119
	0.1	103, 112, 76, 93, 118, 84, 86, 83, 105, 70, 77, 81, 94, 86, 77, 84, 110, 103	18	91	16	70-118
	Overall		37	88	16	70-119
Wheat Forage	0.01**	105, 78, 88, 91	4	91	12	78-105
	0.1	100, 94, 116, 85	4	99	13	85-116
	Overall		8	95	13	78-116
Wheat Hay	0.01**	88, 87, 75	3	83	9	75-88
	0.1	76, 99, 82	3	85	14	76-99
	Overall		6	85	10	75-99
Wheat Straw	0.01**	78, 111, 82	3	90	20	78-111
	0.1	80, 97, 105	3	94	14	80-105
	Overall		6	92	14	78-111
Wheat Grain	0.01**	78, 73	2	76	N/A	73-78
	0.1	97, 75	2	86	N/A	75-97
	Overall		4	81	14	73-97

Matrix	Fortification Level* (mg/kg)	Recovery (%)	n	Mean (%)	RSD (%)	Range (%)
Radish Roots	0.01**	93, 104, 104	3	100	6	93-104
	0.1	119, 107, 117	3	114	6	107 – 119
	Overall		6	107	9	93-119
Radish Tops	0.01**	113, 89, 119, 86	4	102	16	86-119
	0.1	105, 119, 103, 118	4	111	8	103-119
	Overall		8	107	12	86-119
Spinach Leaves	0.01**	119, 112, 98	3	110	10	98-119
	0.1	116, 116, 113	3	115	2	113-116
	Overall		6	112	7	98-119

*Expressed as or CSAA915194

**Limit of quantification, defined by the lowest validated fortification level

***Residues in duplicate control samples and reagent blanks were less than 30% of the LOQ.

N/A = Not applicable.

An independent laboratory validation (ILV) study was conducted for GRM030.05A. Samples for recovery were fortified with bicyclopyrone (for determination as SYN503780) or with CSAA915194 (for determination as CSCD686480). Samples of field corn grain, forage, stover and soya bean seed were fortified at the proposed limit of quantification (0.01 mg/kg) and at ten times LOQ (0.1 mg/kg). The recoveries obtained are detailed in Tables 65 to 68.

Table 65 SYN503780 Recovery Results Obtained During Independent Validation of Method GRM030.05A – primary transition *m/z* = 278 → 202

Crop Matrix	Fortification Level (mg/kg)	Recovery (%)**	n	Mean (%)	RSD (%)	Range (%)
Field Corn Grain	0.01*	84, 99, 110, 108, 102	5	101	10	84-110
	0.1	95, 97, 94, 96, 93	5	95	2	93-97
	Overall		10	96	7	84-110
Field Corn Forage	0.01*	97, 90, 92, 90, 105	5	95	6	90-105
	0.1	91, 87, 79, 81, 92	5	86	7	79-92
	Overall		10	89	8	79-105
Field Corn Stover	0.01*	83, 92, 93, 94, 90	5	90	4	83-94
	0.1	83, 98, 97, 92, 116	5	97	12	83-116
	Overall		10	96	9	83-116
Soya bean Seed	0.01*	93, 101, 104, 103, 93	5	99	5	93-104
	0.1	106, 106, 118, 76, 104	5	102	16	76-118
	Overall		10	100	11	76-118

*Limit of quantification, defined by the lowest validated fortification level

**Residues in control samples and reagent blanks were less than 30% of the LOQ.

Table 66 SYN503780 Recovery Results Obtained During Independent Validation of Method GRM030.05A – confirmatory transition *m/z* = 278 → 176

Crop Matrix	Fortification Level (mg/kg)	Recovery (%)**	n	Mean (%)	RSD (%)	Range (%)
Field Corn Grain	0.01*	87, 104, 107, 113, 98	5	102	10	87-113
	0.1	97, 101, 96, 99, 96	5	98	2	96-101
	Overall		10	100	7	87-113

Crop Matrix	Fortification Level (mg/kg)	Recovery (%)**	n	Mean (%)	RSD (%)	Range (%)
Field Corn Forage	0.01*	93, 86, 94, 82, 92	5	86	6	86-94
	0.1	92, 89, 77, 80, 93	5	86	8	77-93
	Overall		10	88	7	77-94
Field Corn Stover	0.01*	95, 96, 100, 97, 97	5	95	6	95-100
	0.1	87, 98, 96, 90, 115	5	97	11	87-115
	Overall		10	97	7	87-115
Soya bean Seed	0.01*	101, 112, 108, 112, 120	5	111	6	101- 120
	0.1	79, 83, 80, 91, 86	5	84	6	79-91
	Overall		10	97	15	79-120

*Limit of quantification, defined by the lowest validated fortification level

**Residues in control samples and reagent blanks were less than 30% of the LOQ.

Table 67 CSCD686480 Recovery Results Obtained During Independent Validation of Method GRM030.05A– primary transition *m/z* = 264 → 175

Crop Matrix	Fortification Level (mg/kg)	Recovery (%)**	n	Mean (%)	RSD (%)	Range (%)
Field Corn Grain	0.01*	84, 107, 107, 102, 90	5	98	10	84-107
	0.1	109, 114, 111, 112, 109	5	111	2	109-114
	Overall		10	108	9	84-114
Field Corn Forage	0.01*	87, 84, 83, 93, 97	5	89	7	83-97
	0.1	101, 99, 92, 95, 108	5	99	6	92-108
	Overall		10	99	8	83-108
Field Corn Stover	0.01*	69, 80, 83, 82, 83	5	79	8	69-83
	0.1	94, 104, 104, 96, 125	5	105	11	94-125
	Overall		10	101	16	69-125
Soya bean Seed	0.01*	102, 117, 109, 120, 125	5	115	8	102-125
	0.1	86, 80, 76, 72, 70	5	77	8	70-86
	Overall		10	96	21	70-125

*Limit of quantification, defined by the lowest validated fortification level

**Residues in control samples and reagent blanks were less than 30% of the LOQ.

Table 68 CSCD686480 Recovery Results Obtained During Validation of Method GRM030.05A – confirmatory transition *m/z* = 264 → 170

Crop Matrix	Fortification Level (mg/kg)	Recovery (%)**	n	Mean (%)	RSD (%)	Range (%)
Field Corn Grain	0.01*	90, 105, 107, 105, 91	5	100	8	90-107
	0.1	102, 112, 104, 104, 102	5	105	4	102-112
	Overall		10	102	7	90-112
Field Corn Forage	0.01*	89, 88, 90, 97, 102	5	93	6	88-102
	0.1	106, 109, 97, 95, 106	5	103	6	95-109
	Overall		10	98	8	88-109
Field Corn Stover	0.01*	66, 72, 80, 76, 84	5	76	9	66-84
	0.1	97, 113, 109, 99, 133	5	110	13	97-133
	Overall		10	93	23	66-133

Crop Matrix	Fortification Level (mg/kg)	Recovery (%)**	n	Mean (%)	RSD (%)	Range (%)
Soya bean Seed	0.01*	101, 112, 108, 112, 120	5	111	6	101-120
	0.1	79, 83, 80, 91, 86	5	84	6	79-91
	Overall		10	97	15	79-120

*Limit of quantification, defined by the lowest validated fortification level

**Residues in control samples and reagent blanks were less than 30% of the LOQ.

Method GRM030.09A

This LC-MS/MS methods for measuring residues of NOA412101 (CSAA589691) metabolite in crops was reported by Braid (2012, NOA449280_10001).

Crop samples were extracted with acetonitrile:water 80:20 v/v. Samples were centrifuged and an aliquot of the sample evaporated to dryness. Samples were dissolved in water and then filtered into a vial, using a syringe filter and analysed by high performance liquid chromatography with triple-quadrupole mass-spectrometric detection (LC-MS/MS). The limit of quantification of the method was 0.01 mg/kg for NOA412101 (CSAA589691).

Good linearity was observed in the range of 1.0 to 5.0 ng/mL for NOA412101 (CSAA589691). Analysis of control samples resulted in no apparent residues of bicyclopyrone and metabolite (the response in the area of the bicyclopyrone and metabolites peak always corresponded to less than 30% of the limit of determination). Acceptable mean recoveries of between 70% and 120% with a relative standard deviation of < 20% were found for corn kernel matrix. Only the primary transition was quantified during validation. The recoveries obtained are detailed in Table 69.

Table 69 NOA412101 (CSAA589691) Recovery Results Obtained During Validation of Method GRM030.09A – primary transition *m/z* = 157 → 71

Crop Matrix	Fortification Level (mg/kg)	Recovery (%)**	n	Mean (%)	RSD (%)	Range (%)
Field Corn Grain	0.01*	77, 73, 97, 82, 74, 74, 82, 87, 81, 80, 73, 78, 82, 93, 98	15	82	10	73-97
	0.02	69, 70, 69, 70, 74, 70, 74, 101	8	75	15	69-101
	0.04	67, 77	2	72	N/A	67-77
	0.03	73	1	73	N/A	N/A
	0.05	109, 83, 68	2	87	24	68-109
	0.1	79, 81, 80, 70, 72, 75, 76	5	76	5	70-81
	0.2	93	1	93	N/A	N/A
	0.5	100	1	100	N/A	N/A
	Overall		35	80	13	67-109

*Limit of quantification, defined by the lowest validated fortification level

**Residues in control samples and reagent blanks were less than 30% of the LOQ.

Method POPIT MET.117

This LC-MS/MS method for measuring residues of bicyclopyrone and its CSAA915194 and CSAA806573 metabolites as SYN503780 and CSCD686480 in sugar cane, cassava, dried corn, corn and corn plants was reported by Fukimoto (2011a, NOA449280_11475).

Samples were extracted with acetonitrile:water 8:2 v/v. Samples are centrifuged and an aliquot of the sample evaporated to dryness. A solution of 30% hydrogen peroxide and 0.05M sodium

hydroxide solution is added and left at room temperature for 3 hours to hydrolysis bicyclopyrone and relevant metabolites to SYN503780 and CSCD686480. After the reaction, samples are diluted in a solution of acetonitrile:water 7:3 v/v for corn and acetonitrile: water 1:1v/v for other substrates, and filtered. The samples are quantified in terms of SYN503780 and CSCD686480 by liquid chromatography with triple-quadrupole mass-selective detector (LC-MS/MS). The limit of quantification of the method is 0.01 mg/kg for all analytes. The method has been validated in sugar cane, cassava, dried corn, corn and corn plants.

Good linearity was observed in the range of 0.03 to 3.2 µg/mL for SYN503780, CSCD686480 and CSAA915194. Analysis of control samples resulted in no apparent residues of bicyclopyrone and metabolite (the response in the area of the bicyclopyrone and metabolites peak always corresponded to less than 30% of the limit of determination).

Acceptable mean recoveries of between 70% and 120% with relative standard deviations of <20% were found for the five matrices: sugar cane, cassava, dried corn, corn and corn plants. The recoveries obtained are detailed in Tables 70 and 71.

Table 70 Bicyclopyrone Recovery Results Obtained During Validation of Method POPIT 117 – Determined as SYN503780, primary transition *m/z* = 278 → 202

Crop Matrix	Fortification Level (mg/kg)	Recovery (%)**	n	Mean (%)	RSD (%)	Range (%)
Sugar cane	0.01*	77, 76, 83, 77, 85, 87, 77	7	80	5.7	76-87
	0.1	82, 84, 85, 88, 87	5	85	2.8	82-88
	Overall		12	82	5.4	76-88
Cassava	0.01*	96, 90, 81, 92, 87, 78, 78	7	86	8.3	78-96
	0.1	92, 93, 95, 96, 92	5	94	1.9	92-96
	Overall		12	89	7.5	78-96
Corn (dry)	0.01*	84, 85, 86, 85, 88, 91, 93	7	87	3.9	84-93
	0.1	84, 86, 91, 89, 92	5	88	3.8	84-92
	Overall		12	88	3.7	84-93
Corn	0.01*	76, 76, 85, 88, 83, 76, 79	7	80	6.1	76-88
	0.1	86, 90, 91, 87, 87	5	88	2.5	86-91
	Overall		12	84	6.7	76-91
Whole corn plants	0.01*	72, 76, 86, 75, 77, 79, 87	7	79	7.2	72-87
	0.1	83, 75, 90, 72, 90	5	82	10.2	72-90
	Overall		12	80	8.4	72-90

*Limit of quantification, defined by the lowest validated fortification level

**Residues in control samples and reagent blanks were less than 30% of the LOQ.

Table 71 CSAA945194 Recovery Results Obtained During Validation of Method POPIT 117 – Determined as CSCD686480, primary transition *m/z* = 264 → 175

Crop Matrix	Fortification Level (mg/kg)	Recovery (%)**	n	Mean (%)	RSD (%)	Range (%)
Sugar cane	0.01*	88, 91, 91, 88, 92, 77, 89	7	88	5.8	77-92
	0.1	100, 96, 104, 107, 97	5	101	4.6	96-107
	Overall		12	93	8.7	77-107
Cassava	0.01*	89, 87, 92, 93, 89, 86, 90	7	82	4.4	86-93
	0.1	91, 98, 92, 93, 103	5	95	2.7	91-103
	Overall		12	87	8.4	86-103
Corn (dry)	0.01*	79, 79, 76, 83, 83, 84, 79	7	89	2.8	76-84
	0.1	82, 90, 91, 94, 105	5	95	5.3	82-105
	Overall		12	92	5.1	76-105

Crop Matrix	Fortification Level (mg/kg)	Recovery (%)**	n	Mean (%)	RSD (%)	Range (%)
Corn	0.01*	70, 71, 77, 80, 71, 78, 76	7	71	2.2	70-80
	0.1	76, 82, 78, 79, 79	5	83	2.0	76-82
	Overall		12	76	7.9	70-82
Whole corn plants	0.01*	80, 91, 105, 103, 82, 84, 88	7	80	3.7	80-103
	0.1	84, 72, 90, 71, 92	5	92	9.0	71-92
	Overall		12	85	9.6	71-103

*Limit of quantification, defined by the lowest validated fortification level
**Residues in control samples and reagent blanks were less than 30% of the LOQ.

Dixon and Alderman (2010, NOA449280_11098) investigated the extraction efficency of Method GRM030.08A using radiolabelled animal tissue. The method is suitable for the determination of residues of NOA449280 and structurally related metabolites such as CSAA915194 as the moieties SYN503780 and CSCD686480 in animal matrices. The samples analysed in this study were prepared in the poultry and ruminant metabolism studies

Goat liver and hen egg yolk samples were extracted using methodology developed and validated under Syngenta Analytical Method GRM030.08A. Extracts were then subjected to reaction with basic peroxide followed by HPLC analysis. Results of the extractability tests are presented in Table 72.

Table 72 Comparison of Extraction Efficiency from animal matrices using Residue Analytical Method and Exhaustive Extraction (Metabolism Method)

Commodity	Radiolabel	Extraction Method	Radioactive Residues Extracted		Extraction efficiency ($\%TRR_{RES}/\%TRR_{MET}$) x 100
			%TRR	Residue (mg/kg)	
Hen egg yolk	Pyridine	Metabolism [a]	91.1	0.094	91.5
		Residue	83.4	0.089	
Goat liver	Pyridine	Metabolism [a]	91.2	2.489	95.9
		Residue	87.5	2.127	

[a] Results from metabolism studies

The majority of the radioactivity in hen egg yolk (mean 83.4% TRR, total recovered radioactivity) was extracted with acetonitrile: water (50:50, v/v), which compared favourably with the exhaustive extraction procedure used in the hen metabolism study where 91.1% was extracted. The residue method therefore extracted approximately 92% of the radioactivity compared with the metabolism method.

The majority of the radioactivity in goat liver (87.5% TRR) was extracted with acetonitrile: water (50:50, v/v), which again compared favourably with the exhaustive extraction procedure used in the goat metabolism study where 91.2% was extracted. The residue method therefore extracted approximately 96% of the radioactivity compared with the metabolism method. Of the extractable radioactivity remaining after base hydrolysis, 15.2% was converted to SYN503780 and 75.1% was converted to CSCD686480. Extractability of residues from animal matrices using method GRM030.08A was acceptable.

Method GRM030.08A (Bicyclopyrone and its metabolites – animal tissues, milk and eggs)

This LC-MS/MS method for measuring residues of bicyclopyrone directly, or of determining bicyclopyrone and its metabolites as SYN503780 and CSCD686480 in animal tissues, milk and eggs was reported by Crook and Lin (2012, NOA449280_11267).

In this method, animal samples are extracted by homogenisation with acetonitrile: water (50:50 v/v). For the analysis of residues of bicyclopyrone, extracts are centrifuged and an aliquot of the extract is diluted and analysed by high performance liquid chromatography with triple quadrupole mass spectrometric detection (LC-MS/MS).

For the analysis of bicyclopyrone and CSAA915194 and structurally related molecules as the SYN503780 and CSCD686480 moieties, extracts are centrifuged and aliquots (equivalent to 0.1 g) evaporated to dryness. Hydrogen peroxide and 0.05M sodium hydroxide solution are added and the samples left at room temperature for 3 hours to oxidise bicyclopyrone, CSAA915194 and structurally related metabolites to SYN503780 or CSCD686480. After basic oxidation, the samples are acidified with 0.1M HCl and taken though a solid phase extraction (SPE) clean-up procedure. SYN503780 and CSCD686480, are eluted with 60:40, v/v, acetonitrile: 0.2% acetic acid. Samples are diluted and final determination is by high performance liquid chromatography with triple-quadrupole mass-spectrometric detection (LC-MS/MS). Quantitation and confirmation was performed using the following mass transitions:

Analyte	Quantitation	Confirmation
bicyclopyrone	400→324	400→228
SYN503780	278→ 202	278→ 176
CSCD686480	264→ 175	264→ 170
CSAA915194	384→ 137	384→ 175

The linearity of the LC-MS/MS detector response for both primary and confirmatory transitions for bicyclopyrone, CSCD686480 and SYN503780 was tested at concentrations ranging from 0.02–1.0 ng/mL and was found to be linear.

The limit of quantification (LOQ) has been set at 0.01 mg/kg (expressed as NOA449280 equivalents) or 0.01 mg/kg as SYN503780 or CSCD686480. Recovery rates were within guideline requirements (70–120%, RSD ≤ 20%). The recoveries obtained are detailed in Tables 73 to 78.

Table 73 Bicyclopyrone Recovery Results Obtained During Validation of Method GRM030.08A-Determined as bicyclopyrone, primary transition *m/z* = 400 → 324

Matrix	Fortification Level (mg/kg)	Recovery (%)**	n	Mean (%)	RSD (%)	Range (%)
Kidney	0.01*	97, 101,102, 99, 97	5	99	2	97-102
	0.1	103, 103, 104, 106,101	5	103	2	101-106
	Overall		10	101	3	97-106
Muscle	0.01*	103, 102, 99, 102, 104	5	102	2	99-104
	0.1	108, 104, 105, 104, 103	5	105	2	103-108
	Overall		10	103	2	99-108
Egg	0.01*	100, 95, 86, 87, 91	5	92	6	86-100
	0.1	94, 92, 98, 90, 93	5	93	3	90-98
	Overall		10	92	5	86-100
Fat	0.01*	107, 104, 110, 104, 106	5	106	3	104-110
	0.1	107, 108, 106, 109, 111	5	108	2	106-111
	Overall		10	107	2	104-111
Liver	0.01*	103, 105, 97, 92, 100	5	99	5	92-105
	0.1	102, 104, 104, 104, 102	5	103	1	102-104
	Overall		10	101	4	92-105
Milk	0.01*	89, 89, 88, 93, 87	5	89	3	87-93
	0.1	96, 94, 93, 90, 99	5	94	4	90-99
	Overall		10	92	4	87-99

*Limit of quantification, defined by the lowest validated fortification level
**Residues in control samples and reagent blanks were less than 30% of the LOQ.

Table 74 Bicyclopyrone Recovery Results Obtained During Validation of Method GRM030.08A – Determined as bicyclopyrone, confirmatory transition *m/z* = 400 → 228

Matrix	Fortification Level (mg/kg)	Recovery (%)**	n	Mean (%)	RSD (%)	Range (%)
Kidney	0.01*	93, 100, 102, 97, 96	5	98	4	93-102
	0.1	103, 100, 102, 108, 101	5	103	3	100-108
	Overall		10	100	4	93-108
Muscle	0.01*	106, 107, 112, 102, 111	5	107	4	102-112
	0.1	110, 108, 108, 104, 106	5	107	2	104-110
	Overall		10	107	3	102-112
Egg	0.01*	97, 99, 80, 88, 88	5	90	9	80-99
	0.1	96, 93, 98, 93, 91	5	94	3	91-98
	Overall		10	92	6	80-99
Fat	0.01*	105, 101, 113, 116, 113	5	109	6	101-116
	0.1	107, 108, 109, 105, 109	5	108	2	105-109
	Overall		10	108	4	101-116
Liver	0.01*	101, 101, 102, 96, 97	5	99	3	96-102
	0.1	100, 103, 102, 104, 103	5	102	1	100-104
	Overall		10	101	3	96-104
Milk	0.01*	89, 94, 92, 83, 83	5	88	6	83-94
	0.1	96, 93, 94, 90, 97	5	94	3	90-97
	Overall		10	91	5	83-97

*Limit of quantification, defined by the lowest validated fortification level
**Residues in control samples and reagent blanks were less than 30% of the LOQ.

Table 75 CSAA915194 Recovery Results Obtained During Validation of Method GRM030.08A – Determined as CSCD686480, primary transition *m/z* = 264 → 175

Matrix	Fortification Level (mg/kg)	Recovery (%)**	n	Mean (%)	RSD (%)	Range (%)
Kidney	0.01*	89, 83, 99, 104, 107	5	96	11	83-107
	0.1	94, 92, 105, 101, 94	5	97	6	92-105
	Overall		10	97	8	83-107
Muscle	0.01*	83, 62, 89, 84, 74	5	78	14	62-89
	0.1	78, 63, 73, 73, 85	5	74	11	63-85
	Overall		10	76	12	62-89
Egg	0.01*	68, 89, 83, 98, 111	5	90	18	68-111
	0.1	105, 93, 83, 74, 99	5	91	14	74-105
	Overall		10	90	15	68-111
Fat	0.01*	97, 107, 100, 106, 102	5	103	4	97-107
	0.1	109, 108, 84, 100, 100	5	100	10	84-109
	Overall		10	101	7	84-109
Liver	0.01*	89, 98, 87, 95, 95	5	93	5	87-98
	0.1	91, 88, 85, 95, 80	5	88	7	80-95
	Overall		10	90	6	80-98
Milk	0.01*	91, 77, 94, 82, 87	5	86	8	77-94
	0.1	99, 92, 87, 91, 96	5	93	5	87-99
	Overall		10	90	7	77-99

*Limit of quantification, defined by the lowest validated fortification level
**Residues in control samples and reagent blanks were less than 30% of the LOQ.

Table 76 CSAA915194 Recovery Results Obtained During Validation of Method GRM030.08A – Determined as CSCD686480, confirmatory transition *m/z* = 264 → 170

Matrix	Fortification Level (mg/kg)	Recovery (%)**	n	Mean (%)	RSD (%)	Range (%)
Kidney	0.01*	94, 97, 99, 106, 116	5	102	9	94-116
	0.1	91, 98, 95, 95, 92	5	94	3	91-98
	Overall		10	98	8	91-116
Muscle	0.01*	84, 69, 101, 82, 81	5	83	14	69-101
	0.1	85, 90, 79, 88, 90	5	87	5	79-90
	Overall		10	85	10	69-101
Egg	0.01*	78, 109, 74, 93, 115	5	94	19	74-115
	0.1	93, 92, 84, 81, 83	5	86	6	81-93
	Overall		10	90	15	74-115
Fat	0.01*	79, 82, 77, 73, 82	5	79	5	73-82
	0.1	84, 81, 76, 94, 79	5	83	9	76-94
	Overall		10	81	7	73-94
Liver	0.01*	76, 97, 95, 103, 77	5	90	14	76-103
	0.1	86, 105, 104, 83, 80	5	92	13	80-105
	Overall		10	91	13	76-105
Milk	0.01*	88, 78, 88, 80, 85	5	84	6	78-88
	0.1	83, 94, 82, 85, 88	5	86	6	82-94
	Overall		10	85	6	78-94

*Limit of quantification, defined by the lowest validated fortification level
**Residues in control samples and reagent blanks were less than 30% of the LOQ.

Table 77 Bicyclopyrone Recovery Results Obtained During Validation of Method GRM030.08A – Determined as SYN503780, primary transition *m/z* = 278 → 202

Matrix	Fortification Level (mg/kg)	Recovery (%)**	n	Mean (%)	RSD (%)	Range (%)
Kidney	0.01*	93, 98, 95, 97, 93	5	95	2	93-98
	0.1	85, 103, 97, 97, 92	5	95	7	85-103
	Overall		10	95	5	85-103
Muscle	0.01*	86, 83, 88, 89, 91	5	87	3	83-91
	0.1	87, 85, 82, 82, 93	5	86	5	82-93
	Overall		10	86	4	82-93
Egg	0.01*	71, 91, 88, 90, 104	5	89	13	71-104
	0.1	99, 93, 94, 84, 90	5	92	6	84-99
	Overall		10	90	10	71-104
Fat	0.01*	88, 96, 97, 93, 96	5	94	4	88-97
	0.1	102, 99, 103, 99, 101	5	101	2	99-103
	Overall		10	97	5	88-103
Liver	0.01*	88, 117, 111, 91, 98	5	101	12	88-117
	0.1	88, 91, 92, 92, 83	5	89	4	83-92
	Overall		10	95	11	83-117
Milk	0.01*	101, 98, 103, 94, 97	5	98	4	94-103
	0.1	92, 98, 99, 105, 99	5	99	5	92-105
	Overall		10	99	4	92-105

*Limit of quantification, defined by the lowest validated fortification level
**Residues in control samples and reagent blanks were less than 30% of the LOQ.

Table 78 Bicyclopyrone Recovery Results Obtained During Validation of Method GRM030.08A – Determined as SYN503780, confirmatory transition *m/z* = 278 → 176

Matrix	Fortification Level (mg/kg)	Recovery (%)**	n	Mean (%)	RSD (%)	Range (%)
Kidney	0.01*	95, 99, 104, 99, 111	5	102	6	95-111
	0.1	97, 96, 100, 97, 98	5	98	2	96-100
	Overall		10	100	5	95-111
Muscle	0.01*	87, 86, 97, 103, 98	5	94	8	86-103
	0.1	87, 92, 102, 105, 100	5	97	7	87-105
	Overall		10	96	7	86-105
Egg	0.01*	88, 111, 99, 112, 123	5	107	13	88-123
	0.1	106, 111, 102, 100, 106	5	105	4	100-111
	Overall		10	106	9	88-123
Fat	0.01*	76, 84, 88, 89, 92	5	86	7	76-92
	0.1	95, 94, 95, 95, 94	5	95	1	94-95
	Overall		10	90	7	76-95
Liver	0.01*	85, 112, 113, 84, 90	5	97	15	84-113
	0.1	93, 89, 90, 96, 92	5	92	3	89-96
	Overall		10	94	11	84-113
Milk	0.01*	108, 108, 111, 103, 102	5	106	4	102-111
	0.1	106, 111, 97, 99, 98	5	102	6	97-111
	Overall		10	104	5	97-111

*Limit of quantification, defined by the lowest validated fortification level
**Residues in control samples and reagent blanks were less than 30% of the LOQ.

Independent laboratory of GRM030.08A in animal tissues

During an independent laboratory validation (ILV) of GRM030.08A milk, egg, muscle tissue and liver samples were fortified with bicyclopyrone (for determination directly or as SYN503780) or with CSAA915194 (for determination as CSCD686480) at the proposed limit of quantification (0.01 mg/kg) and at ten times LOQ (0.1 mg/kg). The recoveries obtained are detailed in Tables 79 to 84.

Table 79 Bicyclopyrone Recovery Results Obtained During Independent Validation of Method GRM030.08A – Determined as bicyclopyrone, primary transition *m/z* = 400 → 324

Matrix	Fortification Level (mg/kg)	Recovery (%)**	n	Mean (%)	RSD (%)	Range (%)
Milk	0.01*	106, 97, 101, 97, 97	5	100	4	97-106
	0.1	91, 91, 103, 93, 93	5	94	5	91-103
	Overall		10	97	10	91-106
Egg	0.01*	94, 102, 93, 98, 66	5	91	15	66-102
	0.1	95, 94, 93, 96, 98	5	95	2	93-98
	Overall		10	93	11	66-102
Muscle	0.01*	84, 92, 85, 89, 88	5	88	3	84-92
	0.1	88, 85, 88, 86, 87	5	87	1	85-88
	Overall		10	87	2	84-92
Liver	0.01*	108, 107, 109, 100, 93	5	103	7	93-109

Matrix	Fortification Level (mg/kg)	Recovery (%)**	n	Mean (%)	RSD (%)	Range (%)
	0.1	89, 91, 79, 83, 87	5	86	6	79-91
	Overall		10	95	12	79-109

*Limit of quantification, defined by the lowest validated fortification level
**Residues in control samples and reagent blanks were less than 30% of the LOQ.

Table 80 Bicyclopyrone Recovery Results Obtained During Independent Validation of Method GRM030.08A – Determined as bicyclopyrone, confirmatory transition *m/z* = 400 → 228

Matrix	Fortification Level (mg/kg)	Recovery (%)**	n	Mean (%)	RSD (%)	Range (%)
Milk	0.01*	105, 89, 102, 103, 96	5	99	7	89-105
	0.1	87, 91, 103, 91, 99	5	94	7	87-103
	Overall		10	97	7	87-105
Egg	0.01*	95, 104, 102, 108, 73	5	96	15	73-108
	0.1	97, 92, 96, 98, 93	5	95	3	92-98
	Overall		10	96	9	73-108
Muscle	0.01*	107, 94, 90, 97, 92	5	96	7	90-107
	0.1	86, 86, 86, 87, 87	5	86	1	86-87
	Overall		10	91	8	86-107
Liver	0.01*	101, 118, 113, 110, 96	5	108	13	96-118
	0.1	94, 107, 94, 74, 89	5	92	5	74-107
	Overall		10	100	13	74-118

*Limit of quantification, defined by the lowest validated fortification level
**Residues in control samples and reagent blanks were less than 30% of the LOQ.

Table 81 CSAA915194 Recovery Results Obtained During Independent Validation of Method GRM030.08A – Determined as CSCD686480, primary transition m/z = 264 → 175

Matrix	Fortification Level (mg/kg)	Recovery (%)**	n	Mean (%)	RSD (%)	Range (%)
Milk	0.01*	106, 97, 101, 97, 97	5	100	4	97-106
	0.1	91, 91, 103, 93, 93	5	94	5	91-103
	Overall		10	97	10	91-106
Egg	0.01*	94, 102, 93, 98, 66	5	91	15	66-102
	0.1	95, 94, 93, 96, 98	5	95	2	93-98
	Overall		10	93	11	66-102
Muscle	0.01*	84, 92, 85, 89, 88	5	88	3	84-92
	0.1	88, 85, 88, 86, 87	5	87	1	85-88
	Overall		10	87	2	84-92
Liver	0.01*	108, 107, 109, 100, 93	5	103	7	93-109
	0.1	89, 91, 79, 83, 87	5	86	6	79-91
	Overall		10	95	12	79-109

*Limit of quantification, defined by the lowest validated fortification level
**Residues in control samples and reagent blanks were less than 30% of the LOQ.

Table 82 CSAA915194 Recovery Results Obtained During Independent Validation of Method GRM030.08A – Determined as CSCD686480, confirmatory transition *m/z* = 264 → 170

Matrix	Fortification Level (mg/kg)	Recovery (%)**	n	Mean (%)	RSD (%)	Range (%)
Milk	0.01*	105, 89, 102, 103, 96	5	99	7	89-105
	0.1	87, 91, 103, 91, 99	5	94	7	87-103
	Overall		10	97	7	87-105
Egg	0.01*	95, 104, 102, 108, 73	5	96	15	73-108
	0.1	97, 92, 96, 98, 93	5	95	3	92-98
	Overall		10	96	9	73-108
Muscle	0.01*	107, 94, 90, 97, 92	5	96	7	90-107
	0.1	86, 86, 86, 87, 87	5	86	1	86-87
	Overall		10	91	8	86-107
Liver	0.01*	101, 118, 113, 110, 96	5	108	13	96-118
	0.1	94, 107, 94, 74, 89	5	92	5	74-107
	Overall		10	100	13	74-118

*Limit of quantification, defined by the lowest validated fortification level
**Residues in control samples and reagent blanks were less than 30% of the LOQ.

Table 83 Bicyclopyrone Recovery Results Obtained During Independent Validation of Method GRM030.08A – Determined as SYN503780, primary transition *m/z* = 278 → 202

Matrix	Fortification Level (mg/kg)	Recovery (%)**	n	Mean (%)	RSD (%)	Range (%)
Milk	0.01*	96, 88, 87, 87, 102	5	92	8	87-102
	0.1	108, 107, 117, 101, 102	5	107	6	101-117
	Overall		10	100	10	87-117
Egg	0.01*	108, 104, 110, 111, 78	5	102	14	78-111
	0.1	104, 109, 107, 106, 111	5	107	3	104-111
	Overall		10	105	10	78-111
Muscle	0.01*	101, 102, 96, 101, 110	5	102	5	96-110
	0.1	96, 96, 99, 97, 99	5	97	2	96-99
	Overall		10	100	4	96-110
Liver	0.01*	109, 114, 112, 103, 101	5	108	6	101-114
	0.1	91, 96, 94, 54, 89	5	88	20	54-96
	Overall		10	96	18	54-114

*Limit of quantification, defined by the lowest validated fortification level
**Residues in control samples and reagent blanks were less than 30% of the LOQ.

Table 84 Bicyclopyrone Recovery Results Obtained During Independent Validation of Method GRM030.08A – Determined as SYN503780, confirmatory transition *m/z* = 278 → 176

Matrix	Fortification Level (mg/kg)	Recovery (%)**	n	Mean (%)	RSD (%)	Range (%)
Milk	0.01*	93, 91, 77, 115, 123	5	100	19	77-123
	0.1	98, 99, 109, 107, 100	5	103	5	98-109
	Overall		10	101	113	77-123
Egg	0.01*	95, 104, 102, 108, 73	5	104	15	73-108
	0.1	97, 92, 96, 98, 93	5	108	2	92-98
	Overall		10	106	10	73-108
Muscle	0.01*	94, 95, 91, 110, 101	5	98	8	91-110

Matrix	Fortification Level (mg/kg)	Recovery (%)**	n	Mean (%)	RSD (%)	Range (%)
	0.1	95, 94, 92, 97, 95	5	95	2	92-97
	Overall		10	96	6	91-110
Liver	0.01*	115, 109, 113, 109, 102	5	110	5	102-115
	0.1	86, 96, 94, 54, 84	5	83	20	54-96
	Overall		10	96	19	54-115

*Limit of quantification, defined by the lowest validated fortification level
**Residues in control samples and reagent blanks were less than 30% of the LOQ.

Stability of residues in stored analytical samples

The Meeting received information on the stability of residues of bicyclopyrone and its metabolites in fortified samples of raw agricultural commodities (RACs): maize grain, wheat straw, spinach leaves, soya beans, lentils, lemon fruit, potato tubers and sugarcane, in processed commodities: corn grits, corn flour, corn starch, corn oil, sugarcane molasses, sugarcane refined sugar, soya bean meal and soya bean hulls, and in animal commodities: milk, fat, muscle (meat), liver and kidney stored at freezer temperatures of -20±5 °C for up to 24 months (RACs), 12 months (processed commodities) or 12.7 months (bovine commodities).

Plant matrices

In a study reported by Gemrot, (2010, NOA449280_11093), separate representative crop sample replicates were fortified with 0.2 mg/kg bicyclopyrone and SYN503780 and stored at -20 ± 5°C. At least three replicate samples of the crop matrices were analysed initially and at least two replicate samples were removed after 3, 6, 12, 18 and 24 months storage at a temperature of -20±5 °C.

Analytical method GRM030.03A was used in the analysis of stored samples. The method determines bicyclopyrone and SYN503780 residues in the crops.

The residues of bicyclopyrone and SYN503780 showed no significant decrease (>30% as compared with the initial value) in any of the crop matrices studied after storage under deep frozen conditions for at least 24 months. The recoveries of the various analytes after storage are summarised in the following Tables.

Table 85 Stability of residues of bicyclopyrone in Maize Grain during frozen storage

Interval		Uncorrected Residue (mg/kg)	Mean Uncorrected Residue (mg/kg) (A)	Mean Procedural Recovery (%)	Mean Recovered Uncorrected Residue (%) (C)
Months stored	Days (actual)				
0	0	0.17, 0.18, 0.17	0.17	87	100[a]
3	83	0.18, 0.17	0.17	87	99
6	198	0.25, 0.25	0.25	98	142
12	366	0.17, 0.16	0.16	83	93
18	535	0.20, 0.20	0.20	97	115
24	735	0.17, 0.18	0.17	89	100

[a] nominally 100%
C = (A / 0 time A) x 100/

Table 86 Stability of residues of SYN503780 in Maize Grain during frozen storage

Interval		Uncorrected Residue (mg/kg)	Mean Uncorrected Residue (mg/kg) (A)	Mean Procedural Recovery (%)	Mean Recovered Uncorrected Residue (%) (C)
Months stored	Days (actual)				
0	0	0.20, 0.20, 0.20	0.20	100	100[a]
3	83	0.16, 0.17	0.16	82	82
6	198	0.20, 0.21	0.21	103	103

Interval		Uncorrected Residue (mg/kg)	Mean Uncorrected Residue (mg/kg) (A)	Mean Procedural Recovery (%)	Mean Recovered Uncorrected Residue (%) (C)
Months stored	Days (actual)				
12	366	0.18, 0.19	0.19	94	94
18	535	0.20, 0.20	0.20	101	101
24	735	0.19, 0.19	0.19	94	94

[a] nominally 100%

C = (A / 0 time A) x 100/

Table 87 Stability of residues of bicyclopyrone in Wheat Straw during frozen storage

Interval		Uncorrected Residue (mg/kg)	Mean Uncorrected Residue (mg/kg) (A)	Mean Procedural Recovery (%)	Mean Recovered Uncorrected Residue (%) (C)
Months stored	Days (actual)				
0	0	0.21, 0.21, 0.22	0.21	107	100[a]
3	84	0.17, 0.17	0.17	84	79
6	198	0.16, 0.15	0.16	103	73
12	366	0.21, 0.19	0.20	107	93
18	535	0.20, 0.20	0.20	101	95
24	735	0.19, 0.18	0.18	92	86

[a] nominally 100%

C = (A / 0 time A) x 100/

Table 88 Stability of residues of SYN503780 in Wheat Straw during frozen storage

Interval		Uncorrected Residue (mg/kg)	Mean Uncorrected Residue (mg/kg) (A)	Mean Procedural Recovery (%)	Mean Recovered Uncorrected Residue (%) (C)
Months stored	Days (actual)				
0	0	0.20, 0.20, 0.20	0.20	100	100[a]
3	84	0.17, 0.17	0.17	84	83
6	198	0.17, 0.17	0.17	105	86
12	366	0.22, 0.21	0.21	105	106
18	535	0.20, 0.20	0.20	101	102
24	735	0.19, 0.18	0.18	92	92

[a] nominally 100%

C = (A / 0 time A) x 100/

Table 89 Stability of residues of bicyclopyrone in Spinach Leaf during frozen storage

Interval		Uncorrected Residue (mg/kg)	Mean Uncorrected Residue (mg/kg) (A)	Mean Procedural Recovery (%)	Mean Recovered Uncorrected Residue (%) (C)
Months stored	Days (actual)				
0	0	0.21, 0.20, 0.21	0.21	104	100[a]
3	83	0.17, 0.17	0.17	90	82
6	209	0.17, 0.19	0.18	108	87
12	365	0.21, 0.19	0.20	106	96
18	534	0.17, 0.21	0.19	102	92
24	734	0.19, 0.21	0.20	108	96

[a] nominally 100%

C = (A / 0 time A) x 100/

Table 90 Stability of residues of SYN503780 in Spinach Leaf during frozen storage

Interval		Uncorrected Residue (mg/kg)	Mean Uncorrected Residue (mg/kg) (A)	Mean Procedural Recovery (%)	Mean Recovered Uncorrected Residue (%) (C)
Months stored	Days (actual)				
0	0	0.20, 0.19, 0.20	0.19	97	100[a]
3	83	0.18, 0.18	0.18	89	93
6	209	0.19, 0.18	0.19	94	96
12	365	0.21, 0.20	0.21	101	106
18	534	0.19, 0.21	0.20	86	103
24	734	0.20, 0.21	0.21	102	106

[a] nominally 100%

C = (A / 0 time A) x 100/

Table 91 Stability of residues of bicyclopyrone in Soya beans during frozen storage

Interval		Uncorrected Residue (mg/kg)	Mean Uncorrected Residue (mg/kg) (A)	Mean Procedural Recovery (%)	Mean Recovered Uncorrected Residue (%) (C)
Months stored	Days (actual)				
0	0	0.19, 0.18, 0.17	0.18	90	100[a]
3	77	0.19, 0.19	0.19	91	104
6	182	0.17, 0.17	0.17	90	95
12	370	0.16, 0.16	0.16	81	88
18	540	0.20, 0.19	0.20	101	109
24	756	0.19, 0.17	0.18	89	100

[a] nominally 100%

C = (A / 0 time A) x 100/

Table 92 Stability of residues of SYN503780 in Soya beans during frozen storage

Interval		Uncorrected Residue (mg/kg)	Mean Uncorrected Residue (mg/kg) (A)	Mean Procedural Recovery (%)	Mean Recovered Uncorrected Residue (%) (C)
Months stored	Days (actual)				
0	0	0.21, 0.18, 0.19	0.19	96	100[a]
3	77	0.18, 0.18	0.18	98	94
6	182	0.20, 0.20	0.20	107	105
12	370	0.20, 0.21	0.20	93	105
18	540	0.20, 0.19	0.20	98	102
24	756	0.18, 0.19	0.19	94	98

[a] nominally 100%

C = (A / 0 time A) x 100/

Table 93 Stability of residues of bicyclopyrone in Lentil Seeds during frozen storage

Interval		Uncorrected Residue (mg/kg)	Mean Uncorrected Residue (mg/kg) (A)	Mean Procedural Recovery (%)	Mean Recovered Uncorrected Residue (%) (C)
Months stored	Days (actual)				
0	0	0.21, 0.20, 0.21	0.21	104	100[a]
3	82	0.18, 0.18	0.18	99	87
6	196	0.21, 0.21	0.21	87	101
12	364	0.21, 0.22	0.22	109	104
18	533	0.17, 0.17	0.17	98	83
24	733	0.19, 0.18	0.18	101	88

[a] nominally 100%

C = (A / 0 time A) x 100/

Table 94 Stability of residues of SYN503780 in Lentil Seeds during frozen storage

Interval		Uncorrected Residue (mg/kg)	Mean Uncorrected Residue (mg/kg) (A)	Mean Procedural Recovery (%)	Mean Recovered Uncorrected Residue (%) (C)
Months stored	Days (actual)				
0	0	0.20, 0.19, 0.20	0.19	97	100[a]
3	82	0.18, 0.18	0.18	86	93
6	196	0.21, 0.20	0.20	87	105
12	364	0.21, 0.21	0.21	95	107
18	533	0.21, 0.21	0.21	99	110
24	733	0.20, 0.21	0.20	105	104

[a] nominally 100%

C = (A / 0 time A) x 100/

Table 95 Stability of residues of bicyclopyrone in Citrus (Lemon Fruit) during frozen storage

Interval		Uncorrected Residue (mg/kg)	Mean Uncorrected Residue (mg/kg) (A)	Mean Procedural Recovery (%)	Mean Recovered Uncorrected Residue (%) (C)
Months stored	Days (actual)				
0	0	0.20, 0.20, 0.21	0.20	102	100[a]
3	82	0.19, 0.19	0.149	87	93
6	196	0.20, 0.20	0.20	81	99
12	364	0.20, 0.19	0.20	105	97
18	533	0.11, 0.12	0.11	76	56
24	733	0.19, 0.20	0.20	91	96

[a] nominally 100%

C = (A / 0 time A) x 100

Table 96 Stability of residues of SYN503780 in Citrus (Lemon Fruit) during frozen storage

Interval		Uncorrected Residue (mg/kg)	Mean Uncorrected Residue (mg/kg) (A)	Mean Procedural Recovery (%)	Mean Recovered Uncorrected Residue (%) (C)
Months stored	Days (actual)				
0	0	0.19, 0.21, 0.21	0.20	100	100[a]
3	82	0.18, 0.19	0.19	94	93
6	196	0.19, 0.18	0.19	88	93
12	364	0.20, 0.20	0.20	98	100
18	533	0.17, 0.18	0.17	89	87
24	733	0.20, 0.21	0.21	100	102

[a] nominally 100%

C = (A / 0 time A) x 100/

Table 97 Stability of residues of bicyclopyrone in Potato Tuber during frozen storage

Interval		Uncorrected Residue (mg/kg)	Mean Uncorrected Residue (mg/kg) (A)	Mean Procedural Recovery (%)	Mean Recovered Uncorrected Residue (%) (C)
Months stored	Days (actual)				
0	0	0.20, 0.21, 0.21	0.21	103	100[a]
3	83	0.17, 0.18	0.18	87	85
6	196	0.20, 0.21	0.20	80	99
12	364	0.17, 0.18	0.18	88	85
18	533	0.17, 0.17	0.17	97	82
24	733	0.21, 0.20	0.21	95	100

[a] nominally 100%

C = (A / 0 time A) x 100/

Table 98 Stability of residues of SYN503780 in Potato Tuber during frozen storage

Interval		Uncorrected Residue (mg/kg)	Mean Uncorrected Residue (mg/kg) (A)	Mean Procedural Recovery (%)	Mean Recovered Uncorrected Residue (%) (C)
Months stored	Days (actual)				
0	0	0.18, 0.19, 0.19	0.19	94	100[a]
3	83	0.17, 0.17	0.17	85	90
6	196	0.22, 0.22	0.22	97	118
12	364	0.21, 0.21	0.21	101	111
18	533	0.21, 0.22	0.22	103	114
24	733	0.20, 0.21	0.21	96	110

[a] nominally 100%

C = (A / 0 time A) x 100/

In a separate study, storage stability of bicyclopyrone and its metabolites SYN503780, CSAA915194, CSCD686480 in sugarcane were investigated by Keats and Winner (2012, SL_10076). Samples of billets and tops were fortified with 0.1 mg/kg bicyclopyrone and its metabolites SYN503780, CSAA915194, CSCD686480 and stored in the freezer ≤ -18 ºC up to 26 months.

Methods GRM030.03A and GRM030.05A were used to quantify residues in sugarcane billets and tops. Thus, bicyclopyrone was measured directly using GRM030.03A and as SYN503780 using GRM030.05A, SYN503780 was measured directly using GRM030.03A and using GRM030.05A, CSAA915194 was measured as CSCD686480 using GRM030.05A, and CSCD686480 was measured directly using GRM030.05A. There was no significant change in the residue levels of bicyclopyrone, SYN503780, CSAA915194 or CSCD686480 in sugarcane billets or tops when stored at ≤-18 ºC for at least 26 months.

Table 99 Stability of bicyclopyrone and metabolite residues in sugarcane during frozen storage

Commodity	Storage Period (months)	Fortification (0.1 mg/kg)	Mean Recovery (n=5)			
			Method GRM030.03A		Method GRM030.05A	
		Analyte	Bicyclopyrone	SYN503780	SYN503780	CSCD686480
Sugarcane – Billets	25/26	Bicyclopyrone	81.5%		85.0%	
	25/26	SYN503780		95.1%	104.3%	
	26	CSAA915194				87.6%
	26	CSCD686480				98.2%
	26	CSAA806573				
Sugarcane-Tops	24/25	Bicyclopyrone	94.5%		90.0%	
	24/25	SYN503780		90.2%	104.7%	
	25	CSAA915194				88.4%
	25	CSCD686480				94.9%
	25	CSAA806573				

Processed commodities

Plant matrices

The storage stability of bicyclopyrone was investigated in a number of processed commodities for up to 12 months by Hagan (2013, NOA449280_50635).

Samples (10 g was weighed into 250 mL centrifuge bottles, for each time interval and matrix) of corn grits, corn flour, corn starch, corn oil, sugarcane molasses, sugarcane refined sugar, soya bean meal and soya bean hulls were individually fortified with 1.0 mg/kg bicyclopyrone. The samples were stored frozen at a temperature of <-10 ºC up to 12 months. Samples for all matrices were analysed using method GRM030.03A

Each analytical set analysed with the stability/stored samples included one non-fortified control and two laboratory fortified samples (fresh fortified) (QC) prepared just prior to extraction for the stability samples (Month 1, Month 4, Month 12). The Day 0 set of samples consisted of one non-fortified control and four laboratory fortified samples (fresh fortified).

There were no residues of bicyclopyrone detected in any of the non-fortified controls analysed for the corn processed fractions (grits, flour, starch and oil), sugarcane processed fraction (molasses), refined sugar and soya bean processed fractions (meal and hulls) at or above the LOQ of 0.01 mg/kg. A total of ten fortified QC samples were analysed for each of the corn, sugarcane and soya bean processed fractions during the 12 month study.

Bicyclopyrone is stable in corn, sugarcane and soya bean processed fractions for 12 months when stored in a freezer set at ≤-10 °C. Storage stabilities, defined as the difference between the final and initial residue concentrations for in the representative processed fractions, are summarized in the following Tables.

Table 100 Recoveries of bicyclopyrone from Corn Grits during frozen storage

Interval Months stored	Uncorrected Residue(stored) (mg/kg)	Mean Uncorrected Residue (stored) (mg/kg)	Procedural recoveries (fresh) (mg/kg)	Mean procedural recovery (mg/kg)	Mean Procedural Recovery (fresh) (%)	Mean Recovered Uncorrected Residue (stored) (%)	Mean Recovered Corrected Residue (stored) (%)
0	-	-	1.02, 1.13, 1.16, 1.12	1.11	111	-	-
1	1.14, 1.20	1.17	1.01, 0.959	0.985	99	117	118
4	0.902, 0.968	0.935	0.895, 0.859	0.877	88	94	106
12	0.916, 0.888	0.902	1.20, 1.10	1.15	115	91	79

Table 101 Recoveries of bicyclopyrone from Corn Flour during frozen storage

Interval Months stored	Uncorrected Residue(stored) (mg/kg)	Mean Uncorrected Residue (stored) (mg/kg)	Procedural recoveries (fresh) (mg/kg)	Mean procedural recovery (mg/kg)	Mean Procedural Recovery (fresh) (%)	Mean Recovered Uncorrected Residue (stored) (%)	Mean Recovered Corrected Residue (stored) (%)
0	-	-	0.918, 0.914, 0.917, 0.903	0.913	91	-	-
1	1.07, 1.15	1.11	0.756, 1.18	0.968	97	111	115
4	1.06, 1.06	1.06	0.832, 0.905	0.869	87	106	122
12	0.850, 0.906	0.878	1.13, 1.14	1.14	114	88	78

Table 102 Recoveries of bicyclopyrone from Corn Starch during frozen storage

Interval Months stored	Uncorrected Residue(stored) (mg/kg)	Mean Uncorrected Residue (stored) (mg/kg)	Procedural recoveries (fresh) (mg/kg)	Mean procedural recovery (mg/kg)	Mean Procedural Recovery (fresh) (%)	Mean Recovered Uncorrected Residue (stored) (%)	Mean Recovered Corrected Residue (stored) (%)
0	-	-	1.00, 0.772, 1.04, 0.717	0.882	88	-	-
1	1.01, 1.11	1.06	1.15, 1.14	1.15	115	106	93
4	0.881, 0.921	0.901	0.796, 0.854	0.825	83	90	109
12	0.824, 0.869	0.847			117	85	72

Table 203 Recoveries of bicyclopyrone from Corn Oil during frozen storage

Interval Months stored	Uncorrected Residue(stored) (mg/kg)	Mean Uncorrected Residue (stored) (mg/kg)	Procedural recoveries (fresh) (mg/kg)	Mean procedural recovery (mg/kg)	Mean Procedural Recovery (fresh) (%)	Mean Recovered Uncorrected Residue (stored) (%)	Mean Recovered Corrected Residue (stored) (%)
0	-	-	0.829, 0.983, 0.916, 0.768	0.874	88	-	-
1	1.04, 1.02	1.03	1.08, 1.13	1.11	111	103	93
4	0.948, 0.897	0.922	0.848, 0.922	0.885	89	93	104
12	0.823, 0.797	0.810	1.12, 1.11	1.12	112	81	72

Table 104 Recoveries of bicyclopyrone from Sugarcane Molasses during frozen storage

Interval Months stored	Uncorrected Residue(stored) (mg/kg)	Mean Uncorrected Residue (stored) (mg/kg)	Procedural recoveries (fresh) (mg/kg)	Mean procedural recovery (mg/kg)	Mean Procedural Recovery (fresh) (%)	Mean Recovered Uncorrected Residue (stored) (%)	Mean Recovered Corrected Residue (stored) (%)
0	-	-	1.19, 1.11, 1.01, 1.04	1.09	109	-	-
1	0.849, 0.787	0.818	1.06, 0.990	1.03	103	82	80
4	0.985, 0.901	0.943	0.982, 0.925	0.954	96	95	99
12	0.799, 0.759	0.779	1.12, 1.20	1.16	116	78	68

Table 105 Recoveries of bicyclopyrone from Refined Sugar during frozen storage

Interval Months stored	Uncorrected Residue(stored) (mg/kg)	Mean Uncorrected Residue (stored) (mg/kg)	Procedural recoveries (fresh) (mg/kg)	Mean procedural recovery (mg/kg)	Mean Procedural Recovery (fresh) (%)	Mean Recovered Uncorrected Residue (stored) (%)	Mean Recovered Corrected Residue (stored) (%)
0	-	-	1.14, 1.11, 1.02, 1.12	1.10	110	-	-
1	1.13, 1.20	1.17	1.17, 0.861	1.02	102	117	115
4	0.995, 0.997	0.996	0.969, 0.957	0.963	97	100	103
12	0.939, 0.904	0.922	1.20, 1.17	1.19	119	92	78

Table 106 Recoveries of bicyclopyrone from Soya bean Meal during frozen storage

Interval Months stored	Uncorrected Residue(stored) (mg/kg)	Mean Uncorrected Residue (stored) (mg/kg)	Procedural recoveries (fresh) (mg/kg)	Mean procedural recovery (mg/kg)	Mean Procedural Recovery (fresh) (%)	Mean Recovered Uncorrected Residue (stored) (%)	Mean Recovered Corrected Residue (stored) (%)
0	-	-	0.756, 1.15, 0.990, 0.801	0.924	93	-	-
1	1.06, 0.986	1.02	0.902, 1.12	1.01	101	103	102
4	0.964, 0.933	0.949	0.856, 0.861	0.859	86	95	110
12	0.905, 0.860	0.883	1.10, 1.11	1.11	111	89	80

Table 107 Recoveries of bicyclopyrone from Soya bean Hulls during frozen storage

Interval Months stored	Uncorrected Residue(stored) (mg/kg)	Mean Uncorrected Residue (stored) (mg/kg)	Procedural recoveries (fresh) (mg/kg)	Mean procedural recovery (mg/kg)	Mean Procedural Recovery (fresh) (%)	Mean Recovered Uncorrected Residue (stored) (%)	Mean Recovered Corrected Residue (stored) (%)
0	-	-	0.784, 1.01, 1.02, 0.898	0.928	93	-	-
1	1.04, 0.991	1.02	1.12, 1.08	1.10	110	102	93
4	0.882, 0.968	0.925	0.812, 0.845	0.829	83	83	112
12	0.842, 0.892	0.867	1.10, 1.20	1.15	115	87	75

Animal matrices

The stability of residues in animal matrices during frozen storage was measured in both bovine matrices and hens eggs, reported by Walsh, and Herczog (2013, NOA449280_50563).

Samples (10 g) of the homogenized bulk control samples of milk, fat, muscle, liver and kidney were individually fortified with 0.01 mg/kg of the analytes. The samples were stored frozen.

At storage intervals of approximately 0 and 12.7 months, a sample set of each substrate, consisting of a control sample, two freshly fortified samples and two freezer stored fortified samples were analysed using analytical method GRM030.08A. Storage stability results (recoveries >70% corrected for procedural recovery) indicate that bicyclopyrone, SYN503780 and CSCD686480 residues are stable in all bovine matrices during frozen storage for 385 days as shown in the following Tables.

Table 108 Stability of bicyclopyrone in animal commodities during frozen storage

Commodity	Storage Period (months)	bicyclopyrone Concentration – Uncorrected (mg/kg)[a]	Mean Procedural Recovery (%)[b]	bicyclopyrone Concentration – Corrected (mg/kg)[c]	Uncorrected Recovery (%)[d]
Cow-Milk	0	0.00975	97.5	0.01	100
	12.8	0.00985	97.5	0.0101	101
Cow-Fat	0	0.0111	111	0.01	100
	12.8	0.0111	111	0.01	100
Cow-Muscle	0	0.0101	101	0.01	100
	12.8	0.00995	101	0.00985	98.5
Cow-Liver	0	0.0121	121	0.01	100
	12.8	0.0119	121	0.00979	97.9
Cow-Kidney	0	0.0122	122	0.01	100
	12.8	0.0112	122	0.00914	91.4

[a] Mean of two samples, not corrected for procedural recovery

[b] Mean of two procedural recoveries

[c] Mean of two samples, corrected for procedural recovery

[d] Percentage of day 0 using uncorrected residues (mean uncorrected residue at time x / mean uncorrected residue at time 0) × 100%. Day 0 nominally 100%. Note: Calculations performed on un-rounded values.

Table 109 Stability of SYN503780 in animal commodities during frozen storage

Commodity	Storage Period (months)	SYN503780 Concentration – Uncorrected (mg/kg)[a]	Mean Procedural Recovery (%)[b]	SYN503780 Concentration – Corrected (mg/kg)[c]	Uncorrected Recovery (%)[d]
Cow-Milk	0	0.0101	101	0.01	100
	12.8	0.0104	101	0.0103	103
Cow-Fat	0	0.0104	104	0.01	100
	12.8	0.0098	104	0.00947	94.7

Commodity	Storage Period (months)	SYN503780 Concentration – Uncorrected (mg/kg)[a]	Mean Procedural Recovery (%)[b]	SYN503780 Concentration – Corrected (mg/kg)[c]	Uncorrected Recovery (%)[d]
Cow-Muscle	0	0.0103	103	0.01	100
	12.8	0.0100	103	0.00976	97.6
Cow-Liver	0	0.0128	128	0.01	100
	12.8	0.0115	128	0.00902	90.2
Cow-Kidney	0	0.0116	116	0.01	100
	12.8	0.0109	116	0.00939	93.9

[a] Mean of two samples, not corrected for procedural recovery

[b] Mean of two procedural recoveries

[c] Mean of two samples, corrected for procedural recovery

[d] Percentage of day 0 using uncorrected residues (mean uncorrected residue at time x / mean uncorrected residue at time 0) × 100%. Day 0 nominally 100%. Note: Calculations performed on un-rounded values.

Table 110 Stability of CSCD686480 in animal commodities during frozen storage

Commodity	Storage Period (months)	CSCD686480 Concentration – Uncorrected (mg/kg)[a]	Mean Procedural Recovery (%)[b]	CSCD686480 Concentration – Corrected (mg/kg)[c]	Uncorrected Recovery (%)[d]
Cow-Milk	0	0.0136	136	0.01	100
	12.8	0.0124	136	0.00911	91.4
Cow – Fat	0	0.00895	89.5	0.01	100
	12.8	0.00790	89.5	0.00883	88.3
Cow – Muscle	0	0.00885	88.5	0.01	100
	12.8	0.00885	88.5	0.01	100
Cow – Liver	0	0.0119	119	0.01	100
	12.8	0.0107	119	0.00899	89.9
Cow – Kidney	0	0.0112	112	0.01	100
	12.8	0.0104	112	0.00924	92.4

[a] Mean of two samples, not corrected for procedural recovery

[b] Mean of two procedural recoveries

[c] Mean of two samples, corrected for procedural recovery

[d] Percentage of day 0 using uncorrected residues (mean uncorrected residue at time x / mean uncorrected residue at time 0) × 100%. Day 0 nominally 100%. Note: Calculations performed on un-rounded values.

Stability of residues in samples extract

The Meeting received information investigating the stability of bicyclopyrone residues extracts demonstrated as part of the validation of the analytical methods. Recoveries in sample extracts stored alongside fortified samples were within the acceptable ranges of 70 to 120% with standard deviations of < 20%.

In summary, residue stability of bicyclopyrone and its metabolite SYN503780 during frozen storage has been examined in fortified samples of raw agricultural commodities (RACs): maize grain, wheat straw, spinach leaves, soya beans, lentils, lemon fruit, potato tubers and sugarcane, in processed commodities: corn grits, corn flour, corn starch, corn oil, sugarcane molasses, sugarcane refined sugar, soya bean meal and soya bean hulls, and in animal commodities: milk, fat, muscle (meat), liver and kidney. There was no unacceptable decrease in the concentration of bicyclopyrone over periods of at least 24 months (RACs), 12 months (processed commodities) or 12.7 months (bovine commodities).

The stability of residues of CSAA915194 during frozen storage has been examined in fortified samples of raw agricultural commodities of sugarcane (tops and billets). There was no significant decrease in the concentration of CSAA915194 over periods of at least 26 months.

The stability of residues of CSCD686480 during frozen storage has been examined in fortified samples of raw agricultural commodities of sugarcane (tops and billets), and in animal commodities: milk, fat, muscle (meat), liver and kidney. There was no significant decrease in the concentration of CSCD686480 over periods of at least 26 months (sugarcane RACs), or 12.7 months (bovine commodities).

In general, the available storage stability data for bicyclopyrone, SYN503780, CSAA915194 and CSCD686480 are sufficient to demonstrate that residues matching the proposed definition of residue are stable (less than 30% decline in concentration) in frozen storage (nominally <-18 °C) for periods of at least 24 months (RACs), 12 months (processed commodities) or 12.7 months (bovine commodities). The demonstrated periods of stability are sufficient to cover the periods for which samples have been stored during routine residues analyses.

USE PATTERNS

Information on GAP in Belize, Canada, Uruguay and USA was available to the Meeting on the use of bicyclopyrone (EC or SC or mixed CS and SC formulations).

Bicyclopyrone is intended for use to control broad-leaf weeds and annual grasses in maize, sweet corn, barley, wheat and sugarcane. Bicyclopyrone is to be applied from pre-emergence through to early post-emergence using standard spraying equipment. Bicyclopyrone is generally applied once annually, however a split application pre-emergent and early post emergent maybe used equating to the maximum recommended application/year. The authorized uses relevant to the supervised trial data submitted to the current Meeting are summarized in Table 111.

Table 111 List of registered uses

Crop	Country	Product Type (g/L)	Maximum Annual Application Bicyclopyrone (g/ha)	Number of treatments	Application timing	Treatment interval (days)	PHI (days)	Commodity	Product Name
Barley	USA	Emulsifiable Concentrate Bicyclopyrone 37.5 g/L Bromoxynil 175 g /L [as Bromoxynil octanoate 255 g /L] [Safener: Cloquintocet-mexyl 9.4 g/L]	50	1	Post-emergence 2-leaf to pre-boot	NA	30	Hay	Talinor
							60	Grain, straw	
Barley	Canada	Emulsifiable Concentrate Bicyclopyrone 37.5 g/L Bromoxynil 175 g /L [as Bromoxynil octanoate 255 g /L] [Safener: Cloquintocet-mexyl 9.4 g/L]	37.5	1	Post-emergence BBCH 12-37	NA	30	Forage, hay	Talinor
							60	Grain, straw	
Maize	USA	Soluble Concentrate Bicyclopyrone 200 g/L	50	1-2	Pre-emergence – Up to 30 inches tall or up to the 8-leaf stage	14	45	Forage, sweet corn ears	SYN-A16003 Herbicide

Crop	Country	Product Type (g/L)	Maximum Annual Application Bicyclopyrone (g/ha)	Number of treatments	Application timing	Treatment interval (days)	PHI (days)	Commodity	Product Name
Maize	USA	Mixed formulation of capsule suspension (CS) and suspension concentrate (SC) Bicyclopyrone 7.13 g/L Mesotrione 28.5 g/L Atrazine 119.7 g/L S-metolachlor 256 g/L	50	1-2	Pre-plant, pre emergence Up to 12 inches tall		45	Grazing	Acuron
						Defined by application timings	60	Grain, seed, silage and forage	
Maize	USA	Mixed formulation of capsule suspension (CS) and suspension concentrate (SC) Bicyclopyrone 9.6 g/L Mesotrione 38.3 g/L S-metolachlor 343 g/L	50	1-2	Pre-plant, pre emergence-up to 30 inches tall or up to the 8-leaf stage (post-emerg allowed for field corn, seed corn & silage corn only)	Defined by application timings	45	Forage, sweet corn ears	Acuron flexi
							60	Forage, grain, stover after post-emergence use	
Maize	Canada	Soluble Concentrate Bicyclopyrone 200 g/L	37.5-50	1	Pre-emergence-up to and including 6-leaf corn (post-emerg allowed for field corn, only)	NA	45	Field corn forage and sweet corn	Solo
							At maturity	Field corn grain and stover	
Maize	Canada	Mixed formulation of capsule suspension (CS) and suspension concentrate (SC) Bicyclopyrone 7.1 g/L Mesotrione 28.5 g/L Atrazine 120 g/L S-metolachlor 257 g/L	35	1	Pre-emergence-up to and including 2-leaf corn (post-emerg allowed for field corn, only)	NA	45	Sweet corn forage	Acuron
							50	Sweet corn ears	
							90	Field corn forage	
							At maturity	Field corn grain and stover	

Crop	Country	Product Type (g/L)	Maximum Annual Application Bicyclopyrone (g/ha)	Number of treatments	Application timing	Treatment interval (days)	PHI (days)	Commodity	Product Name
Maize	Uruguay	Soluble Concentrate Bicyclopyrone 200 g/L	160-200	1	Pre-emergence	-	Defined by application timings	-	Acuron Uno
Wheat	USA	Emulsifiable Concentrate Bicyclopyrone 37.5 g/L Bromoxynil 175 g /L [as Bromoxynil Octanoate 255 g /L]	50	1	Post-emergence 2-leaf to pre-boot	NA	30	Hay	Talinor
							60	Grain, straw	
Wheat	Canada	Emulsifiable Concentrate Bicyclopyrone 37.5 g/L Bromoxynil 175 g /L [as Bromoxynil octanoate 255 g /L] Cloquintocet-mexyl 9.4 g/L	37.5	1	Post-emergence BBCH 12-37	NA	30	Forage, hay	Talinor
							60	Grain, straw	
Sugarcane	Belize	Soluble Concentrate Bicyclopyrone 75 g/L Hexazinone 94 g/L	262.5	1	Pre-emergence – BBCH 12	NA	Defined by application timings	-	Crestivo 16.9 SL
					Post-emergence-2 to 4 leaves	NA	Defined by application timings	-	

RESIDUES RESULTING FROM SUPERVISED TRIALS

The Meeting received information on supervised trials conducted with bicyclopyrone used as a selective herbicide for the control of annual grass weeds to the following crops.

Codex group	Commodity	Use	Table No.
Fruiting vegetables, other than cucurbits	Sweetcorn	Pre- and post-emergence herbicide to control grass and broad leaf weeds	Table 113
Cereal grains	Barley	Post-emergence herbicide to control grass and broad leaf weeds	Table 115
	Maize	Pre- and post-emergence herbicide to control grass and broad leaf weeds	Table 116
	Wheat	Post-emergence herbicide to control grass and broad leaf weeds	Table 118
Grasses, for sugar or syrup production	Sugar cane	Pre-and post-emergence herbicide to control grass and broad leaf weeds	Table 119

The supervised trials were well documented with laboratory and field reports. Laboratory reports included method validation including procedural 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. Although trials included control plots, no control data are recorded in the tables unless residues in control samples exceeded the LOQ. Residue data are recorded unadjusted for recovery.

Bicyclopyrone residues are calculated as the sum of two common moieties (SYN503780 and CSCD686480) expressed as bicyclopyrone equivalents. Where residues have been measured in duplicate samples, a mean total value is presented. Residues and application rates have been reported as provided in the study reports except for finite values below the LOQ, where these have been reported as < 0.01 mg/kg.

The results from trials used for the estimation of maximum residue levels (underlined) have been rounded to two significant digits (or if close to the LOQ, rounded to one significant digit) in the Appraisal. The designation "ND" is used for treated samples for which the residue was <LOD (below the limit of detection); < 0.01 mg/kg. When determining the total bicyclopyrone equivalent residue, where residues were classified as not detected, a value of half the LOQ was used in calculations and where a residue below the limit of quantification was detected, the LOQ value was used.

Where a residue of both common moieties has been detected, the sum of the two values is used. Where both values are reported as < 0.01, the total bicyclopyrone equivalent residue is reported as < 0.02 mg/kg and where both values are reported as < 0.005, the total bicyclopyrone equivalent residue is reported as < 0.01 mg/kg.

Correction factors have been applied as follows:

To correct SYN503780 to bicyclopyrone equivalents: 399/279 = **1.43**

To correct CSCD686480 to bicyclopyrone equivalents: 399/265 = **1.51**

To correct CSCD686480 to CSAA915194 equivalents: 385/265 = **1.45**

To correct CSAA915194 to bicyclopyrone equivalents: 399/385 = **1.04**

Fruiting vegetables, other than cucurbits

Sweetcorn

The supported GAP for the use of bicyclopyrone on sweetcorn in Uruguay and the United States is as a selective, pre- or post-emergence herbicide. The regional GAPs are detailed in Table 112.

Table 112 Use pattern (GAP) for bicyclopyrone on sweetcorn

Region	Crop	Outdoor/ Protected	Max No of Apps	App Interval (days)	Growth stage at application (BBCH)	App Rate (g ai/ha)	Min PHI (days)
Uruguay	Maize	Outdoor	1	NA	Pre-emergence	200	-
United States	Maize	Outdoor	1-2*	14	Up to 30 inches tall or up to the 8-leaf stage	50	45 (Forage, sweet corn ears)

DBH—Days before harvest

*-The maximum application of 50 g ai/ha may be split across two applications, pre- and post-emergence

Residue data have been collected from four field trials in maize (field corn) located in the Brazil. Trials were conducted using one or two applications at rates of 100 or 200 g ai/ha. The formulations used in the trials were 18.5% SL formulation. Method POPIT.117 was used for analysis of bicyclopyrone residues samples corresponding to sweetcorn quantifying the analyte by Liquid chromatography mass spectrometry (LC-MS/MS) with a limit of quantitation of 0.01 mg/kg. The measured residues are presented as bicyclopyrone (determined as SYN503780) and CSAA915194

(determined as CSCD686480). All samples were analysed within the demonstrated period of stability. Mean recoveries from control sweetcorn samples fortified with bicyclopyrone or metabolites were within the required range, 89–110% for all analytes, with standard deviations below 20%.

Fourteen trials in sweetcorn were conducted in USA to determine the residue level of bicyclopyrone in/on immature cobs, ears, forage/ plants for silage, grain and stover. At each trial, one foliar application was made to the treated plot at a rate of 50 g ai/ha. The formulations used in the trials were 18.5% SL formulation. Method GRM030.05A was used for analysis of bicyclopyrone residues in immature cobs quantifying the analyte by Liquid chromatography mass spectrometry (LC-MS/MS) with a limit of quantitation of 0.01 mg/kg. The measured residues are presented as bicyclopyrone (determined as SYN503780) and CSAA915194 (determined as CSCD686480). All samples were analysed within the demonstrated period of stability. Mean recoveries from control sweetcorn commodities samples fortified with bicyclopyrone or metabolites were within the required range, 108–113% for all analytes, with standard deviations below 20%.

Table 113 Residues in sweetcorn from supervised trials in Brazil and the USA following application of bicyclopyrone SL formulation

GLP and Trial Details	Crop (Variety)	Country (Region) (Postcode)	Application		PHI (days)	Crop Part	Residue Found (Uncorrected, mg/kg)		
			Rate (g ai/ha) (Formulation)	Growth Stage			Bicyclopyrone eq. (SYN503780)	Bicyclopyrone eq. (CSCD686480)	Total Mean[a]
GAP	Sweetcorn	Uruguay	200	Pre-emergence	Defined by application timing				
Report: M09107 Study: M09107 Trial: M09107-JJB - Study to GLP - Study carried out in 2009	Maize (Impacto)	Brazil (Uberlandia-MG)	200 (SL)	BBCH 00 (pre-em.)	82	Immature cobs	< 0.01	< 0.01	<0.02
			100 100 (SL)	BBCH 14 BBCH 18	47	Immature cobs	< 0.01	< 0.01	<0.02
Report: M09107 Study: M09107 Trial: M09107-LZF - Study to GLP - Study carried out in 2009	Maize (BR 106)	Brazil (Holambra-SP)	200 (SL)	BBCH 00 (pre-em.)	98	Immature cobs	< 0.01	< 0.01	<0.02
			100 100 (SL)	BBCH 14 BBCH 18	45	Immature cobs	< 0.01	< 0.01	<0.02
Report: M09107 Study: M09107 Trial: M09107-MFG - Study to GLP - Study carried out in 2009	Maize (Impacto)	Brazil (Goiania-GO)	200 (SL)	BBCH 00 (pre-em.)	87	Immature cobs	< 0.01	< 0.01	<0.02
			100	BBCH 14	55	Immature cobs	< 0.01	< 0.01	< 0.02

GLP and Trial Details	Crop (Variety)	Country (Region) (Postcode)	Application		PHI (days)	Crop Part	Residue Found (Uncorrected, mg/kg)		
			Rate (g ai/ha) (Formulation)	Growth Stage			Bicyclopyrone eq. (SYN503780)	Bicyclopyrone eq. (CSCD686480)	Total Mean[a]
			100 (SL)	BBCH 18					
Report: M09107 Study: M09107 Trial: M09107-DMO - Study to GLP - Study carried out in 2009	Maize (Sprint)	Brazil (Itabera-SP)	200 (SL)	BBCH 00 (pre-em.)	80	Immature cobs	< 0.01	< 0.01	< 0.02
			100 100 (SL)	BBCH 14-15 BBCH 18-19	48	Immature cobs	< 0.01	< 0.01	< 0.02
GAP	Sweetcorn	USA	50	Up to 30 inches tall or up to the 8-leaf stage	45				
Report: TK0112879 Study: TK0112879 Trial: TK0112879-01 - Study to GLP - Study carried out in 2012	Corn (Pioneer 34F07)	USA (EPA/Region 1)	51.5 (SL)	BBCH 17-19 30”corn/V8	39	Ears	< 0.01	< 0.01	< 0.02 (< 0.02, < 0.02)
							< 0.01	< 0.01	
Report: TK0112879 Study: TK0112879 Trial: TK0112879-02 - Study to GLP - Study carried out in 2012	Corn (DKC66-96)	USA (EPA/Region 2)	50.4 (SL)	BBCH 18-19 30”corn/V8	37	Ears	< 0.01	< 0.01	< 0.02 (< 0.02, < 0.02)
							< 0.01	< 0.01	
Report: TK0112879 Study: TK0112879 Trial: TK0112879-03 - Study to GLP - Study carried out in 2012	Corn (A1022967/ A1027871)	USA (EPA/Region 5)	51.5 (SL)	BBCH 17-19 30”corn/V8	54	Ears	< 0.01	< 0.01	< 0.02 (< 0.02, < 0.02)
							< 0.01	< 0.01	
Report: TK0112879 Study: TK0112879 Trial: TK0112879-04	Corn (33Z74)	USA (EPA/Region 5)	50.4 (SL)	BBCH 17-19 30”corn/V8	40	Ears	< 0.01	< 0.01	< 0.02 (< 0.02, < 0.02)

GLP and Trial Details	Crop (Variety)	Country (Region) (Postcode)	Application		PHI (days)	Crop Part	Residue Found (Uncorrected, mg/kg)		
			Rate (g ai/ha) (Formulation)	Growth Stage			Bicyclopyrone eq. (SYN503780)	Bicyclopyrone eq. (CSCD686480)	Total Mean[a]
- Study to GLP - Study carried out in 2012							< 0.01	< 0.01	
Report: TK0112879 Study: TK0112879 Trial: TK0112879-05 - Study to GLP - Study carried out in 2012	Corn (Pioneer P1948)	USA (EPA/Region 5)	50.4 (SL)	BBCH 17-19 30”corn/V8	40	Ears	< 0.01 < 0.01	< 0.01 < 0.01	< 0.02 (< 0.02, < 0.02)
Report: TK0112879 Study: TK0112879 Trial: TK0112879-06 - Study to GLP - Study carried out in 2012	Corn (DKC 33-54)	USA (EPA/Region 5)	50.4 (SL)	BBCH 18 30”corn/V8	39	Ears	< 0.01 < 0.01	< 0.01 < 0.01	< 0.02 (< 0.02, < 0.02)
Report: TK0112879 Study: TK0112879 Trial: TK0112879-07 - Study to GLP - Study carried out in 2012	Corn (P1151HR)	USA (EPA/Region 5)	50.4 (SL)	BBCH 16-17 30”corn/V8	42	Ears	< 0.01 < 0.01	< 0.01 < 0.01	< 0.02 (< 0.02, < 0.02)
Report: TK0112879 Study: TK0112879 Trial: TK0112879-09 - Study to GLP - Study carried out in 2012	Corn (Super Sweet Jubilee Plus)	USA (EPA/Region 3)	49.3 (SL)	BBCH 38 30”corn/V8	26	Ears	< 0.01 < 0.01	0.0132 0.0136	0.0234 (0.0232, 0.0236)
Report: TK0112879 Study: TK0112879 Trial: TK0112879-10 - Study to GLP - Study carried out in 2012	Corn (Legion)	USA (EPA/Region 1)	49.3 (SL)	BBCH 18 30”corn/V8	43	Ears	< 0.01 < 0.01	< 0.01 < 0.01	< 0.02 (< 0.02, < 0.02)

GLP and Trial Details	Crop (Variety)	Country (Region) (Postcode)	Application		PHI (days)	Crop Part	Residue Found (Uncorrected, mg/kg)		
			Rate (g ai/ha) (Formulation)	Growth Stage			Bicyclopyrone eq. (SYN503780)	Bicyclopyrone eq. (CSCD686480)	Total Mean[a]
Report: TK0112879 Study: TK0112879 Trial: TK0112879-17 - Study to GLP	Corn (SS Garrison)	USA (EPA/Region 5)	50.4 (SL)	BBCH 17-18 30"corn/V8	25	Ears	< 0.01	< 0.01	< 0.02 (< 0.02, < 0.02)
- Study carried out in 2012							< 0.01	< 0.01	
Report: TK0112879 Study: TK0112879 Trial: TK0112879-27 - Study to GLP	Corn (Golden Beauty SU)	USA (EPA/Region 7)	51.5 (SL)	BBCH 18-19 30"corn/V8	34	Ears	< 0.01	< 0.01	< 0.02 (< 0.02, < 0.02)
- Study carried out in 2012							< 0.01	< 0.01	
Report: TK0112879 Study: TK0112879 Trial: TK0112879-28 - Study to GLP	Corn (BSS0982)	USA (EPA/Region 10)	54.9 (SL)	BBCH 33-34 30"corn/V8	38	Ears	< 0.01	< 0.01	< 0.02 (< 0.02, < 0.02)
- Study carried out in 2012							< 0.01	< 0.01	
Report: TK0112879 Study: TK0112879 Trial: TK0112879-29 - Study to GLP	Corn (Ambrosia)	USA (EPA/Region 11)	52.6 (SL)	BBCH 18 30"corn/V8	45	Ears	< 0.01	< 0.01	< 0.02 (< 0.02, < 0.02)
- Study carried out in 2012							< 0.01	< 0.01	
Report: TK0112879 Study: TK0112879 Trial: TK0112879-30 - Study to GLP	Corn (Jubilee)	USA (EPA/Region 12)	50.4 (SL)	BBCH 17-19 30"corn/V8	51	Ears	< 0.01	0.0132	0.023 (0.0237, 0.0236)
- Study carried out in 2012							< 0.01	0.0136	

[a] Determined as the sum of common moieties (SYN503780 and CSCD686480 expressed as bicyclopyrone equivalents).

LOQ – Limit of quantification-The limit of quantification (LOQ) was 0.01 mg/kg for bicyclopyrone equivalents from SYN503780 and for bicyclopyrone equivalents from CSCD686480

A further seventeen trials on sweetcorn or maize were conducted in the USA to determine the residue level of bicyclopyrone. Bicyclopyrone was applied once or twice using the SL formulation at a rate of 200 g ai/ha. Method GRM030.05A was used for analysis of bicyclopyrone residues in samples quantifying the analyte by HPLC-MS/MS with a limit of quantitation of 0.01 mg/kg expressed as bicyclopyrone equivalents. The residues in these trials measured as CSCD686480 have been converted mathematically to bicyclopyrone equivalents. In these studies, SYN503780 was corrected to bicyclopyrone equivalents. All samples were analysed within the demonstrated period of stability. Mean recoveries of the analytes from sweetcorn commodities were within the required range, 88–111% for all analytes, with standard deviations below 20%.

Table 114 Residues in sweetcorn from supervised trials in US involving one or two applications of bicyclopyrone formulations

GLP and Trial Details	Crop (Variety)	Country (Region) (Postcode)	Application Rate (g ai/ha) (Formulation)	Growth Stage at Application	PHI (days)	Crop Part	Residue Found (Uncorrected, mg/kg)		
							Bicyclopyrone eq. (SYN503780)	Bicyclopyrone eq (CSCD686480)	Total Mean [a]
GAP	Sweetcorn	USA	50	V8/8-leaf stage	45				
Report: T019378-04 Study: 09SYN253A.REP Trial: E10NC081383 - Study to GLP - Study carried out in 2008	Corn (Garst 8377YG1/RR)	USA (EPA Region 2)	200 + 200 (soil surface + post-emergence foliar) (EC)	Pre-plant BBCH 36 (V8)	45	Ears	< 0.01 < 0.01	< < 0.01	< 0.02 (< 0.02, < 0.02)
			200 (post-emergence foliar) (EC)	BBCH 36 (V8)	45		< 0.01 < 0.01	< 0.01 < 0.01	< 0.02 (< 0.02, < 0.02)
Report: T019378-04 Study: 09SYN253A.REP Trial: C19MO081385 - Study to GLP - Study carried out in 2008	Corn (Pioneer 33D47)	USA (EPA Region 5)	200 + 200 (soil surface + post-emergence foliar) (EC)	Pre-plant BBCH 36 (V8)	49	Ears	< 0.01 < 0.01	< < 0.01	< 0.02 (< 0.02, < 0.02)
			200 (post-emergence foliar) (EC)	BBCH 36 (V8)	49		< 0.01 < 0.01	< 0.01 < 0.01	< 0.02 (< 0.02, < 0.02)
Report: T019378-04 Study: 09SYN253A.REP Trial: C19KS081386 - Study to GLP - Study carried out in 2008	Corn (DK 6019)	USA (EPA Region 5)	200 + 200 (soil surface + post-emergence foliar) (EC)	Pre-plant BBCH 37 (V8)	50	Ears	< 0.01 < 0.01	< 0.01 < 0.01	< 0.02 (< 0.02, < 0.02)
			200 (post-emergence foliar) (EC)	BBCH 37 (V8)	50		< 0.01 < 0.01	< 0.01 < 0.01	< 0.02 (< 0.02, < 0.02)
Report: T019378-04 Study: 09SYN253A.REP Trial: C01MI081387 - Study to GLP - Study carried	Corn (Pioneer 38N85 RR)	USA (EPA Region 5)	200 + 200 (soil surface + post-emergence foliar) (EC)	Pre-plant BBCH 19 (V8)	50	Ears	< 0.01 < 0.01	< 0.01 < 0.01	< 0.02 (< 0.02, < 0.02)
			200	BBCH 19	50		< 0.01	< 0.01	< 0.02

GLP and Trial Details	Crop (Variety)	Country (Region) (Postcode)	Application Rate (g ai/ha) (Formulation)	Growth Stage at Application	PHI (days)	Crop Part	Residue Found (Uncorrected, mg/kg)		
							Bicyclopyrone eq. (SYN503780)	Bicyclopyrone eq (CSCD686480)	Total Mean [a]
out in 2008			(post-emergence foliar) (EC)	(V8)			< 0.01	< 0.01	(< 0.02, < 0.02)
Report: T019378-04 Study: 09SYN253A.REP Trial: C01OH081388 - Study to GLP - Study carried out in 2008	Corn (691RR2)	USA (EPA Region 5)	200 + 200 (soil surface + post-emergence foliar) (EC)	Pre-plant BBCH 18 (V8)	47	Ears	< 0.01	< 0.01	< 0.02
							< 0.01	< 0.01	(< 0.02, < 0.02)
			200 (post-emergence foliar) (EC)	BBCH 19 (V8)	47		< 0.01	< 0.01	< 0.02
							< 0.01	< 0.01	(< 0.02, < 0.02)
Report: T019378-04 Study: 09SYN253A.REP Trial: C08WI081389 - Study to GLP - Study carried out in 2008	Corn (Dekalb DK43-27 (VT3))	USA (EPA Region 5)	200 + 200 (soil surface + post-emergence foliar) (EC)	Pre-plant BBCH 18 (V8)	43	Ears	< 0.01	< 0.01	< 0.02
							< 0.01	< 0.01	(< 0.02, < 0.02)
			200 (post-emergence foliar) (EC)	BBCH 18 (V8)	43		< 0.01	< 0.01	< 0.02
							< 0.01	< 0.01	(< 0.02, < 0.02)
Report: T019378-04 Study: 09SYN253A.REP Trial: W32CA081404 - Study to GLP - Study carried out in 2008	Corn (Bodacious)	USA (EPA Region 10)	200 + 200 (soil surface + post-emergence foliar) (EC)	Pre-plant BBCH 18 (V8)	76	Ears	< 0.01	< 0.01	< 0.02 (< 0.02, < 0.02)
					83		< 0.01	< 0.01	< 0.02 (< 0.02, < 0.02)
					90		< 0.01	< 0.01	< 0.02 (< 0.02, < 0.02)
					97		< 0.01	< 0.01	< 0.02
							< 0.01	< 0.01	(< 0.02, < 0.02)
					104		< 0.01	< 0.01	< 0.02 (< 0.02, < 0.02)
			200 (post-emergence foliar) (EC)	BBCH 18 (V8)	76		< 0.01	< 0.01	< 0.02 (< 0.02, < 0.02)
					83		< 0.01	< 0.01	< 0.02 (< 0.02, < 0.02)
					90		< 0.01	< 0.01	< 0.02 (< 0.02, < 0.02)
					97		< 0.01	< 0.01	< 0.02
							< 0.01	< 0.01	(< 0.02, < 0.02)
					104		< 0.01	< 0.01	< 0.02 (< 0.02, < 0.02)
Report: T019378-04 Study: 09SYN253A.REP Trial: W15ID081405 - Study to GLP - Study carried	Corn (Honey 'N Pearl)	USA (EPA Region 11)	200 + 200 (soil surface + post-emergence foliar) (EC)	Pre-plant BBCH 18 (V8)	45	Ears	< 0.01	< 0.01	< 0.02
							< 0.01	< 0.01	(< 0.02, < 0.02)
			200	BBCH 18	45		< 0.01	< 0.01	< 0.02

GLP and Trial Details	Crop (Variety)	Country (Region) (Postcode)	Application Rate (g ai/ha) (Formulation)	Growth Stage at Application	PHI (days)	Crop Part	Residue Found (Uncorrected, mg/kg)		
							Bicyclopyrone eq. (SYN503780)	Bicyclopyrone eq (CSCD686480)	Total Mean [a]
out in 2008			(post-emergence foliar) (EC)	(V8)			< 0.01	< 0.01	(< 0.02, < 0.02)
Report: T019378-04 Study: 09SYN253A.REP Trial: W21OR081406 - Study to GLP - Study carried out in 2008	Corn (Honey and Pearls)	USA (EPA Region 12)	200 + 200 (soil surface + post-emergence foliar) (EC)	Pre-plant BBCH 22 (V8)	47	Ears	< 0.01	< 0.01	< 0.02
							< 0.01	< 0.01	(< 0.02, < 0.02)
			200 (post-emergence foliar) (EC)	BBCH 22 (V8)	47		< 0.01	< 0.01	< 0.02
							< 0.01	< 0.01	(< 0.02, < 0.02)
Report: T019378-04 Study: 09SYN253A.REP Trial: E19FL081407 - Study to GLP - Study carried out in 2008	Corn ("Awesome")	USA (EPA Region 3)	200 + 200 (soil surface + post-emergence foliar) (EC)	Pre-plant BBCH 18 (V8)	42	Ears	< 0.01	< 0.01	< 0.02
							< 0.01	< 0.01	(< 0.02, < 0.02)
Report: T019378-04 Study: 09SYN253A.REP Trial: E04PA081411 - Study to GLP - Study carried out in 2008	Corn (Mycogen Hybrid Seed (Hybrid 2D324))	USA (EPA Region 1)	200 + 200 (soil surface + post-emergence foliar) (EC)	Pre-plant BBCH 18 (V8)	45	Ears	< 0.01	< 0.01	< 0.02
							< 0.01	< 0.01	(< 0.02, < 0.02)
			200 (post-emergence foliar) (EC)	BBCH 18 (V8)	45		< 0.01	< 0.01	< 0.02
							< 0.01	< 0.01	(< 0.02, < 0.02)
			200 + 200 (pre-plant +post-emergence foliar) (EC)	Pre-plant BBCH 35 (V8)	45		< 0.01	< 0.01	< 0.02
							< 0.01	< 0.01	(< 0.02, < 0.02)
Report: T019378-04 Study: 09SYN253A.REP Trial: E04PA081412 - Study to GLP - Study carried out in 2008	Corn (Mirai 421 W Insect Guard F1)	USA (EPA Region 1)	200 + 200 (soil surface + post-emergence foliar) (EC)	Pre-plant BBCH 35 (V8)	45	Ears	< 0.01	< 0.01	< 0.02
							< 0.01	< 0.01	(< 0.02, < 0.02)
			200 (post-emergence foliar) (EC)	BBCH 35 (V8)	45		< 0.01	< 0.01	< 0.02
							< 0.01	< 0.01	(< 0.02, < 0.02)
			200 + 200 (pre-plant +post-emergence foliar) (EC)	Pre-plant BBCH 35 (V8)	45		< 0.01	< 0.01	< 0.02
							< 0.01	< 0.01	(< 0.02, < 0.02)

GLP and Trial Details	Crop (Variety)	Country (Region) (Postcode)	Application Rate (g ai/ha) (Formulation)	Growth Stage at Application	PHI (days)	Crop Part	Residue Found (Uncorrected, mg/kg)		
							Bicyclopyrone eq. (SYN503780)	Bicyclopyrone eq (CSCD686480)	Total Mean [a]
Report: T019378-04 Study: 09SYN268A.REP Trial: E15-9451/FL - Study to GLP - Study carried out in 2009	Corn (Hybrid Sweet Corn #274A)	USA (NAFTA Region 3)	200 + 200 (soil surface + post-emergence foliar) (EC)	Pre-plant BBCH 53 (V8)	30	Ears	< 0.01 < 0.01	0.012 < 0.01	0.021 (0.022, 0.02)
			200 + 200 (pre-plant +post-emergence foliar) (EC)	Pre-plant BBCH 53 (V8)	30		< 0.01 < 0.01	0.020 0.015	0.028 (0.030, 0.025)
Report: T019378-04 Study: 09SYN268A.REP Trial: C19-9452/MO - Study to GLP - Study carried out in 2009	Corn (Bodacious)	USA (NAFTA Region 5)	200 + 200 (soil surface + post-emergence foliar) (EC)	Pre-plant BBCH 32 (V8)	46	Ears	< 0.01 < 0.01	0.015 0.017	0.026 (0.025, 0.026)
			200 + 200 (pre-plant +post-emergence foliar) (EC)	Pre-plant BBCH 32 (V8)	46		< 0.01 < 0.01	0.011 0.013	0.022 (0.021, 0.023)
Report: T019378-04 Study: 09SYN268A.REP Trial: C30-9453/IA - Study to GLP - Study carried out in 2009	Corn (33D47)	USA (NAFTA Region 5)	200 + 200 (soil surface + post-emergence foliar) (EC)	Pre-plant BBCH 31 (V8)	45	Ears	< 0.01 < 0.01	< 0.01 < 0.01	< 0.02 (< 0.02, < 0.02)
			200 + 200 (pre-plant +post-emergence foliar) (EC)	Pre-plant BBCH 31 (V8)	45		< 0.01 < 0.01	< 0.01 < 0.01	< 0.02 (< 0.02, < 0.02)
Report: T019378-04 Study: 09SYN268A.REP Trial: C13-9454/ND - Study to GLP - Study carried out in 2009	Corn (9618888)	USA (NAFTA Region 5)	200 + 200 (soil surface + post-emergence foliar) (EC)	Pre-plant BBCH 37 (V8)	45	Ears	< 0.01 < 0.01	< 0.01 < 0.01	< 0.02 (< 0.02, < 0.02)
			200 + 200 (pre-plant +post-emergence foliar) (EC)	Pre-plant BBCH 37 (V8)	45		< 0.01 < 0.01	< 0.01 < 0.01	< 0.02 (< 0.02, < 0.02)
Report: T019378-04 Study: 09SYN268A.REP Trial: C19-9455/MO - Study to GLP - Study carried out in 2009	Corn (Pioneer 33T56)	USA (NAFTA Region 5)	200 + 200 (soil surface + post-emergence foliar) (EC)	Pre-plant BBCH 37 (V8)	39	Ears	< 0.01 < 0.01	< 0.01 < 0.01	< 0.02 (< 0.02, < 0.02)

GLP and Trial Details	Crop (Variety)	Country (Region) (Postcode)	Application Rate (g ai/ha) (Formulation)	Growth Stage at Application	PHI (days)	Crop Part	Residue Found (Uncorrected, mg/kg)		
							Bicyclopyrone eq. (SYN503780)	Bicyclopyrone eq (CSCD686480)	Total Mean [a]
			200 + 200 (pre-plant +post-emergence foliar) (EC)	Pre-plant BBCH 37 (V8)	39		< 0.01 < 0.01	< 0.01 < 0.01	< 0.02 (< 0.02, < 0.02)

[a] Determined as the sum of common moieties SYN503780 (expressed as bicyclopyrone equivalents) and CSCD686480 (expressed as bicyclopyrone equivalents).

LOQ – Limit of quantification-The limit of quantification (LOQ) was 0.0050 mg/kg for bicyclopyrone equivalents from SYN503780 and 0.0054 mg/kg for bicyclopyrone equivalents from CSCD686480 in the Canadian study and 0.005 mg/kg for both analytes in the USA study.

DBH = Days Before Harvest

Residues in All Untreated Samples (controls) were <LOQ.

Cereal grains

Barley

Residue data have been collected from 12 field trials located in the USA. At each trial, one plot was treated 30 days before normal harvest of hay and a second plot was treated 60 days before normal harvest of grain and straw. The formulation used in the trials was 18.5% SL formulation. The common moiety analytical method GRM030.05A was used for analysis of bicyclopyrone residues in barley grain, hay, and straw quantifying the analyte by liquid chromatography mass spectrometry (LC-MS/MS) with a limit of quantitation of 0.005 mg/kg in all matrices for bicyclopyrone equivalents from SYN503780 and CSCD686480. Residues of both SYN503780 and CSCD686480 have been corrected to bicyclopyrone equivalents.

Nine trials in barley were conducted in Canada to determine the residue level of bicyclopyrone in barley. The SL formulation was applied to the plots as foliar application at rate 50 g ai/h. The common moiety analytical method GRM030.05A was used for analysis of bicyclopyrone residues in barley grain, hay and straw quantifying the analyte by liquid chromatography mass spectrometry (LC-MS/MS) with a limit of quantitation of 0.005 mg/kg in all matrices for bicyclopyrone equivalents from SYN503780 and CSCD686480. Residues of both SYN503780 and CSCD686480 have been corrected to bicyclopyrone equivalents.

Table 115 Residues in barley grain from supervised trials in USA and Canada involving one foliar applications of bicyclopyrone

GLP and Trial Details	Crop (Variety)	Country (Region) (Postcode)	Application		DAT	Crop Part	Residue Found (Uncorrected) (mg/kg)		
			Rate (g ai/ha) (Formulation)	Growth Stage			Bicyclopyrone eq. (SYN503780)	Bicyclopyrone eq. (CSCD686480)	Total Mean [a]
GAP	Barley	USA	50	2-leaf stage to pre-boot stage	PHI:60 days	Grain	-	-	-
Report: TK0024326 Study: TK0024326 Trial: TK0024326-01 - Study to GLP - Study carried out in 2012	Barley (Thoroughbred)	USA (NAFTA/Region 2)	52 (EC)	BBCH 32-33 60 DBH	60	Grain	< 0.005, < 0.005	0.0157, 0.0161	0.021 (0.0207, 0.0210)
Report: TK0024326 Study:	Barley (Robust)	USA (NAFTA/Region 5)	50 (EC)	BBCH 73 60 DBH	60	Grain	0.0370, 0.0398	0.0121, 0.0123	0.051 (0.0491, 0.0522)

GLP and Trial Details	Crop (Variety)	Country (Region) (Postcode)	Application		DAT	Crop Part	Residue Found (Uncorrected) (mg/kg)		
			Rate (g ai/ha) (Formulation)	Growth Stage			Bicyclopyrone eq. (SYN503780)	Bicyclopyrone eq. (CSCD686480)	Total Mean [a]
TK0024326 Trial: TK0024326-02 - Study to GLP - Study carried out in 2012									
Report: TK0024326 Study: TK0024326 Trial: TK0024326-03 - Study to GLP - Study carried out in 2012	Barley (Robust)	USA (NAFTA/Region 5)	50 (EC)	BBCH 45-47	50	Grain	< 0.005, < 0.005	0.0127, 0.0118	0.0177, 0.0168
					55		< 0.005, < 0.005	0.0154, 0.0141	0.0204, 0.0191
					61		< 0.005, < 0.005	0.0118, 0.0112	0.017 (0.0168, 0.0162)
					65		< 0.005, < 0.005	0.0115, 0.0123	0.017 (0.0165, 0.0173)
					70		< 0.005, < 0.005	0.00743, 0.00747	0.0124, 0.0125
Report: TK0024326 Study: TK0024326 Trial: TK0024326-04 - Study to GLP - Study carried out in 2012	Barley (Tradition)	USA (NAFTA/Region 5)	54 (EC)	BBCH 40-42	50	Grain	< 0.005, < 0.005	0.00668, < 0.005	0.0117, < 0.005
					55		< 0.005, NA	< 0.005, NA	< 0.005, NA
					61		< 0.005, < 0.005	< 0.005, < 0.005	< 0.01 (< 0.01, < 0.01)
					65		< 0.005, NA	< 0.005, NA	< 0.005, NA
					70		< 0.005, < 0.005	< 0.005, < 0.005	< 0.005, < 0.005
Report: TK0024326 Study: TK0024326 Trial: TK0024326-05 - Study to GLP - Study carried out in 2012	Barley (Tradition)	USA (NAFTA/Region 7)	49 (EC)	BBCH 30-35	59	Grain	< 0.005, < 0.005	< 0.005, < 0.005	< 0.01 (< 0.01, < 0.01)
Report: TK0024326 Study: TK0024326 Trial: TK0024326-06 - Study to GLP - Study carried out in 2012	Barley (Lacey)	USA (NAFTA/Region 7)	50 (EC)	BBCH 30-31 60 DBH	57	Grain	< 0.005, < 0.005	< 0.005, < 0.005	< 0.01 (< 0.01, < 0.01)
Report: TK0024326 Study: TK0024326 Trial: TK0024326-07 - Study to GLP - Study carried out in 2012	Barley (Tradition)	USA (NAFTA/Region 7)	49 (EC)	BBCH 25-30 60 DBH	59	Grain	< 0.005, < 0.005	< 0.005, < 0.005	< 0.01 (< 0.01, < 0.01)
Report: TK0024326 Study: TK0024326 Trial: TK0024326-08 - Study to GLP - Study carried out in 2012	Barley (Robust)	USA (NAFTA/Region 7)	49 (EC)	BBCH 21-22 60 DBH	60	Grain	< 0.005, < 0.005	< 0.005, < 0.005	< 0.01 (< 0.01, < 0.01)
Report: TK0024326 Study: TK0024326 Trial: TK0024326-09 - Study to GLP - Study carried	Barley (Moravian 69)	USA (NAFTA/Region 9)	50 (EC)	BBCH 65-69 60 DBH	60	Grain	0.0130, 0.0129	0.0125, 0.0124	0.025 (0.0254, 0.0254)

GLP and Trial Details	Crop (Variety)	Country (Region) (Postcode)	Application		DAT	Crop Part	Residue Found (Uncorrected) (mg/kg)		
			Rate (g ai/ha) (Formulation)	Growth Stage			Bicyclopyrone eq. (SYN503780)	Bicyclopyrone eq. (CSCD686480)	Total Mean [a]
out in 2012									
Report: TK0024326 Study: TK0024326 Trial: TK0024326-10 - Study to GLP - Study carried out in 2012	Barley (UC937)	USA (NAFTA/Region 10)	49 (EC)	BBCH 77-82 60 DBH	58	Grain	0.0200, 0.0170	0.00930, 0.00627	0.026 (0.0293, 0.0232)
Report: TK0024326 Study: TK0024326 Trial: TK0024326-11 - Study to GLP - Study carried out in 2012	Barley (Champion)	USA (NAFTA/Region 11)	50 (EC)	BBCH 65-69 60 DBH	58	Grain	0.00934, 0.0107	0.0119, 0.0117	0.022 (0.0212, 0.0223)
Report: TK0024326 Study: TK0024326 Trial: TK0024326-12 - Study to GLP - Study carried out in 2012	Barley (Baroness)	USA (NAFTA/Region 11)	50 (EC)	BBCH 49-52 60 DBH	61	Grain	0.0125, 0.0124	0.0184, 0.0230	0.033 (0.0309, 0.0353)
Report: TK0147009 Study: TK0147009 Trial: T487 - Study to GLP - Study carried out in 2013	Barley (CDC Austenson)	Canada (NAFTA/ Region 7A)	51.3 (EC)	BBCH 34-37	60	Grain	< 0.0050, < 0.0050	0.0062, 0.0063	0.011 (0.0113, 0.0112)
Report: TK0147009 Study: TK0147009 Trial: T488 - Study to GLP - Study carried out in 2013	Barley (CDC Austenson)	Canada (NAFTA/ Region 14)	53.0 (EC)	BBCH 30-32	60	Grain	< 0.0050, < 0.0050	< 0.0054, < 0.0054	0.026 (< 0.0104, < 0.0104)
Report: TK0147009 Study: TK0147009 Trial: T489 - Study to GLP - Study carried out in 2013	Barley (Bentley)	Canada (NAFTA/ Region 14)	50.2 (EC)	BBCH 14-15	61	Grain	< 0.0050, < 0.0050	0.010, 0.0086	0.014 (0.0150, 0.0136)
Report: TK0147009 Study: TK0147009 Trial: T490 - Study to GLP - Study carried out in 2013	Barley (AC Metcalfe)	Canada (NAFTA/ Region 14)	54.6 (EC)	BBCH 58-59	61	Grain	0.012, 0.0076	0.012, 0.0087	0.020 (0.024, 0.0163)
Report: TK0147009 Study: TK0147009 Trial: T491 - Study to GLP - Study carried out in 2013	Barley (AC Metcalfe)	Canada (NAFTA/ Region 14)	49.5 (EC)	BBCH 51-59	59	Grain	< 0.0050, < 0.0050	0.0065, 0.0075	0.012 (0.0115, 0.0125)
Report:	Barley	Canada	54.7	BBCH	63	Grain	0.012, 0.0097	0.015, 0.012	0.024

GLP and Trial Details	Crop (Variety)	Country (Region) (Postcode)	Application		DAT	Crop Part	Residue Found (Uncorrected) (mg/kg)		
			Rate (g ai/ha) (Formulation)	Growth Stage			Bicyclopyrone eq. (SYN503780)	Bicyclopyrone eq. (CSCD686480)	Total Mean [a]
TK0147009 Study: TK0147009 Trial: T492 - Study to GLP - Study carried out in 2013	(AC Metcalfe)	(NAFTA/ Region 14)	(EC)	51-52					(0.027, 0.0217)
Report: TK0147009 Study: TK0147009 Trial: T493 - Study to GLP - Study carried out in 2013	Barley (Coalition)	Canada (NAFTA/ Region 14)	53.2 (EC)	BBCH 45-51	60	Grain	< 0.0050, < 0.0050	0.0061, 0.0066	0.011 (0.0111, 0.0116)
Report: TK0147009 Study: TK0147009 Trial: T494 - Study to GLP - Study carried out in 2013	Barley (Bentley)	Canada (NAFTA/ Region 14)	50 (EC)	BBCH 13-14 (majority 14)	51	Grain	< 0.0050	< 0.0054	< 0.0104
					56	Grain	< 0.0050	< 0.0054	< 0.0104
					61	Grain	< 0.0050, < 0.0050	< 0.0054, < 0.0054	< 0.011 (< 0.0104, < 0.0104)
					65	Grain	< 0.0050	< 0.0054	< 0.0104
					70	Grain	< 0.0050	< 0.0054	< 0.0104
Report: TK0147009 Study: TK0147009 Trial: T495 - Study to GLP - Study carried out in 2013	Barley (Coalition)	Canada (NAFTA/ Region 14)	52.3 (EC)	BBCH 13-14 (majority 14)	51	Grain	< 0.0050	0.0062	0.0112
					56	Grain	< 0.0050	0.0065	0.0115
					61	Grain	< 0.0050, < 0.0050	0.0060, 0.0058	0.011 (0.0110, 0.0108)
					65	Grain	< 0.0050	0.0079	0.013
					70	Grain	< 0.0050	0.0078	0.0128

[a] Determined as the sum of common moieties SYN503780 (expressed as bicyclopyrone equivalents) and CSCD686480 (expressed as bicyclopyrone equivalents).

LOQ – Limit of quantification-The limit of quantification (LOQ) was 0.0050 mg/kg for bicyclopyrone equivalents from SYN503780 and 0.0054 mg/kg for bicyclopyrone equivalents from CSCD686480 in the Canadian study and 0.005 mg/kg for both analytes in the USA study.

DBH = Days Before Harvest

Residues in All Untreated Samples (controls) were <LOQ (< 0.005 mg/kg for SYN503780 and CSCD686480 expressed as bicyclopyrone equivalents).

Total Residues = Sum of SYN503780 and CSCD686480 expressed as bicyclopyrone equivalents (LOQ = 0.01 mg/kg).

Maize

Residue data have been collected from three field trials located in Brazil. At each trial, the SL formulation was applied either once as foliar application at rate of 200 g ai/h or twice at rate of 100 g ai/h to the treated plot. Method POPIT.117, a common-moiety method based upon GRM030.05A method was used for analysis of bicyclopyrone (determined as SYN503780) and CSAA915194 (determined as CSCD686480) residues in maize grains quantifying the analytes by liquid chromatography/ mass spectrometry (LC-MS/MS) The limit of quantification (LOQ) was 0.01 mg/kg expressed as bicyclopyrone equivalents.

Twenty two trials in maize were conducted in the USA to determine the residue level of bicyclopyrone on maize. At each trial, the SL formulation was applied once as foliar application at rate of 50 g ai/h to the treated plots. The common-moiety analytical method GRM030.05A was used for analysis of bicyclopyrone (determined as SYN503780) and CSAA915194 (determined as CSCD686480) residues in maize grains quantifying the analyte by HPLC-MS/MS with a limit of

Table 116 Residues in maize from supervised trials in Brazil and the United States involving foliar application of bicyclopyrone

0GLP and Trial Details	Crop (Variety)	Country (Region) (Postcode)	Application		DALA	Crop Part	Residue Found (Uncorrected, mg/kg)		
			Rate (g ai/ha) (Formulation)	Growth Stage			Bicyclopyrone eq. (SYN503780)	Bicyclopyroneeq. (CSCD686480)	Total Mean[a]
GAP	Maize	Uruguay	200	Pre-emergence	PHI: Defined by application timing				
Report: M09107 Study: M09107 Trial: M09107-JJB - Study to GLP - Study carried out in 2009	Maize (Impacto)	Brazil (Uberlandia-MG)	200 (SL)	BBCH 00	125	Grain	<0.01	<0.01	<0.02
			100 100 (SL)	BBCH 14 BBCH 18	90	Grain	<0.01	<0.01	<0.02
Report: M09107 Study: M09107 Trial: M09107-LZF - Study to GLP - Study carried out in 2009	Maize (BR 106)	Brazil (Holambra-SP)	200 (SL)	BBCH 00	138	Grain	<0.01	<0.01	<0.02
			100 100 (SL)	BBCH 14 BBCH 18	85	Grain	< 0.01	< 0.01	< 0.02
Report: M09107 Study: M09107 Trial: M09107-MFG - Study to GLP - Study carried out in 2009	Maize (Impacto)	Brazil (Goiania- GO)	200 (SL)	BBCH 00	127	Grain	< 0.01	< 0.01	< 0.02
			100 100 (SL)	BBCH 14 BBCH 18	95	Grain	< 0.01	< 0.01	<0.02
GAP	Maize	USA	50	V8/8-leaf stage	60	Grain			
Report: TK0112879 Study: TK0112879 Trial: TK0112879-01 - Study to GLP - Study carried out in 2012	Maize (Pioneer 34F07)	USA (EPA/Region 1)	51.5 (SL)	BBCH 17-19 30”corn/V8	100	Grain	< 0.01	< 0.01	< 0.02 (< 0.02, < 0.02)
							< 0.01	< 0.01	

0GLP and Trial Details	Crop (Variety)	Country (Region) (Postcode)	Application		DALA	Crop Part	Residue Found (Uncorrected, mg/kg)		
			Rate (g ai/ha) (Formulation)	Growth Stage			Bicyclopyrone eq. (SYN503780)	Bicyclopyroneeq. (CSCD686480)	Total Mean[a]
Report: TK0112879 Study: TK0112879 Trial: TK0112879-02 - Study to GLP - Study carried out in 2012	Maize (DKC66-96)	USA (EPA/Region 2)	50.4 (SL)	BBCH 18-19 30”corn/V8	94	Grain	< 0.01	< 0.01	< 0.02 (< 0.02, < 0.02)
							< 0.01	< 0.01	
Report: TK0112879 Study: TK0112879 Trial: TK0112879-03 - Study to GLP - Study carried out in 2012	Maize (A1022967/ A1027871)	USA (EPA/Region 5)	51.5 (SL)	BBCH 17-19 30”corn/V8	90	Grain	< 0.01	< 0.01	< 0.02 (< 0.02, < 0.02)
							< 0.01	< 0.01	
Report: TK0112879 Study: TK0112879 Trial: TK0112879-04 - Study to GLP - Study carried out in 2012	Maize (33Z74)	USA (EPA/Region 5)	50.4 (SL)	BBCH 17-19 30”corn/V8	110	Grain	< 0.01	< 0.01	< 0.02 (< 0.02, < 0.02)
							< 0.01	< 0.01	
Report: TK0112879 Study: TK0112879 Trial: TK0112879-05 - Study to GLP - Study carried out in 2012	Maize (Pioneer P1948)	USA (EPA/Region 5)	50.4 (SL)	BBCH 17-19 30”corn/V8	92	Grain	< 0.01	< 0.01	< 0.02 (< 0.02, < 0.02)
							< 0.01	< 0.01	
Report: TK0112879 Study: TK0112879 Trial: TK0112879-06 - Study to GLP - Study carried out in 2012	Maize (DKC 33-54)	USA (EPA/Region 5)	50.4 (SL)	BBCH 18 30”corn/V8	79	Grain	< 0.01	< 0.01	< 0.02 (< 0.02, < 0.02)
							< 0.01	< 0.01	
Report: TK0112879 Study: TK0112879 Trial:	Maize (P1151HR)	USA (EPA/Region 5)	50.4 (SL)	BBCH 16-17 30”corn/V8	98	Grain	< 0.01	< 0.01	< 0.02 (< 0.02, < 0.02)

0GLP and Trial Details	Crop (Variety)	Country (Region) (Postcode)	Application		DALA	Crop Part	Residue Found (Uncorrected, mg/kg)		
			Rate (g ai/ha) (Formulation)	Growth Stage			Bicyclopyrone eq. (SYN503780)	Bicyclopyroneeq. (CSCD686480)	Total Mean[a]
TK0112879-07 - Study to GLP - Study carried out in 2012									
							< 0.01	< 0.01	
Report: TK0112879 Study: TK0112879 Trial: TK0112879-14 - Study to GLP - Study carried out in 2012	Maize (Pioneer)	USA (EPA/Region 5)	51.5 (SL)	BBCH 17-19 30”corn/V8	103	Grain	< 0.01	< 0.01	< 0.02 (< 0.02, < 0.02)
							< 0.01	< 0.01	
Report: TK0112879 Study: TK0112879 Trial: TK0112879-15 - Study to GLP - Study carried out in 2012	Maize (DKC 45-51 RIB)	USA (EPA/Region 5)	49.3 (SL)	BBCH 17-19 30”corn/V8	100	Grain	< 0.01	< 0.01	< 0.02 (< 0.02, < 0.02)
							< 0.01	< 0.01	
Report: TK0112879 Study: TK0112879 Trial: TK0112879-16 - Study to GLP - Study carried out in 2012	Maize (DKC 45-51 RIB)	USA (EPA/Region 5)	51.5 (SL)	BBCH 17-19 30”corn/V8	100	Grain	< 0.01	< 0.01	< 0.02 (< 0.02, < 0.02)
							ND	< 0.01	
Report: TK0112879 Study: TK0112879 Trial: TK0112879-18 - Study to GLP - Study carried out in 2012	Maize -8066846	USA (EPA/Region)	50.4 (SL)	BBCH 18 30”corn/V8	80	Grain	< 0.01	< 0.01	< 0.02 (< 0.02, < 0.02)
							< 0.01	< 0.01	
Report: TK0112879 Study: TK0112879 Trial: TK0112879-19 - Study to GLP - Study	Maize -8066846	USA (EPA/Region 5)	50.4 (SL)	BBCH 18 30”corn/V8	80	Grain	< 0.01	< 0.01	< 0.02 (< 0.02, < 0.02)
							< 0.01	< 0.01	

0GLP and Trial Details	Crop (Variety)	Country (Region) (Postcode)	Application		DALA	Crop Part	Residue Found (Uncorrected, mg/kg)		
			Rate (g ai/ha) (Formulation)	Growth Stage			Bicyclopyrone eq. (SYN503780)	Bicyclopyroneeq. (CSCD686480)	Total Mean[a]
carried out in 2012									
Report: TK0112879 Study: TK0112879 Trial: TK0112879-20 - Study to GLP - Study carried out in 2012	Maize (P1360HR)	USA (EPA/Region 5)	50.4 (SL)	BBCH 18 30”corn/V8	99	Grain	< 0.01	< 0.01	< 0.02 (< 0.02, < 0.02)
							< 0.01	< 0.01	
Report: TK0112879 Study: TK0112879 Trial: TK0112879-21 - Study to GLP - Study carried out in 2012	Maize (Pioneer P9675)	USA (EPA/Region 5)	51.5 (SL)	BBCH 19 30”corn/V8	106	Grain	< 0.01	< 0.01	< 0.02 (< 0.02, < 0.02)
							< 0.01	< 0.01	
Report: TK0112879 Study: TK0112879 Trial: TK0112879-22 - Study to GLP - Study carried out in 2012	Maize (N77H-3000Gt)	USA (EPA/Region5)	51.5 (SL)	BBCH 17-18 30”corn/V8	113	Grain	< 0.01	< 0.01	< 0.02 (< 0.02, < 0.02)
							< 0.01	< 0.01	
Report: TK0112879 Study: TK0112879 Trial: TK0112879-23 - Study to GLP - Study carried out in 2012	Maize (PB878RRCB)	USA (EPA/Region 5)	50.4 (SL)	BBCH 18 30”corn/V8	98	Grain	< 0.01	< 0.01	< 0.02 (< 0.02, < 0.02)
							< 0.01	< 0.01	
Report: TK0112879 Study: TK0112879 Trial: TK0112879-24 - Study to GLP - Study carried out in 2012	Maize (89T43-3000GT)	USA (EPA/Region 5)	50.4 (SL)	BBCH 18 30”corn/V8	86	Grain	< 0.01	< 0.01	< 0.02 (< 0.02, < 0.02)
							< 0.01	< 0.01	
Report: TK0112879 Study:	Maize (DKC52-59	USA (EPA/Region	51.5 (SL)	BBCH 17-18 30”corn/V8	109	Grain	< 0.01	< 0.01	< 0.02 (< 0.02,

0GLP and Trial Details	Crop (Variety)	Country (Region) (Postcode)	Application		DALA	Crop Part	Residue Found (Uncorrected, mg/kg)		
			Rate (g ai/ha) (Formulation)	Growth Stage			Bicyclopyrone eq. (SYN503780)	Bicyclopyroneeq. (CSCD686480)	Total Mean[a]
TK0112879 Trial: TK0112879-25 - Study to GLP - Study carried out in 2012	(VT3))	5)							< 0.02)
							< 0.01	< 0.01	
Report: TK0112879 Study: TK0112879 Trial: TK0112879-26 - Study to GLP - Study carried out in 2012	Maize (33Z74)	USA (EPA/Region 5)	51.5 (SL)	BBCH 17-19 30”corn/V8	96	Grain	< 0.01	< 0.01	< 0.02 (< 0.02, < 0.02)
							< 0.01	< 0.01	
Report: TK0112879 Study: TK0112879 Trial: TK0112879-11 - Study to GLP - Study carried out in 2012	Popcorn (997 Yellow F1)	USA (EPA/Region 5)	50.3 (SL)	BBCH 18 30”corn/V8	100	Grain	< 0.01	< 0.01	< 0.02 (< 0.02, < 0.02)
							< 0.01	< 0.01	
Report: TK0112879 Study: TK0112879 Trial: TK0112879-12 - Study to GLP - Study carried out in 2012	Popcorn (997 Yellow F1)	USA (EPA/Region 5)	50.4 (SL)	BBCH 18 30”corn/V8	100	Grain	< 0.01	< 0.01	< 0.02 (< 0.02, < 0.02)
							< 0.01	< 0.01	
Report: TK0112879 Study: TK0112879 Trial: TK0112879-13 - Study to GLP - Study carried out in 2012	Popcorn (Robust Yellow Popcorn)	USA (EPA/Region 5)	50.4 (SL)	BBCH 16-17 30”corn/V8	98	Grain	< 0.01	< 0.01	< 0.02 (< 0.02, < 0.02)
							< 0.01	< 0.01	

[a] Determined as the sum of common moieties SYN503780 (expressed as bicyclopyrone equivalents) and CSCD686480 (expressed as bicyclopyrone equivalents).

LOQ – Limit of quantification-The limit of quantification (LOQ) was 0.01 mg/kg for bicyclopyrone equivalents from SYN503780 and for bicyclopyrone equivalents from CSCD686480

During the growing seasons 2008/2009, twenty-six trials were conducted in maize in USA to determine the residue level of bicyclopyrone. The SL formulation of bicyclopyrone was applied once or twice at a rate of 200 g ai/ha to the soil surface pre-emergence of the crop and as a foliar spray post-emergence, or as a single post-emergence foliar spray. The common-moiety analytical method GRM030.05A was used to analyse maize samples for the residues of bicyclopyrone by liquid chromatography and mass/mass detector (LC-MS/MS) with a limit of quantitation (LOQ) of 0.01 mg/kg expressed as bicyclopyrone equivalents. This method includes hydrolysis of the bridge between the two rings of bicyclopyrone to release the structurally-related moieties SYN503780 and CSCD686480. In these studies, SYN503780 was corrected to bicyclopyrone equivalents and CSCD686480 was corrected to CSAA915194 equivalents (principle metabolite).

Table 117 Residues in maize from supervised trials in the USA involving one or two application of bicyclopyrone SL formulation at a rate of 200 g ai/ha.

GLP and Trial Details	Crop (Variety)	Country (Region)	Application		DALA	Crop Part	Residue Found (Uncorrected, mg/kg)		
			Rate (g ai/ha) (Formulation)	Growth Stage			Bicyclopyrone eq. (SYN503780)	Bicyclopyrone eq. (CSCD686480)	Total Mean[a]
GAP	Maize	USA	50	V8/8-leaf stage	45				
Report: T019378-04 Study: 09SYN253A.REP Trial: E10NC081383 - Study to GLP - Study carried out in 2008	Maize (Garst 8377YG1/RR)	USA (EPA Region 2)	200 + 200 (soil surface + post-emergence foliar) (EC)	Pre-plant BBCH 36 (V8)	82	Grain	< 0.01 < 0.01	< 0.01 < 0.01	< 0.02 (< 0.02, < 0.02)
			200 (post-emergence foliar) (EC)	BBCH 36 (V8)	82		< 0.01 < 0.01	< 0.01 < 0.01	< 0.02 (< 0.02, < 0.02)
Report: T019378-04 Study: 09SYN253A.REP Trial: C19MO081385 - Study to GLP - Study carried out in 2008	Maize (Pioneer 33D47)	USA (EPA Region 5)	200 + 200 (soil surface + post-emergence foliar) (EC)	Pre-plant BBCH 36 (V8)	111	Grain	< 0.01 < 0.01	< 0.01 < 0.01	< 0.02 (< 0.02, < 0.02)
			200 (post-emergence foliar) (EC)	BBCH 36 (V8)	111		< 0.01 < 0.01	< 0.01 < 0.01	< 0.02 (< 0.02, < 0.02)
Report: T019378-04 Study: 09SYN253A.REP Trial: C19KS081386 - Study to GLP - Study carried out in 2008	Maize (DK 6019)	USA (EPA Region 5)	200 + 200 (soil surface + post-emergence foliar) (EC)	Pre-plant BBCH 18 (V8)	109	Grain	< 0.01 < 0.01	< 0.01 < 0.01	< 0.02 (< 0.02, < 0.02)
			200 (post-emergence foliar) (EC)	BBCH 18 (V8)	109		< 0.01 < 0.01	< 0.01 < 0.01	< 0.02 (< 0.02, < 0.02)
Report: T019378-04 Study: 09SYN253A.REP Trial: C01MI081387 - Study to GLP - Study carried out in 2008	Maize (Pioneer 38N85 RR)	USA (EPA Region 5)	200 + 200 (soil surface + post-emergence foliar) (EC)	Pre-plant BBCH 18 (V8)	114	Grain	< 0.01 < 0.01	< 0.01 < 0.01	< 0.02 (< 0.02, < 0.02)
			200 (post-emergence foliar) (EC)	BBCH 18 (V8)	114		< 0.01 < 0.01	< 0.01 < 0.01	< 0.02 (< 0.02, < 0.02)
Report: T019378-04 Study: 09SYN253A.REP Trial: C01OH081388 - Study to GLP - Study carried out in 2008	Maize (691RR2)	USA (EPA Region 5)	200 + 200 (soil surface + post-emergence foliar) (EC)	Pre-plant BBCH 18 (V8)	112	Grain	< 0.01 < 0.01	< 0.01 < 0.01	< 0.02 (< 0.02, < 0.02)
			200	BBCH	112		< 0.01	< 0.01	< 0.02

GLP and Trial Details	Crop (Variety)	Country (Region)	Application		DALA	Crop Part	Residue Found (Uncorrected, mg/kg)		
			Rate (g ai/ha) (Formulation)	Growth Stage			Bicyclopyrone eq. (SYN503780)	Bicyclopyrone eq. (CSCD686480)	Total Mean[a]
			(post-emergence foliar) (EC)	18 (V8)			< 0.01	< 0.01	(< 0.02, < 0.02)
Report: T019378-04 Study: 09SYN253A.REP Trial: C08WI081389 - Study to GLP - Study carried out in 2008	Maize (Dekalb DK43-27 (VT3))	USA (EPA Region 5)	200 + 200 (soil surface + post-emergence foliar) (EC)	Pre-plant	115	Grain	< 0.01	< 0.01	< 0.02
				BBCH 18 (V8)			< 0.01	< 0.01	(< 0.02, < 0.02)
			200 (post-emergence foliar) (EC)	BBCH 18 (V8)	115		< 0.01	< 0.01	< 0.02
							< 0.01	< 0.01	(< 0.02, < 0.02)
Report: T019378-04 Study: 09SYN253A.REP Trial: C08WI081390 - Study to GLP - Study carried out in 2008	Maize (Pioneer 37Y12)	USA (EPA Region 5)	200 + 200 (soil surface + post-emergence foliar) (EC)	Pre-plant	109	Grain	< 0.01	< 0.01	< 0.02
				BBCH 18 (V8)			< 0.01	< 0.01	(< 0.02, < 0.02)
			200 (post-emergence foliar) (EC)	BBCH 18 (V8)	109		< 0.01	< 0.01	< 0.02
							< 0.01	< 0.01	(< 0.02, < 0.02)
Report: T019378-04 Study: 09SYN253A.REP Trial: C08WI081391 - Study to GLP - Study carried out in 2008	Maize (H-7151CB/LL/RW)	USA (EPA Region 5)	200 + 200 (soil surface + post-emergence foliar) (EC)	Pre-plant	119	Grain	< 0.01	< 0.01	< 0.02
				BBCH 18 (V8)			< 0.01	< 0.01	(< 0.02, < 0.02)
			200 (post-emergence foliar) (EC)	BBCH 18 (V8)	119		< 0.01	< 0.01	< 0.02
							< 0.01	< 0.01	(< 0.02, < 0.02)
Report: T019378-04 Study: 09SYN253A.REP Trial: C13ND081392 - Study to GLP - Study carried out in 2008	Maize (238 RR2/BT)	USA (EPA Region 5)	200 + 200 (soil surface + post-emergence foliar) (EC)	Pre-plant	99	Grain	< 0.01	< 0.01	< 0.02
					107		< 0.01	< 0.01	< 0.02
					113		< 0.01	< 0.01	< 0.02
				BBCH 18 (V8)	120		< 0.01	0.01	< 0.02
							< 0.01	< 0.01	
					127		< 0.01	< 0.01	< 0.02
			200 (post-emergence foliar) (EC)	BBCH 18 (V8)	99		< 0.01	< 0.01	< 0.02
					107		< 0.01	0.01	< 0.02
					113		< 0.01	0.01	< 0.02
					120		< 0.01	< 0.01	< 0.02
							< 0.01	0.01	
					127		< 0.01	< 0.01	< 0.02
Report: T019378-04 Study: 09SYN253A.REP Trial: C13ND081393 - Study to GLP - Study carried out in 2008	Maize (238 RR2/BT)	USA (EPA Region 5)	200 + 200 (soil surface + post-emergence foliar) (EC)	Pre-plant	110	Grain	< 0.01	< 0.01	< 0.02
				BBCH 18 (V8)			< 0.01	< 0.01	(< 0.02, < 0.02)
			200 (post-emergence foliar) (EC)	BBCH 18 (V8)	110		< 0.01	< 0.01	< 0.02
							< 0.01	< 0.01	(< 0.02, < 0.02)
Report: T019378-04 Study: 09SYN253A.REP Trial: E19IA081395 - Study to GLP - Study carried out in 2008	Maize (B0000948 Hybrid Seed Corn)	USA (EPA Region 5)	200 + 200 (soil surface + post-emergence foliar) (EC)	Pre-plant	80	Grain	< 0.01	< 0.01	< 0.02
				BBCH 18 (V8)			< 0.01	< 0.01	(< 0.02, < 0.02)
			200 (post-emergence foliar) (EC)	BBCH 18 (V8)	80		0.01	< 0.01	< 0.02
							< 0.01	< 0.01	(< 0.02, < 0.02)

GLP and Trial Details	Crop (Variety)	Country (Region)	Application		DALA	Crop Part	Residue Found (Uncorrected, mg/kg)		
			Rate (g ai/ha) (Formulation)	Growth Stage			Bicyclopyrone eq. (SYN503780)	Bicyclopyrone eq. (CSCD686480)	Total Mean[a]
Report: T019378-04 Study: 09SYN253A.REP Trial: E19IA081396 - Study to GLP - Study carried out in 2008	Maize (B0000948 Hybrid Seed Corn)	USA (EPA Region 5)	200 + 200 (soil surface + post-emergence foliar) (EC)	Pre-plant BBCH 18 (V8)	88	Grain	< 0.01 < 0.01	< 0.01 < 0.01	< 0.02 (< 0.02, < 0.02)
			200 (post-emergence foliar) (EC)	BBCH 18 (V8)	88		< 0.01 < 0.01	< 0.01 < 0.01	< 0.02 (< 0.02, < 0.02)
Report: T019378-04 Study: 09SYN253A.REP Trial: E19IA081397 - Study to GLP - Study carried out in 2008	Maize (B0000948 Hybrid Seed Corn)	USA (EPA Region 5)	200 + 200 (soil surface + post-emergence foliar) (EC)	Pre-plant BBCH 18 (V8)	79	Grain	< 0.01 < 0.01	< 0.01 < 0.01	< 0.02 (< 0.02, < 0.02)
			200 (post-emergence foliar) (EC)	BBCH 18 (V8)	79		< 0.01 < 0.01	< 0.01 < 0.01	< 0.02 (< 0.02, < 0.02)
Report: T019378-04 Study: 09SYN253A.REP Trial: E19IA081398 - Study to GLP - Study carried out in 2008	Maize (B0000948 Hybrid Seed Corn)	USA (EPA Region 5)	200 + 200 (soil surface + post-emergence foliar) (EC)	Pre-plant BBCH 18 (V8)	87	Grain	< 0.01 < 0.01	< 0.01 < 0.01	< 0.02 (< 0.02, < 0.02)
			200 (post-emergence foliar) (EC)	BBCH 18 (V8)	87		< 0.01 < 0.01	< 0.01 < 0.01	< 0.02 (< 0.02, < 0.02)
Report: T019378-04 Study: 09SYN253A.REP Trial: C30IA081399 - Study to GLP - Study carried out in 2008	Maize (33H27)	USA (EPA Region 5)	200 + 200 (soil surface + post-emergence foliar) (EC)	Pre-plant BBCH 18 (V8)	106	Grain	< 0.01 < 0.01	< 0.01 < 0.01	< 0.02 (< 0.02, < 0.02)
			200 (post-emergence foliar) (EC)	BBCH 18 (V8)	106		< 0.01 < 0.01	< 0.01 < 0.01	< 0.02 (< 0.02, < 0.02)
Report: T019378-04 Study: 09SYN253A.REP Trial: C30IA081400 - Study to GLP - Study carried out in 2008	Maize (FA5614R)	USA (EPA Region 5)	200 + 200 (soil surface + post-emergence foliar) (EC)	Pre-plant BBCH 18 (V8)	76	Grain	< 0.01	< 0.01	< 0.02
					83		< 0.01	< 0.01	< 0.02
					90		< 0.01	< 0.01	< 0.02
					97		< 0.01 < 0.01	< 0.01 < 0.01	< 0.02
					104		< 0.01	< 0.01	< 0.02
			200 (post-emergence foliar) (EC)	BBCH 18 (V8)	76		< 0.01	< 0.01	< 0.02
					83		< 0.01	< 0.01	< 0.02
					90		< 0.01	< 0.01	< 0.02
					97		< 0.01 < 0.01	< 0.01 < 0.01	< 0.02
					104		< 0.01	< 0.01	< 0.02
Report: T019378-04 Study: 09SYN253A.REP Trial: C30IA081401 - Study to GLP - Study carried out in 2008	Maize (Stine 903228VT3)	USA (EPA Region 5)	200 + 200 (soil surface + post-emergence foliar) (EC)	Pre-plant BBCH 18 (V8)	83	Grain	< 0.01 < 0.01	< 0.01 < 0.01	< 0.02 (< 0.02, < 0.02)
			200 (post-emergence foliar) (EC)	BBCH 18 (V8)	83		< 0.01 < 0.01	< 0.01 < 0.01	< 0.02 (< 0.02, < 0.02)
Report: T019378-04 Study: 09SYN253A.REP Trial: W07TX081402 - Study to GLP - Study carried out in	Maize (DKC69-44)	USA (EPA Region 6)	200 + 200 (soil surface + post-emergence foliar) (EC)	Pre-plant BBCH 18 (V8)	115	Grain	< 0.01 < 0.01	< 0.01 < 0.01	< 0.02 (< 0.02, < 0.02)

GLP and Trial Details	Crop (Variety)	Country (Region)	Application		DALA	Crop Part	Residue Found (Uncorrected, mg/kg)		
			Rate (g ai/ha) (Formulation)	Growth Stage			Bicyclopyrone eq. (SYN503780)	Bicyclopyrone eq. (CSCD686480)	Total Mean[a]
2008			200 (post-emergence foliar) (EC)	BBCH 18 (V8)	115		< 0.01 < 0.01	< 0.01 < 0.01	< 0.02 (< 0.02, < 0.02)
Report: T019378-04 Study: 09SYN253A.REP Trial: E13TX081403 - Study to GLP - Study carried out in 2008	Maize (Robust 128YH F1)	USA (EPA Region 8)	200 + 200 (soil surface + post-emergence foliar) (EC)	Pre-plant BBCH 18 (V8)	124	Grain	< 0.01 < 0.01	< 0.01 < 0.01	< 0.02 (< 0.02, < 0.02)
			200 (post-emergence foliar) (EC)	BBCH 18 (V8)	124		< 0.01 < 0.01	< 0.01 < 0.01	< 0.02 (< 0.02, < 0.02)
Report: T019378-04 Study: 09SYN253A.REP Trial: C13ND081408 - Study to GLP - Study carried out in 2008	Maize (Croplan Genetics 9618888)	USA (EPA Region 5)	200 + 200 (soil surface + post-emergence foliar) (EC)	Pre-plant BBCH 18 (V8)	110	Grain	< 0.01 < 0.01	< 0.01 < 0.01	< 0.02 (< 0.02, < 0.02)
			200 (post-emergence foliar) (EC)	BBCH 18 (V8)	110		< 0.01 < 0.01	< 0.01 < 0.01	< 0.02 (< 0.02, < 0.02)
Report: T019378-04 Study: 09SYN253A.REP Trial: E04PA081411 - Study to GLP - Study carried out in 2008	Maize (Mycogen Hybrid Seed (Hybrid 2D324))	USA (EPA Region 1)	200 + 200 (soil surface + post-emergence foliar) (EC)	Pre-plant BBCH 18 (V8)	85	Grain	< 0.01 < 0.01	< 0.01 < 0.01	< 0.02 (< 0.02, < 0.02)
			200 (post-emergence foliar) (EC)	BBCH 18 (V8)	85		< 0.01 < 0.01	< 0.01 < 0.01	< 0.02 (< 0.02, < 0.02)
			200 + 200 (pre-plant +post-emergence foliar) (EC)	Pre-plant BBCH 18 (V8)	85		< 0.01 < 0.01	< 0.01 < 0.01	< 0.02
Report: T019378-04 Study: 09SYN268A.REP Trial: C30-9453/IA - Study to GLP - Study carried out in 2009	Maize (33D47)	USA (NAFTA Region 5)	200 + 200 (soil surface + post-emergence foliar) (EC)	Pre-plant BBCH 31 (V8)	111	Grain	< 0.01 < 0.01	< 0.01 < 0.01	< 0.02 (< 0.02, < 0.02)
			200 + 200 (pre-plant +post-emergence foliar) (EC)	Pre-plant BBCH 31 (V8)	111		< 0.01 < 0.01	< 0.01 < 0.01	< 0.02 (< 0.02, < 0.02)
Report: T019378-04 Study: 09SYN268A.REP Trial: C13-9454/ND - Study to GLP - Study carried out in 2009	Maize (9618888)	USA (NAFTA Region 5)	200 + 200 (soil surface + post-emergence foliar) (EC)	Pre-plant BBCH 37 (V8)	104	Grain	< 0.01 < 0.01	< 0.01 0.01	< 0.02 (< 0.02, < 0.02)
			200 + 200 (pre-plant +post-emergence foliar) (EC)	Pre-plant BBCH 37 (V8)	104		< 0.01 < 0.01	< 0.01 < 0.01	< 0.02 (< 0.02, < 0.02)

GLP and Trial Details	Crop (Variety)	Country (Region)	Application		DALA	Crop Part	Residue Found (Uncorrected, mg/kg)		
			Rate (g ai/ha) (Formulation)	Growth Stage			Bicyclopyrone eq. (SYN503780)	Bicyclopyrone eq. (CSCD686480)	Total Mean[a]
Report: T019378-04 Study: 09SYN268A.REP Trial: C19-9455/MO - Study to GLP - Study carried out in 2009	Maize (Pioneer 33T56)	USA (NAFTA Region 5)	200 + 200 (soil surface + post-emergence foliar) (EC)	Pre-plant BBCH 37 (V8)	94	Grain	< 0.01 < 0.01	< 0.01 < 0.01	< 0.02 (< 0.02, < 0.02)
			200 + 200 (pre-plant +post-emergence foliar) (EC)	Pre-plant BBCH 37 (V8)	94		< 0.01 < 0.01	< 0.01 < 0.01	< 0.02 (< 0.02, < 0.02)
Report: T019378-04 Study: 09SYN268A.REP Trial: C12-9456/ND - Study to GLP - Study carried out in 2009	Maize (INT65D85R)	USA (NAFTA Region 5)	200 + 200 (soil surface + post-emergence foliar) (EC)	Pre-plant BBCH 18 (V8)	109	Grain	< 0.01 < 0.01	< 0.01 < 0.01	< 0.02 (< 0.02, < 0.02)
			200 + 200 (pre-plant +post-emergence foliar) (EC)	Pre-plant BBCH 18 (V8)	109		< 0.01 < 0.01	< 0.01 < 0.01	< 0.02 (< 0.02, < 0.02)
Report: T019378-04 Study: 09SYN268A.REP Trial: C12-9457/ND - Study to GLP - Study carried out in 2009	Maize (INT65D85R)	USA (NAFTA Region 5)	200 + 200 (soil surface + post-emergence foliar) (EC)	Pre-plant BBCH 18 (V8)	105	Grain	< 0.01 < 0.01	< 0.01 < 0.01	< 0.02 (< 0.02, < 0.02)
			200 + 200 (pre-plant +post-emergence foliar) (EC)	Pre-plant BBCH 18 (V8)	105		< 0.01 < 0.01	< 0.01 < 0.01	< 0.02 (< 0.02, < 0.02)

[a] Determined as the sum of common moieties SYN503780 (expressed as bicyclopyrone equivalents) and CSCD686480 (expressed as bicyclopyrone equivalents).

LOQ – Limit of quantification-The limit of quantification (LOQ) was 0.01 mg/kg for bicyclopyrone equivalents from SYN503780 and for bicyclopyrone equivalents from CSCD686480

Wheat

The trials were conducted at two locations in Canada and USA to determine the residue level of bicyclopyrone in/on wheat. Each trial contained two treated plots. The SL formulation of bicyclopyrone, were applied once at a rate equivalent to 50 g ai/ha to each treated plot. One plot was treated 30 days before normal harvest of forage and hay and a second plot was treated 60 days before normal harvest of grain and straw. The common moiety analytical method GRM030.05A (in the Canadian study, GRM030.05B was used only for the calculation of final residues expressed as bicyclopyrone) was used for the determination of residues of bicyclopyrone in wheat. The limit of quantification (LOQ) in the US study was 0.005 mg/kg for SYN503780 or CSCD686480 expressed as bicyclopyrone equivalents, whereas in the Canadian study the limits of quantification were 0.005 mg/kg for SYN503780 and 0.0054 mg/kg for CSCD686480 expressed as bicyclopyrone equivalents.

Table 118 Bicyclopyrone residues on wheat grain from supervised trials in Canada and the USA

GLP and Trial Details	Crop (Variety)	Country (Region) (Postcode)	Application		DALA	Crop Part	Residue Found (Uncorrected) (mg/kg)		
			Rate (g ai/ha) (Formulation)	Growth Stage			Bicyclopyrone eq. (SYN503780)	Bicyclopyrone eq. (CSCD686480)	Total Mean[a]
GAP	Wheat	USA	50	2-leaf to pre-boot stage	PHI: 60	Grain	-	-	-
Report: TK0021323 Study: TK0021323 Trial: TK0021323-01 - Study to GLP - Study carried out in 2012	Wheat (Pioneer 26R12)	USA (NAFTA/Region 2)	50 (EC)	BBCH 32-34 60 DBH	58	Grain	< 0.005, < 0.005	< 0.005, < 0.005	0.01 (< 0.010, < 0.010)
Report: TK0021323 Study: TK0021323 Trial: TK0021323-02 - Study to GLP - Study carried out in 2012	Wheat (Oakes)	USA (NAFTA/Region 4)	52 (EC)	BBCH 30-32 60 DBH	60	Grain	< 0.005, < 0.005	0.00617, 0.00655	0.011 (0.0112, 0.0116)
Report: TK0021323 Study: TK0021323 Trial: TK0021323-03 - Study to GLP - Study carried out in 2012	Wheat (Armour)	USA (NAFTA/Region 5)	49 (EC)	BBCH 31-32 60 DBH	57	Grain	< 0.005, < 0.005	0.00757, 0.00941	0.014 (0.0126, 0.0144)
Report: TK0021323 Study: TK0021323 Trial: TK0021323-04 - Study to GLP - Study carried out in 2012	Wheat (Croplan 9201)	USA (NAFTA/Region 5)	52 (EC)	BBCH 45-47	49	Grain	< 0.005, < 0.005	0.0143, 0.0158	0.0193, 0.0208
					54		< 0.005, < 0.005	0.00511, 0.00623	0.0101, 0.0112
					58		< 0.005, < 0.005	0.00691, 0.00790	(0.0119, 0.0129)
					63		< 0.005, < 0.005	0.00630, 0.00680	0.0113, 0.0118
					68		< 0.005, < 0.005	0.0139, 0.0120	0.018 0.0189, 0.0169
Report: TK0021323 Study: TK0021323 Trial: TK0021323-05 - Study to GLP - Study carried out in 2012	Wheat (Faller)	USA (NAFTA/Region 5)	50 (EC)	BBCH 45-47 60 DBH	61	Grain	< 0.005, < 0.005	0.0112, 0.0105	0.016 (0.0162, 0.0155
Report: TK0021323 Study: TK0021323 Trial: TK0021323-06 - Study to GLP - Study carried out in 2012	Wheat (Beretta)	USA (NAFTA/Region 5)	50 (EC)	BBCH 30-32 60 DBH	60	Grain	< 0.005, < 0.005	< 0.005, < 0.005	0.01 (< 0.010, < 0.010)
Report: TK0021323 Study: TK0021323 Trial: TK0021323-07 - Study to GLP - Study carried	Wheat (Divide)	USA (NAFTA/Region 7)	50 (EC)	BBCH 30-35	50	Grain	< 0.005, < 0.005	< 0.005, 0.00565	< 0.010, 0.0106
					55		< 0.005, < 0.005	0.00571, 0.00565	< 0.010, 0.010
					59		< 0.005, < 0.005	< 0.005, < 0.005	0.01 (< 0.010, 0.010)
					64		< 0.005, < 0.005	< 0.005, < 0.005	< 0.010, 0.010

GLP and Trial Details	Crop (Variety)	Country (Region) (Postcode)	Application		DALA	Crop Part	Residue Found (Uncorrected) (mg/kg)		
			Rate (g ai/ha) (Formulation)	Growth Stage			Bicyclopyrone eq. (SYN503780)	Bicyclopyrone eq. (CSCD686480)	Total Mean[a]
out in 2012					70		< 0.005, < 0.005	< 0.005, < 0.005	< 0.010, 0.010
Report: TK0021323 Study: TK0021323 Trial: TK0021323-08 - Study to GLP - Study carried out in 2012	Wheat (TAM 304)	USA (NAFTA/Region 6)	53 (EC)	BBCH 37-51 60 DBH	60	Grain	< 0.005, < 0.005	< 0.005, < 0.005	0.01 (< 0.010, < 0.010)
Report: TK0021323 Study: TK0021323 Trial: TK0021323-09 - Study to GLP - Study carried out in 2012	Wheat (Traverse)	USA (NAFTA/Region 7)	50 (EC)	BBCH 30-31 60 DBH	57	Grain	< 0.005, < 0.005	< 0.005, < 0.005	0.01 (< 0.010, 0.010)
Report: TK0021323 Study: TK0021323 Trial: TK0021323-10 - Study to GLP - Study carried out in 2012	Wheat (Glenn)	USA (NAFTA/Region 7)	50 (EC)	BBCH 30-35 60 DBH	59	Grain	< 0.005, < 0.005	0.00624, 0.00663	0.011 (0.0112, < 0.010)
Report: TK0021323 Study: TK0021323 Trial: TK0021323-11 - Study to GLP - Study carried out in 2012	Wheat (Faller)	USA (NAFTA/Region 7)	53 (EC)	BBCH 15-21 60 DBH	60	Grain	< 0.005, < 0.005	< 0.005, < 0.005	< 0.01 (< 0.005, < 0.005)
Report: TK0021323 Study: TK0021323 Trial: TK0021323-12 - Study to GLP - Study carried out in 2012	Wheat (Prosper)	USA (NAFTA/Region 7)	52 (EC)	BBCH 30-35 30 DBH	59	Grain	< 0.005, < 0.005	< 0.005, < 0.005	0.01 (< 0.005, < 0.005)
Report: TK0021323 Study: TK0021323 Trial: TK0021323-13 - Study to GLP - Study carried out in 2012	Wheat (Duster)	USA (NAFTA/Region 8)	53 (EC)	BBCH 32-33 60 DBH	62	Grain	< 0.005, < 0.005	0.00653, 0.00636	0.011 (0.0115, 0.0114)
Report: TK0021323 Study: TK0021323 Trial: TK0021323-14 - Study to GLP - Study carried out in 2012	Wheat (Duster)	USA (NAFTA/Region 8)	52 (EC)	BBCH 35	51	Grain	< 0.005, < 0.005	< 0.005, < 0.005	< 0.010, < 0.010
					56		< 0.005, < 0.005	< 0.005, < 0.005	< 0.010, < 0.010
					60		< 0.005, < 0.005	< 0.005, < 0.005	0.01 (< 0.010, < 0.010)
					65		< 0.005, < 0.005	< 0.005, < 0.005	< 0.010, < 0.010
					70		< 0.005, < 0.005	< 0.005, < 0.005	< 0.010, < 0.010

GLP and Trial Details	Crop (Variety)	Country (Region) (Postcode)	Application		DALA	Crop Part	Residue Found (Uncorrected) (mg/kg)		
			Rate (g ai/ha) (Formulation)	Growth Stage			Bicyclopyrone eq. (SYN503780)	Bicyclopyrone eq. (CSCD686480)	Total Mean[a]
Report: TK0021323 Study: TK0021323 Trial: TK0021323-15 - Study to GLP - Study carried out in 2012	Wheat (Blend)	USA (NAFTA/Region 8)	48 (EC)	BBCH 31-34 60 DBH	57	Grain	< 0.005, < 0.005	0.0109, 0.0113	0.016 (0.0159, 0.0163)
Report: TK0021323 Study: TK0021323 Trial: TK0021323-16 - Study to GLP - Study carried out in 2012	Wheat (Tam 111 Hard Red Winter)	USA (NAFTA/Region 8)	52 (EC)	BBCH 43-47 60 DBH	60	Grain	0.00545, <LOQ	0.0121, 0.00923	0.016 (0.0175, 0.0142)
Report: TK0021323 Study: TK0021323 Trial: TK0021323-17 - Study to GLP - Study carried out in 2012	Wheat (Coronado)	USA (NAFTA/Region 8)	50 (EC)	BBCH 34-35 60 DBH	60	Grain	< 0.005, < 0.005	< 0.005, < 0.005	0.01 (< 0.010, < 0.010)
Report: TK0021323 Study: TK0021323 Trial: TK0021323-18 - Study to GLP - Study carried out in 2012	Wheat (Stephens)	USA (NAFTA/Region 11)	50 (EC)	BBCH 71-73 60 DBH	58	Grain	0.00812, 0.00700	0.00918, 0.00749	0.016 (0.0173, 0.0145)
Report: TK0021323 Study: TK0021323 Trial: TK0021323-19 - Study to GLP - Study carried out in 2012	Wheat (Willcross 748 SRW)	USA (NAFTA/Region 5)	50 (EC)	BBCH 71 60 DBH	61	Grain	0.0169, 0.0111	0.0200, 0.0138	0.031 (0.0370, 0.0249)
			149 (3X) (EC)	BBCH 71 60 DBH	60	Grain PP	0.0397, 0.0418 0.0396, 0.0403 0.0398, 0.0459	0.0508, 0.0521 0.0507, 0.0502 0.0515, 0.0590	0.094 (0.0905, 0.0939, 0.0903, 0.0905, 0.0913, 0.105)
Report: TK0021323 Study: TK0021323 Trial: TK0021323-20 - Study to GLP - Study carried out in 2012	Wheat (Duster)	USA (NAFTA/Region 6)	47 (EC)	BBCH 31-32 60 DBH	63	Grain	< 0.005, < 0.005	0.00753, 0.00820	0.013 (0.0125, 0.0132)
			148 (3X) (EC)		60	Grain PP	< 0.005, < 0.005 < 0.005, < 0.005 < 0.005, < 0.005	0.0393, 0.0430 0.0387, 0.0404 0.0344, 0.0333	0.043 (0.0443, 0.0480, 0.0437, 0.0454, 0.0394, 0.0383)
Report: TK0044065 Study: TK0044065 Trial: T474 - Study to GLP - Study carried out in 2013	Wheat (Shaw VB)	Canada (NAFTA/ Region 7)	50.0 (EC)	BBCH 51-53	61	Grain	0.0081, 0.0077	0.012, 0.012	0.020 (0.0201, 0.0197)

GLP and Trial Details	Crop (Variety)	Country (Region) (Postcode)	Application		DALA	Crop Part	Residue Found (Uncorrected) (mg/kg)		
			Rate (g ai/ha) (Formulation)	Growth Stage			Bicyclopyrone eq. (SYN503780)	Bicyclopyrone eq. (CSCD686480)	Total Mean[a]
Report: TK0044065 Study: TK0044065 Trial: T475 - Study to GLP - Study carried out in 2013	Wheat (Unity)	Canada (NAFTA/ Region 7)	50.8 (EC)	BBCH 55-57	60	Grain	0.0060, 0.0063	0.014, 0.014	0.020 (0.02, 0.0203)
Report: TK0044065 Study: TK0044065 Trial: T476 - Study to GLP - Study carried out in 2013	Wheat (AC Cranberry)	Canada (NAFTA/ Region 7A)	49.6 (EC)	BBCH 34-37	60	Grain	< 0.0050, < 0.0050	0.0057, 0.0056	0.011 (0.0107, 0.0106)
Report: TK0044065 Study: TK0044065 Trial: T477 - Study to GLP - Study carried out in 2013	Wheat (Harvest)	Canada (NAFTA/ Region 14)	48.9 (EC)	BBCH 33-37	60	Grain	< 0.0050, < 0.0050	< 0.0054, < 0.0054	0.01 (< 0.0104, < 0.0104)
Report: TK0044065 Study: TK0044065 Trial: T478 - Study to GLP - Study carried out in 2013	Wheat (AC Cranberry)	Canada (NAFTA/ Region14)	52.3 (EC)	BBCH 31-33	61	Grain	< 0.0050, < 0.0050	< 0.0054, < 0.0054	0.01 (< 0.0104, < 0.0104)
Report: TK0044065 Study: TK0044065 Trial: T479 - Study to GLP - Study carried out in 2013	Wheat (Unity VB)	Canada (NAFTA/ Region 14)	51.0 (EC)	BBCH 34-37	60	Grain	< 0.0050, < 0.0050	0.018, 0.015	0.022 (0.023, 0.02)
Report: TK0044065 Study: TK0044065 Trial: T480 - Study to GLP - Study carried out in 2013	Wheat (Shaw)	Canada (NAFTA/ Region 14)	52.3 (EC)	BBCH 59-61	61	Grain	0.010, 0.0098	0.016, 0.016	0.026 (0.026, 0.0258)
Report: TK0044065 Study: TK0044065 Trial: T481 - Study to GLP - Study carried out in 2013	Wheat (Shaw)	Canada (NAFTA/ Region 14)	51.2 (EC)	BBCH 51-59	59	Grain	< 0.0050, < 0.0050	< 0.0054, 0.0088	0.012 (< 0.0104, 0.0133)
Report: TK0044065 Study: TK0044065 Trial: T482 - Study to GLP - Study carried out in 2013	Wheat (Harvest)	Canada (NAFTA/ Region 14)	49.1 (EC)	BBCH 39-41	59	Grain	< 0.0050, < 0.0050	< 0.0054, < 0.0054	0.01 (< 0.0104, < 0.0104)

GLP and Trial Details	Crop (Variety)	Country (Region) (Postcode)	Application		DALA	Crop Part	Residue Found (Uncorrected) (mg/kg)		
			Rate (g ai/ha) (Formulation)	Growth Stage			Bicyclopyrone eq. (SYN503780)	Bicyclopyrone eq. (CSCD686480)	Total Mean[a]
Report: TK0044065 Study: TK0044065 Trial: T483 - Study to GLP - Study carried out in 2013	Wheat (Harvest)	Canada (NAFTA/ Region 14)	51.5 (EC)	BBCH 29-43	61	Grain	< 0.0050, < 0.0050	0.0064, 0.0082	0.012 (0.0114, 0.0132)
Report: TK0044065 Study: TK0044065 Trial: T484 - Study to GLP - Study carried out in 2013	Wheat (Harvest)	Canada (NAFTA/ Region 14)	51.7 (EC)	BBCH 49-55	60	Grain	< 0.0050, < 0.0050	0.0079, 0.0067	0.012 (0.0129, 0.0117)
Report: TK0044065 Study: TK0044065 Trial: T485 - Study to GLP - Study carried out in 2013	Wheat (Vesper VB)	Canada (NAFTA/ Region 14)	50.6 (EC)	BBCH 16, 33-37	50	Grain	< 0.0050	0.0079	0.0129
					56		< 0.0050	0.009	0.014
					60		< 0.0050, < 0.0050	0.011, 0.011	0.016 (0.016, 0.016)
					65		< 0.0050	0.012	0.017
					71		< 0.0050	0.0062	0.0112
Report: TK0044065 Study: TK0044065 Trial: T486 - Study to GLP - Study carried out in 2013	Wheat (Unity VB)	Canada (NAFTA/ Region 14)	52.5 (EC)	BBCH 32-33 (majority 14)	51	Grain	< 0.0050	0.0078	0.0128
					56		< 0.0050	0.011	0.016
					61		< 0.0050, < 0.0050	0.011, 0.082	0.015 (0.016, 0.0132)
					65		< 0.0050	0.0087	0.0137
					70		< 0.0050	0.0084	0.0134

[a] Determined as the sum of common moieties SYN503780 (expressed as bicyclopyrone equivalents) and CSCD686480 (expressed as bicyclopyrone equivalents).

LOQ – Limit of quantification-The limit of quantification (LOQ) was 0.0050 mg/kg for bicyclopyrone equivalents from SYN503780 and 0.0054 mg/kg for bicyclopyrone equivalents from CSCD686480 in the Canadian study and 0.005 mg/kg for both analytes in the USA study.

DBH = Days Before Harvest

Residues in All Untreated Samples (controls) were <LOQ (< 0.005 mg/kg for SYN503780 and CSCD686480 expressed as bicyclopyrone equivalents).

Total Residues = Sum of SYN503780 and CSCD686480 expressed as bicyclopyrone equivalents (LOQ = 0.01 mg/kg).
*Residues of SYN503780 and CSCD686480 both ND, therefore mean presented as 0.005.

Grasses, for sugar or syrup production

Sugar cane

The trials were conducted at two locations in Australia and Brazil to determine the residue level of bicyclopyrone in/on sugar cane.

A total of 19 trials were conducted on sugar cane in Brazil. In seventeen trials from Brazil, bicyclopyrone was applied under three different regimes: once pre-emergence of the crop (BBCH 0), once after emergence of the crop (up to BBCH 17), or twice as a split application, pre-emergence and post-emergence up to BBCH 33. The single applications were made using the SL formulation containing 185 g/L at a rate of 300 g ai/ha. The split application was made using the SL formulation at a rate of 150 + 150 g ai/ha. Two trials in Brazil were treated at exaggerated rates (900 and 1500 g ai/ha, nominally 3× and 5×) with SL formulation of bicyclopyrone to provide samples for processing studies. Method POPIT.117 which includes hydrolysis of the bridge between the two rings of bicyclopyrone to release the structurally-related moieties SYN503780 and CSCD686480 were used

for analysis of residues in sugar cane. Measurement was accomplished by LC-MS/MS. The limit of quantification (LOQ) was 0.01 mg/kg expressed as bicyclopyrone equivalents.

In the growing seasons 2009/2011, trials were conducted in Australia to determine the residue level of bicyclopyrone in/on sugar cane. The SL formulation of bicyclopyrone was applied under three different regimes: once pre-emergence of the crop (BBCH 0), once after emergence of the crop (up to BBCH 17), or twice as a split application, pre-emergence and post-emergence up to BBCH 33. All applications were made at rates of 300 g ai/ha or 600 g ai/ha, or as split applications at rates of 150 + 150 g ai/ha or 300 + 300 g ai/ha. Bicyclopyrone was analysed in the sugar cane matrices using method GRM030.05A. Quantitation was accomplished with LC-MS/MS. The LOQ of the method is 0.01 mg/kg expressed as bicyclopyrone equivalents.

Table 119 Bicyclopyrone residues in sugar cane from supervised trials in Brazil and Australia

GLP and Trial Details	Crop (Variety)	Country (Region) (Postcode)	Application		DALA	Crop Part	Residue Found (Uncorrected) (mg/kg)		
			Rate (g ai/ha) (Formulation)	Growth Stage			Bicyclopyrone eq. (SYN503780)	Bicyclopyrone eq. (CSCD686480)	Total[a]
GAP	Sugarcane	Belize	262.5	Pre-or post-emergence	PHI: n/a	-	-	-	-
Report: M09097 Study: M09097 Trial: M09097-LZF1 - Study to GLP - Study carried out in 2009-2010	Sugarcane (RB 86-3129)	Brazil (Carpina – PE)	900 (3×) (SL)	BBCH 00	244	Sugarcane stalks	< 0.01	< 0.01	< 0.02
			1500 (5×) (SL)	BBCH 00	244		< 0.01	< 0.01	< 0.02
Report: M09097 Study: M09097 Trial: M09097-LZF2 - Study to GLP - Study carried out in 2009-2010	Sugarcane (RB 86-3129)	Brazil (Ares – RN)	900 (3×) (SL)	BBCH 00	243	Sugarcane stalks	< 0.01	< 0.01	< 0.02
			1500 (5×) (SL)	BBCH 00	243		< 0.01	< 0.01	< 0.02
Report: M09183 Study: M09183 Trial: M09183-LZF1 - Study to GLP - Study carried out in 2009-2010	Sugarcane (RB 85 7515)	Brazil (Itápolis – SP)	300 (SL)	BBCH 00	248	Sugarcane stalks	< 0.01	< 0.01	< 0.02
				BBCH 15	242		< 0.01	< 0.01	< 0.02
Report: M09183 Study: M09183 Trial: M09183-LZF2 - Study to GLP - Study carried out in 2009-2010	Sugarcane (RB 7515)	Brazil (Rio das Pedras – SP)	300 (SL)	BBCH 00	229	Sugarcane stalks	< 0.01	< 0.01	< 0.02
			300 (SL)	BBCH 15-16	204		< 0.01	< 0.01	< 0.02
Report: M09183 Study: M09183 Trial: M09183-LZF3 - Study to GLP - Study carried out in 2009-2010	Sugarcane (RB-145)	Brazil (Bandeirantes – PR)	300 (SL)	BBCH 00	246	Sugarcane stalks	< 0.01	< 0.01	< 0.02
			300 (SL)	BBCH 15	183		< 0.01	< 0.01	< 0.02
Report: M09183 Study: M09183 Trial: M09183-LZF4 - Study to GLP - Study carried out in 2009-2010	Sugarcane (SP 80 3280)	Brazil (Jaboticabal-SP)	300 (SL)	BBCH 00	242	Sugarcane stalks	< 0.01	< 0.01	< 0.02
			300 (SL)	BBCH 15	221		< 0.01	< 0.01	< 0.02

GLP and Trial Details	Crop (Variety)	Country (Region) (Postcode)	Application		DALA	Crop Part	Residue Found (Uncorrected) (mg/kg)		
			Rate (g ai/ha) (Formulation)	Growth Stage			Bicyclopyrone eq. (SYN503780)	Bicyclopyrone eq. (CSCD686480)	Total[a]
Report: M09183 Study: M09183 Trial: M09183-JJB - Study to GLP - Study carried out in 2009-2010	Sugarcane (SP 813250)	Brazil (Uberlândia – MG)	300 (SL)	BBCH 00	187	Sugarcane stalks	< 0.01	< 0.01	< 0.02
			300 (SL)	BBCH 14	168		< 0.01	< 0.01	< 0.02
Report: M09110 Study: M09110 Trial: M09110-LZF1 - Study to GLP - Study carried out in 2008-2009	Sugarcane (RB 86 7515)	Brazil (Rio das Pedras – SP)	300 (SL)	BBCH 00	267	Sugarcane stalks	< 0.01	< 0.01	< 0.02
			300 (SL)	BBCH 15-16	197		< 0.01	< 0.01	< 0.02
Report: M09110 Study: M09110 Trial: M09110-LZF2 - Study to GLP - Study carried out in 2008-2009	Sugarcane (RB 72 454)	Brazil (Bandeirantes – PR)	300 (SL)	BBCH 00	249	Sugarcane stalks	< 0.01	< 0.01	< 0.02
			300 (SL)	BBCH 15-16	236		< 0.01	< 0.01	< 0.02
Report: M09110 Study: M09110 Trial: M09110-LZF3 - Study to GLP - Study carried out in 2008-2009	Sugarcane (RB 72 454)	Brazil (Jaboticabal – SP)	300 (SL)	BBCH 00	260	Sugarcane stalks	< 0.01	< 0.01	< 0.02
			300 (SL)	BBCH 14-16	235		< 0.01	< 0.01	< 0.02
Report: M09110 Study: M09110 Trial: M09110-JJB - Study to GLP - Study carried out in 2008-2009	Sugarcane (SP 81-3250)	Brazil (Tupaciguara – MG)	300 (SL)	BBCH 00	242	Sugarcane stalks	< 0.01	< 0.01	< 0.02
			300 (SL)	BBCH 15-16	214		< 0.01	< 0.01	< 0.02
Report: M10108 Study: M10108 Trial: M10108-AMA - Study to GLP - Study carried out in 2010	Sugarcane (SP803280)	Brazil (Jaboticabal-SP)	300 (SL)	BBCH 00	151	Sugarcane stalks	< 0.01	< 0.01	< 0.02
					269		< 0.01	< 0.01	< 0.02
			300 (SL)	BBCH 16	151		< 0.01	< 0.01	< 0.02
					232		< 0.01	< 0.01	< 0.02
			150 150 (SL)	BBCH 00 BBCH 29-31	151		< 0.01	< 0.01	< 0.02
					180		< 0.01	< 0.01	< 0.02
Report: M10108 Study: M10108 Trial: M10108-JJB - Study to GLP - Study carried out in 2010	Sugarcane (RB867515)	Brazil (Tupaciguara-MG)	300 (SL)	BBCH 00	151	Sugarcane stalks	< 0.01	< 0.01	< 0.02
					274		< 0.01	< 0.01	< 0.02
			300 (SL)	BBCH 15-17	151		< 0.01	< 0.01	< 0.02
					230		< 0.01	< 0.01	< 0.02
			150 150 (SL)	BBCH 00 BBCH 33	151		< 0.01	< 0.01	< 0.02
					174		< 0.01	< 0.01	< 0.02
Report: M10108 Study: M10108 Trial: M10108-LZF1 - Study to GLP - Study carried out in 2010	Sugarcane (SP803280)	Brazil (Rio das Pedras-SP)	300 (SL)	BBCH 00	151	Sugarcane stalks	< 0.01	< 0.01	< 0.02
					339		< 0.01	< 0.01	< 0.02
			300 (SL)	BBCH 15-17	151		< 0.01	< 0.01	< 0.02
					308		< 0.01	< 0.01	< 0.02
			150 150 (SL)	BBCH 00 BBCH 29-30	151		< 0.01	< 0.01	< 0.02
					266		< 0.01	< 0.01	< 0.02

GLP and Trial Details	Crop (Variety)	Country (Region) (Postcode)	Application		DALA	Crop Part	Residue Found (Uncorrected) (mg/kg)		
			Rate (g ai/ha) (Formulation)	Growth Stage			Bicyclopyrone eq. (SYN503780)	Bicyclopyrone eq. (CSCD686480)	Total[a]
Report: M10108 Study: M10108 Trial: M10108-LZF2 - Study to GLP - Study carried out in 2010	Sugarcane (SP803280)	Brazil (Engenheiro Coelho-SP)	300 (SL)	BBCH 00	151	Sugarcane stalks	< 0.01	< 0.01	< 0.02
					251		< 0.01	< 0.01	< 0.02
			300 (SL)	BBCH 31	151		< 0.01	< 0.01	< 0.02
					219		< 0.01	< 0.01	< 0.02
			150 150 (SL)	BBCH 00 BBCH 31-32	151		< 0.01	< 0.01	< 0.02
					160		< 0.01	< 0.01	< 0.02
Report: M11151 Study: M11151 Trial: M11151-AMA - Study to GLP - Study carried out in 2011	Sugarcane (SP 80 1842)	Brazil (Jaboticabal-SP)	195 (SL)	BBCH 00	151	Sugarcane stalks	< 0.01	< 0.01	< 0.02
					278		< 0.01	< 0.01	< 0.02
			195 (SL)	BBCH 16-17	151		< 0.01	< 0.01	< 0.02
					246		< 0.01	< 0.01	< 0.02
			150 150 (SL)	BBCH 00 BBCH 19	151		< 0.01	< 0.01	< 0.02
					169		< 0.01	< 0.01	< 0.02
Report: M11151 Study: M11151 Trial: M11151-RWC1 - Study to GLP - Study carried out in 2011	Sugarcane (7515)	Brazil (Holambra-SP)	195 (SL)	BBCH 00	151	Sugarcane stalks	< 0.01	< 0.01	< 0.02
			195 (SL)	BBCH 14-16	151		< 0.01	< 0.01	< 0.02
			150 150 (SL)	BBCH 00 BBCH 18	151		< 0.01	< 0.01	< 0.02
Report: M11151 Study: M11151 Trial: M11151-RWC2 - Study to GLP - Study carried out in 2011	Sugarcane (RB72454)	Brazil (Bandeirantes-PR)	195 (SL)	BBCH 00	266	Sugarcane stalks	< 0.01	< 0.01	< 0.02
			195 (SL)	BBCH 17	151		< 0.01	< 0.01	< 0.02
					212		< 0.01	< 0.01	< 0.02
			150 150 (SL)	BBCH 00 BBCH 19	151		< 0.01	< 0.01	< 0.02
					178		< 0.01	< 0.01	< 0.02
Report: M11151 Study: M11151 Trial: M11151-JJB - Study to GLP - Study carried out in 2011	Sugarcane (SP801842)	Brazil (Tupaciguara-MG)	195 (SL)	BBCH 00	270	Sugarcane stalks	< 0.01	< 0.01	< 0.02
			195 (SL)	BBCH 16	151		< 0.01	< 0.01	< 0.02
					220		< 0.01	< 0.01	< 0.02
			150 150 (SL)	BBCH 00 BBCH 19	151		< 0.01	< 0.01	< 0.02
					175		< 0.01	< 0.01	< 0.02
Report: SYN0903 Study: SYN0903 Trial: Site 1 Tweed Valley - Study to GLP - Study carried out in 2009-2010	Sugarcane (Q120)	Australia (NSW)	150 150 (SL)	60-80cm Just before row closure	1	Tops	0.03	< 0.01	0.04
						Billets	0.02	< 0.01	0.03
					7	Tops	0.01	< 0.01	0.02
						Billets	0.01	< 0.01	0.02
					16	Tops	< 0.01	< 0.01	< 0.02
						Billets	< 0.01	< 0.01	< 0.02
					28	Tops	< 0.01	< 0.01	< 0.02
						Billets	< 0.01	< 0.01	< 0.02
					56	Tops	< 0.01	< 0.01	< 0.02
						Billets	< 0.01	< 0.01	< 0.02
					112	Tops	< 0.01	< 0.01	< 0.02
						Billets	< 0.01	< 0.01	< 0.02
			300 300 (SL)	60-80cm Just before row closure	1	Tops	0.06	0.01	0.07
						Billets	0.04	0.01	0.05
					7	Tops	0.02	0.01	0.03
						Billets	0.02	< 0.01	0.03
					16	Tops	< 0.01	< 0.01	< 0.02

GLP and Trial Details	Crop (Variety)	Country (Region) (Postcode)	Application		DALA	Crop Part	Residue Found (Uncorrected) (mg/kg)		
			Rate (g ai/ha) (Formulation)	Growth Stage			Bicyclopyrone eq. (SYN503780)	Bicyclopyrone eq. (CSCD686480)	Total[a]
						Billets	< 0.01	< 0.01	< 0.02
					28	Tops	< 0.01	< 0.01	< 0.02
						Billets	< 0.01	< 0.01	< 0.02
					56	Tops	< 0.01	< 0.01	< 0.02
						Billets	< 0.01	< 0.01	< 0.02
					112	Tops	< 0.01	< 0.01	< 0.02
						Billets	< 0.01	< 0.01	< 0.02
Report: SYN0903 Study: SYN0903 Trial: Site 2 Proserpine, - Study to GLP - Study carried out in 2009-2010	Sugarcane (Q228)	Australia (QLD)	150 150 (SL)	60-80cm Just before row closure	1	Tops	0.01	< 0.01	0.02
						Billets	0.01	< 0.01	0.02
					7	Tops	< 0.01	< 0.01	< 0.02
						Billets	< 0.01	< 0.01	< 0.02
					14	Tops	< 0.01	< 0.01	< 0.02
						Billets	< 0.01	< 0.01	< 0.02
					28	Tops	< 0.01	< 0.01	< 0.02
						Billets	< 0.01	< 0.01	< 0.02
					56	Tops	< 0.01	< 0.01	< 0.02
						Billets	< 0.01	< 0.01	< 0.02
					112	Tops	< 0.01	< 0.01	< 0.02
						Billets	< 0.01	< 0.01	< 0.02
			300 300 (SL)	60-80cm Just before row closure	1	Tops	0.04	0.03	0.07
						Billets	0.04	< 0.01	0.05
					7	Tops	0.03	< 0.01	0.04
						Billets	0.01	< 0.01	0.02
					14	Tops	< 0.01	< 0.01	< 0.02
						Billets	< 0.01	< 0.01	< 0.02
					28	Tops	< 0.01	< 0.01	< 0.02
						Billets	< 0.01	< 0.01	< 0.02
					56	Tops	< 0.01	< 0.01	< 0.02
						Billets	< 0.01	< 0.01	< 0.02
					112	Tops	< 0.01	< 0.01	< 0.02
						Billets	< 0.01	< 0.01	< 0.02
Report: SYN0903 Study: SYN0903 Trial: Site 3 El Arish - Study to GLP - Study carried out in 2009-2010	Sugarcane (Q230)	Australia (QLD)	150 150 (SL)	60-80cm Just before row closure	1	Tops	0.04	< 0.01	0.05
						Billets	0.02	< 0.01	0.03
					7	Tops	0.02	< 0.01	0.03
						Billets	0.03	< 0.01	0.04
					14	Tops	< 0.01	< 0.01	< 0.02
						Billets	< 0.01	< 0.01	< 0.02
					28	Tops	< 0.01	< 0.01	< 0.02
						Billets	< 0.01	< 0.01	< 0.02
					56	Tops	< 0.01	< 0.01	< 0.02
						Billets	< 0.01	< 0.01	< 0.02
					112	Tops	< 0.01	< 0.01	< 0.02
						Billets	< 0.01	< 0.01	< 0.02
			300 300 (SL)	60-80cm Just before row closure	1	Tops	0.10	0.04	0.14
						Billets	0.09	0.03	0.12
					7	Tops	0.05	< 0.01	0.06
						Billets	0.02	0.01	0.03
					14	Tops	< 0.01	0.02	0.03
						Billets	< 0.01	< 0.01	< 0.02
					28	Tops	< 0.01	< 0.01	< 0.02
						Billets	< 0.01	< 0.01	< 0.02
					56	Tops	< 0.01	< 0.01	< 0.02
						Billets	< 0.01	< 0.01	< 0.02
					112	Tops	< 0.01	< 0.01	< 0.02
						Billets	< 0.01	< 0.01	< 0.02
Report: SYN0903 Study: SYN0903 Trial: Site 4 Mareeba - Study to GLP - Study carried out in 2009-2010	Sugarcane (Q200)	Australia (QLD)	150 150 (SL)	60-80cm Just before row closure	1	Tops	0.03	< 0.01	0.04
						Billets	0.01	< 0.01	0.02
					7	Tops	0.01	< 0.01	0.02
						Billets	0.01	< 0.01	0.02
					14	Tops	< 0.01	< 0.01	< 0.02
						Billets	< 0.01	< 0.01	< 0.02
					28	Tops	< 0.01	< 0.01	< 0.02
						Billets	< 0.01	< 0.01	< 0.02
					56	Tops	< 0.01	< 0.01	< 0.02
						Billets	< 0.01	< 0.01	< 0.02

GLP and Trial Details	Crop (Variety)	Country (Region) (Postcode)	Application		DALA	Crop Part	Residue Found (Uncorrected) (mg/kg)		
			Rate (g ai/ha) (Formulation)	Growth Stage			Bicyclopyrone eq. (SYN503780)	Bicyclopyrone eq. (CSCD686480)	Total[a]
					112	Tops	< 0.01	< 0.01	< 0.02
						Billets	< 0.01	< 0.01	< 0.02
			300 300 (SL)	60-80cm Just before row closure	1	Tops	0.10	0.01	0.11
						Billets	0.06	< 0.01	0.07
					7	Tops	0.04	< 0.01	0.05
						Billets	0.03	< 0.01	0.04
					14	Tops	< 0.01	< 0.01	< 0.02
						Billets	< 0.01	< 0.01	< 0.02
					28	Tops	< 0.01	< 0.01	< 0.02
						Billets	< 0.01	< 0.01	< 0.02
					56	Tops	< 0.01	< 0.01	< 0.02
						Billets	< 0.01	< 0.01	< 0.02
					112	Tops	< 0.01	< 0.01	< 0.02
						Billets	< 0.01	< 0.01	< 0.02
Report: SYN0903 Study: SYN0903 Trial: Site 5 Gunalda - Study to GLP - Study carried out in 2009-2010	Sugarcane (Q122)	Australia (QLD)	300 (SL)	Just before row closure	1	Tops	0.03	< 0.01	0.04
						Billets	0.01	< 0.01	0.02
					7	Tops	0.01	< 0.01	0.02
						Billets	0.01	< 0.01	0.02
					14	Tops	< 0.01	< 0.01	< 0.02
						Billets	< 0.01	< 0.01	< 0.02
					28	Tops	< 0.01	< 0.01	< 0.02
						Billets	< 0.01	< 0.01	< 0.02
					56	Tops	< 0.01	< 0.01	< 0.02
						Billets	< 0.01	< 0.01	< 0.02
					112	Tops	< 0.01	< 0.01	< 0.02
						Billets	< 0.01	< 0.01	< 0.02
			600 (SL)	Just before row closure	1	Tops	0.08	< 0.01	0.09
						Billets	0.08	< 0.01	0.09
					7	Tops	0.04	< 0.01	0.05
						Billets	0.03	< 0.01	0.04
					14	Tops	0.01	< 0.01	0.02
						Billets	< 0.01	< 0.01	< 0.02
					28	Tops	< 0.01	< 0.01	< 0.02
						Billets	< 0.01	< 0.01	< 0.02
					56	Tops	< 0.01	< 0.01	< 0.02
						Billets	< 0.01	< 0.01	< 0.02
					112	Tops	< 0.01	< 0.01	< 0.02
						Billets	< 0.01	< 0.01	< 0.02
Report: SYN0903 Study: SYN0903 Trial: Site 6 Gargett - Study to GLP - Study carried out in 2009-2010	Sugarcane (Q138)	Australia (QLD)	300 (SL)	Just before row closure	1	Tops	0.03	< 0.01	0.04
						Billets	0.03	< 0.01	0.04
					7	Tops	< 0.01	< 0.01	< 0.02
						Billets	0.01	< 0.01	0.02
					14	Tops	< 0.01	< 0.01	< 0.02
						Billets	< 0.01	< 0.01	< 0.02
					28	Tops	< 0.01	< 0.01	< 0.02
						Billets	< 0.01	< 0.01	< 0.02
					56	Tops	< 0.01	< 0.01	< 0.02
						Billets	< 0.01	< 0.01	< 0.02
					112	Tops	< 0.01	< 0.01	< 0.02
						Billets	< 0.01	< 0.01	< 0.02
			600 (SL)	Just before row closure	1	Tops	0.08	< 0.01	0.09
						Billets	0.08	< 0.01	0.09
					7	Tops	0.04	< 0.01	0.05
						Billets	0.04	< 0.01	0.05
					14	Tops	0.01	< 0.01	0.02
						Billets	< 0.01	< 0.01	< 0.02
					28	Tops	< 0.01	< 0.01	< 0.02
						Billets	< 0.01	< 0.01	< 0.02
					56	Tops	< 0.01	< 0.01	< 0.02
						Billets	< 0.01	< 0.01	< 0.02
					112	Tops	< 0.01	< 0.01	< 0.02
						Billets	< 0.01	< 0.01	< 0.02
Report: SYN0903 Study: SYN0903 Trial: Site 7	Sugarcane (Q183)	Australia (QLD)	300 (SL)	Just before row	1	Tops	0.05	< 0.01	0.06
						Billets	0.05	< 0.01	0.06
					7	Tops	0.04	< 0.01	0.05

GLP and Trial Details	Crop (Variety)	Country (Region) (Postcode)	Application		DALA	Crop Part	Residue Found (Uncorrected) (mg/kg)		
			Rate (g ai/ha) (Formulation)	Growth Stage			Bicyclopyrone eq. (SYN503780)	Bicyclopyrone eq. (CSCD686480)	Total[a]
McDesme - Study to GLP - Study carried out in 2009-2010				closure		Billets	0.01	< 0.01	0.02
					14	Tops	< 0.01	< 0.01	< 0.02
						Billets	< 0.01	< 0.01	< 0.02
					28	Tops	< 0.01	< 0.01	< 0.02
						Billets	< 0.01	< 0.01	< 0.02
					56	Tops	< 0.01	< 0.01	< 0.02
						Billets	< 0.01	< 0.01	< 0.02
					112	Tops	< 0.01	< 0.01	< 0.02
						Billets	< 0.01	< 0.01	< 0.02
			600 (SL)	Just before row closure	1	Tops	0.20	< 0.01	0.21
						Billets	0.10	< 0.01	0.11
					7	Tops	0.01	< 0.01	0.02
						Billets	0.06	< 0.01	0.07
					14	Tops	0.02	< 0.01	0.03
						Billets	< 0.01	< 0.01	< 0.02
					28	Tops	< 0.01	< 0.01	< 0.02
						Billets	< 0.01	< 0.01	< 0.02
					56	Tops	< 0.01	< 0.01	< 0.02
						Billets	< 0.01	< 0.01	< 0.02
					112	Tops	< 0.01	< 0.01	< 0.02
						Billets	< 0.01	< 0.01	< 0.02
Report: SYN0903 Study: SYN0903 Trial: Site 8 Gordonvale - Study to GLP - Study carried out in 2009-2010	Sugarcane (Q183)	Australia (QLD)	300 (SL)	Just before row closure	1	Tops	0.03	< 0.01	0.04
						Billets	0.03	< 0.01	0.04
					7	Tops	0.01	< 0.01	0.02
						Billets	0.01	< 0.01	< 0.02
					14	Tops	< 0.01	< 0.01	< 0.02
						Billets	< 0.01	< 0.01	< 0.02
					28	Tops	< 0.01	< 0.01	< 0.02
						Billets	< 0.01	< 0.01	< 0.02
					56	Tops	< 0.01	< 0.01	< 0.02
						Billets	< 0.01	< 0.01	< 0.02
					112	Tops	< 0.01	< 0.01	< 0.02
						Billets	< 0.01	< 0.01	< 0.02
			600 (SL)	Just before row closure	1	Tops	0.14	< 0.01	0.15
						Billets	0.16	< 0.01	0.17
					7	Tops	0.04	< 0.01	0.05
						Billets	0.04	< 0.01	0.05
					14	Tops	< 0.01	< 0.01	< 0.02
						Billets	< 0.01	< 0.01	< 0.02
					28	Tops	< 0.01	< 0.01	< 0.02
						Billets	< 0.01	< 0.01	< 0.02
					56	Tops	< 0.01	< 0.01	< 0.02
						Billets	< 0.01	< 0.01	< 0.02
					112	Tops	< 0.01	< 0.01	< 0.02
						Billets	< 0.01	< 0.01	< 0.02

[a] Determined as the sum of common moieties SYN503780 and CSCD686480 (both expressed as bicyclopyrone equivalents).

Straw, fodder and forage of cereal grains and grasses, except grasses for sugar production (including buckwheat fodder)

Barley hay and straw

Residue data have been collected from 21 field trials located in Canada and the USA. The common moiety analytical method GRM030.05A was used for residue analysis of bicyclopyrone (as SYN503780) and CSAA915194 (as CSCD686480) in barley hay and straw quantifying the analytes by liquid chromatography mass spectrometry (LC-MS/MS) with a limit of quantitation of 0.005 mg/kg in all matrices for bicyclopyrone equivalents from SYN503780 and CSAA915194 equivalents from CSCD686480. Residues of both SYN503780 and CSCD686480 have been corrected to bicyclopyrone equivalents.

Table 120 Bicyclopyrone residues on barley hay from supervised trails conducted in the USA and Canada

GLP and Trial Details	Crop (Variety)	Country (Region) (Postcode)	Application		DALA	Crop Part	Residue Found (Uncorrected, mg/kg)		
			Rate(g ai/ha) (Formulation)	Growth Stage			Bicyclopyrone eq. (SYN503780)	Bicyclopyrone eq. (CSCD686480)	Total Mean [a]
GAP	Barley	USA	50	30 DBH	30	-	-	-	-
Report: TK0024326 Study: TK0024326 Trial: TK0024326-01 - Study to GLP - Study carried out in 2012	Barley (Thoroughbred)	USA (NAFTA/Region 2)	50 (EC)	BBCH 31-33 30 DBH	30	Hay	0.00885, 0.00945	0.0669, 0.0786	0.082 (0.0754, 0.0881)
Report: TK0024326 Study: TK0024326 Trial: TK0024326-02 - Study to GLP - Study carried out in 2012	Barley (Robust)	USA (NAFTA/Region 5)	50 (EC)	BBCH 31 30 DBH	30	Hay	0.0162, 0.0135	0.0427, 0.0417	0.057 (0.0589, 0.0551)
Report: TK0024326 Study: TK0024326 Trial: TK0024326-03 - Study to GLP - Study carried out in 2012	Barley (Robust)	USA (NAFTA/Region 5)	52 (EC)	BBCH 21	20	Hay	0.0311, 0.0321	0.0218, 0.0247	0.0529, 0.0568
					25		0.0180, 0.0202	0.0139, 0.0124	0.0319, 0.0327
					30		0.0142, 0.0137	0.0106, 0.00943	0.024 (0.0248, 0.0231)
					35		0.00539, 0.00576	< 0.005, < 0.005	0.0104, 0.0108
					40		< 0.005, < 0.005	< 0.005, < 0.005	< 0.005, < 0.005
Report: TK0024326 Study: TK0024326 Trial: TK0024326-04 - Study to GLP - Study carried out in 2012	Barley (Tradition)	USA (NAFTA/Region 5)	52 (EC)	BBCH 24-25	20	Hay	0.0194, 0.0143	0.0417, 0.0375	0.0612, 0.0518
					25		0.00678, 0.00826	0.0181, 0.0220	0.0249, 0.0303
					30		0.0102, 0.00969	0.0251, 0.0253	0.035 (0.0353, 0.0350)
					35		0.00616, 0.00749	0.0192, 0.0189	0.0253, 0.0264
					40		< 0.005, < 0.005	0.00984, 0.00909	0.0148, 0.0141
Report: TK0024326 Study: TK0024326 Trial: TK0024326-05 - Study to GLP - Study carried out in 2012	Barley (Tradition)	USA (NAFTA/Region 7)	54 (EC)	BBCH 20-21 30 DBH	29	Hay	0.00955, 0.00622	0.0431, 0.0371	0.048 (0.0527, 0.0433)

GLP and Trial Details	Crop (Variety)	Country (Region) (Postcode)	Application		DALA	Crop Part	Residue Found (Uncorrected, mg/kg)		
			Rate(g ai/ha) (Formulation)	Growth Stage			Bicyclopyrone eq. (SYN503780)	Bicyclopyrone eq. (CSCD686480)	Total Mean [a]
Report: TK0024326 Study: TK0024326 Trial: TK0024326-06 - Study to GLP - Study carried out in 2012	Barley (Lacey)	USA (NAFTA/Region 7)	50 (EC)	BBCH 30-31 30 DBH	30	Hay	0.00541, 0.00607	0.0194, 0.0172	0.024 (0.0248, 0.0233)
Report: TK0024326 Study: TK0024326 Trial: TK0024326-07 - Study to GLP - Study carried out in 2012	Barley (Tradition)	USA (NAFTA/Region 7)	50 (EC)	BBCH 10-12 30 DBH	29	Hay	0.00580, 0.00516	0.00802, 0.00670	0.013 (0.0138, 0.0119)
Report: TK0024326 Study: TK0024326 Trial: TK0024326-08 - Study to GLP - Study carried out in 2012	Barley (Robust)	USA (NAFTA/Region 7)	50 (EC)	BBCH 21-22 30 DBH	30	Hay	< 0.005, < 0.005	0.0632, 0.0587	0.066 (0.0682, 0.0637)
Report: TK0024326 Study: TK0024326 Trial: TK0024326-09 - Study to GLP - Study carried out in 2012	Barley (Moravian 69)	USA (NAFTA/Region 9)	49 (EC)	BBCH 65-69 30 DBH	29	Hay	0.0473, 0.0500	0.0794, 0.0837	0.130 (0.127, 0.134)
Report: TK0024326 Study: TK0024326 Trial: TK0024326-10 - Study to GLP - Study carried out in 2012	Barley (UC937)	USA (NAFTA/Region 10)	50 (EC)	BBCH 69-71 30 DBH	30	Hay	0.100, 0.121	0.0810, 0.0920	0.197 (0.181, 0.213)

GLP and Trial Details	Crop (Variety)	Country (Region) (Postcode)	Application		DALA	Crop Part	Residue Found (Uncorrected, mg/kg)		
			Rate(g ai/ha) (Formulation)	Growth Stage			Bicyclopyrone eq. (SYN503780)	Bicyclopyrone eq. (CSCD686480)	Total Mean [a]
Report: TK0024326 Study: TK0024326 Trial: TK0024326-11 - Study to GLP - Study carried out in 2012	Barley (Champion)	USA (NAFTA/Region 11)	50 (EC)	BBCH 34-37 30 DBH	29	Hay	0.0653, 0.0818	0.0722, 0.0945	0.157 (0.138, 0.176)
Report: TK0024326 Study: TK0024326 Trial: TK0024326-12 - Study to GLP - Study carried out in 2012	Barley (Baroness)	USA (NAFTA/Region 11)	50 (EC)	BBCH 32-33 30 DBH	28	Hay	0.0367, 0.0275	0.0501, 0.0476	0.081 (0.0867, 0.0751)
Report: TK0147009 Study: TK0147009 Trial: T487 - Study to GLP - Study carried out in 2013	Barley (CDC Austenson)	Canada (NAFTA/ Region 7A)	50.7 (EC)	BBCH 12-20	30	Hay	0.011, 0.011	0.015, 0.015	0.026 (0.026, 0.026)
Report: TK0147009 Study: TK0147009 Trial: T488 - Study to GLP - Study carried out in 2013	Barley (CDC Austenson)	Canada (NAFTA/ Region 14)	50.0 (EC)	BBCH 13-22	31	Hay	< 0.0050, < 0.0050	0.0065, 0.0065	0.012 (0.0115, 0.0115)
Report: TK0147009 Study: TK0147009 Trial: T489 - Study to GLP - Study carried out in 2013	Barley (Bentley)	Canada (NAFTA/ Region 14)	49.5 (EC)	BBCH 13-14	30	Hay	< 0.0050, 0.0051	0.011, 0.012	0.017 (0.0160, 0.0171)
Report: TK0147009 Study: TK0147009 Trial: T490 - Study to GLP - Study carried out in 2013	Barley (AC Metcalfe)	Canada (NAFTA/ Region 14)	51.1 (EC)	BBCH 14-22	30	Hay	0.011, 0.0079	0.0096, 0.0070	0.018 (0.0206, 0.0149)

GLP and Trial Details	Crop (Variety)	Country (Region) (Postcode)	Application		DALA	Crop Part	Residue Found (Uncorrected, mg/kg)		
			Rate(g ai/ha) (Formulation)	Growth Stage			Bicyclopyrone eq. (SYN503780)	Bicyclopyrone eq. (CSCD686480)	Total Mean [a]
Report: TK0147009 Study: TK0147009 Trial: T491 - Study to GLP - Study carried out in 2013	Barley (AC Metcalfe)	Canada (NAFTA/ Region 14)	52.0 (EC)	BBCH 12-13	30	Hay	0.0065, 0.0079	0.0072, 0.0082	0.015 (0.0137, 0.0161)
Report: TK0147009 Study: TK0147009 Trial: T492 - Study to GLP - Study carried out in 2013	Barley (AC Metcalfe)	Canada (NAFTA/ Region 14)	52.2 (EC)	BBCH 13-15	30	Hay	0.014, 0.019	0.031, 0.032	0.047 (0.045, 0.048)
Report: TK0147009 Study: TK0147009 Trial: T493 - Study to GLP - Study carried out in 2013	Barley (Coalition)	Canada (NAFTA/ Region 14)	51.6 (EC)	BBCH 12-14	31	Hay	0.0068, 0.0097	0.019, 0.027	0.031 (0.0258, 0.0367)
Report: TK0147009 Study: TK0147009 Trial: T494 - Study to GLP - Study carried out in 2013	Barley (Bentley)	Canada (NAFTA/ Region 14)	49.9 (EC)	BBCH 13-14 (majority 14)	20	Hay	0.026	0.066	0.0920
					25	Hay	0.014	0.041	0.0550
					30	Hay	0.0096, 0.0073	0.029, 0.025	0.036 (0.0386, 0.0323)
					35	Hay	< 0.0050	0.016	0.0210
					40	Hay	< 0.0050	0.0080	0.0130
Report: TK0147009 Study: TK0147009 Trial: T495 - Study to GLP - Study carried out in 2013	Barley (Coalition)	Canada (NAFTA/ Region 14)	52.2 (EC)	BBCH 13-14 (majority 14)	20	Hay	0.11	0.032	0.043
					26	Hay	0.024	0.061	0.085
					29	Hay	0.0082,0.0095	0.027, 0.033	0.039 (0.0352, 0.0425)
					34	Hay	0.0071	0.025	0.0321
					40	Hay	< 0.0050	0.011	0.016

[a] Determined as the sum of common moieties SYN503780 (expressed as bicyclopyrone equivalents) and CSCD686480 (expressed as bicyclopyrone equivalents).

The limit of quantification (LOQ) was 0.0050 mg/kg for bicyclopyrone equivalents from SYN503780 and 0.0054 mg/kg for bicyclopyrone equivalents from CSCD686480 in the Canadian study and 0.005 mg/kg for both analytes in the USA study.

DBH = Days Before Harvest

Residues in All Untreated Samples (controls) were <LOQ (< 0.005 mg/kg for SYN503780 and CSCD686480 expressed as bicyclopyrone equivalents).

Total Residues = Sum of SYN503780 and CSCD686480 expressed as bicyclopyrone equivalents (LOQ = 0.01 mg/kg).

Table 121 Bicyclopyrone residues on barley straw from supervised trails conducted in the USA and Canada

GLP and Trial Details	Crop (Variety)	Country (Region) (Postcode)	Application		DALA	Crop Part	Residue Found (Uncorrected, mg/kg)		
			Rate (g ai/ha) (Formulation)	Growth Stage			Bicyclopyrone eq. (SYN503780)	Bicyclopyrone eq. (CSCD686480)	Total Mean[a]
GAP	Barley	USA	50	60 DBH	60	-	-	-	-
Report: TK0024326 Study: TK0024326 Trial: TK0024326-01 - Study to GLP - Study carried out in 2012	Barley (Thoroughbred)	USA (NAFTA/Region 2)	52 (EC)	BBCH 32-33 60 DBH	60	Straw	0.0228, 0.0229	0.144, 0.017	0.188 (0.170, 0.209)
Report: TK0024326 Study: TK0024326 Trial: TK0024326-02 - Study to GLP - Study carried out in 2012	Barley (Robust)	USA (NAFTA/Region 5)	50 (EC)	BBCH 73 60 DBH	60	Straw	0.0199, 0.0164	0.0173, 0.0138	0.034 (0.0372, 0.0302)
Report: TK0024326 Study: TK0024326 Trial: TK0024326-03 - Study to GLP - Study carried out in 2012	Barley (Robust)	USA (NAFTA/Region 5)	50 (EC)	BBCH 45-47	50	Straw	0.109, 0.0860	0.243, 0.206	0.352, 0.292
					55		0.130, 0.121	0.304, 0.302	0.434, 0.423
					61		0.0633, 0.0700	0.144, 0.184	0.231 (0.207, 0.254)
					65		0.0425, 0.0644	0.111, 0.146	0.153, 0.211
					70		0.0252, 0.0165	0.0672, 0.0824	0.0923, 0.0990
Report: TK0024326 Study: TK0024326 Trial: TK0024326-04 - Study to GLP - Study carried out in 2012	Barley (Tradition)	USA (NAFTA/Region 5)	54 (EC)	BBCH 40-42	50	Straw	0.0337, 0.0246	0.116, 0.100	0.150, 0.125
					55		0.0166, NA	0.0503, n/a	0.0669, NA
					61		< 0.005, < 0.005	0.0111, 0.0113	0.016 (0.0161, 0.0163)
					65		NA, 0.00551	NA, 0.0219	NA, 0.0274
					70		< 0.005, 0.00528	0.0101, 0.0188	0.0151, 0.0240
Report: TK0024326 Study: TK0024326 Trial: TK0024326-05 - Study to GLP - Study carried out in 2012	Barley (Tradition)	USA (NAFTA/Region 7)	49 (EC)	BBCH 30-35	59	Straw	0.00969, 0.0121	0.0357, 0.0540	0.056 (0.0454, 0.0661)

GLP and Trial Details	Crop (Variety)	Country (Region) (Postcode)	Application		DALA	Crop Part	Residue Found (Uncorrected, mg/kg)		
			Rate (g ai/ha) (Formulation)	Growth Stage			Bicyclopyrone eq. (SYN503780)	Bicyclopyrone eq. (CSCD686480)	Total Mean[a]
Report: TK0024326 Study: TK0024326 Trial: TK0024326-06 - Study to GLP - Study carried out in 2012	Barley (Lacey)	USA (NAFTA/Region 7)	50 (EC)	BBCH 30-31 60 DBH	57	Straw	< 0.005, < 0.005	0.00813, 0.00914	0.014 (0.0131, 0.0141)
Report: TK0024326 Study: TK0024326 Trial: TK0024326-07 - Study to GLP - Study carried out in 2012	Barley (Tradition)	USA (NAFTA/Region 7)	49 (EC)	BBCH 25-30 60 DBH	59	Straw	< 0.005, < 0.005	0.0157, 0.0246	0.025 (0.0207, 0.0296)
Report: TK0024326 Study: TK0024326 Trial: TK0024326-08 - Study to GLP - Study carried out in 2012	Barley (Robust)	USA (NAFTA/Region 7)	49 (EC)	BBCH 21-22 60 DBH	60	Straw	< 0.005, < 0.005	0.0237, 0.0247	0.029 (0.0287, 0.0297)
Report: TK0024326 Study: TK0024326 Trial: TK0024326-09 - Study to GLP - Study carried out in 2012	Barley (Moravian 69)	USA (NAFTA/Region 9)	50 (EC)	BBCH 65-69 60 DBH	60	Straw	0.0461, 0.0413	0.100, 0.0899	0.139 (0.146, 0.131)
Report: TK0024326 Study: TK0024326 Trial: TK0024326-10 - Study to GLP - Study carried out in 2012	Barley (UC937)	USA (NAFTA/Region 10)	49 (EC)	BBCH 77-82 60 DBH	58	Straw	0.0496, 0.0472	0.0372, 0.0343	0.084 (0.0867, 0.0815)

GLP and Trial Details	Crop (Variety)	Country (Region) (Postcode)	Application		DALA	Crop Part	Residue Found (Uncorrected, mg/kg)		
			Rate (g ai/ha) (Formulation)	Growth Stage			Bicyclopyrone eq. (SYN503780)	Bicyclopyrone eq. (CSCD686480)	Total Mean[a]
Report: TK0024326 Study: TK0024326 Trial: TK0024326-11 - Study to GLP - Study carried out in 2012	Barley (Champion)	USA (NAFTA/Region 11)	50 (EC)	BBCH 65-69 60 DBH	58	Straw	0.0544, 0.102	0.0700, 0.128	0.177 (0.124, 0.230)
Report: TK0024326 Study: TK0024326 Trial: TK0024326-12 - Study to GLP - Study carried out in 2012	Barley (Baroness)	USA (NAFTA/Region 11)	50 (EC)	BBCH 49-52 60 DBH	61	Straw	0.0539, 0.0954	0.0939, 0.163	0.203 (0.148, 0.259)
Report: TK0147009 Study: TK0147009 Trial: T487 - Study to GLP - Study carried out in 2013	Barley (CDC Austenson)	Canada (NAFTA/ Region 7A)	51.3 (EC)	BBCH 34-37	60	Straw	0.023, 0.020	0.042,0.037	0.061 (0.065, 0.057)
Report: TK0147009 Study: TK0147009 Trial: T488 - Study to GLP - Study carried out in 2013	Barley (CDC Austenson)	Canada (NAFTA/ Region 14)	53.0 (EC)	BBCH 30-32	60	Straw	< 0.0050, < 0.0050	0.0076, 0.0064	0.012 (0.0126, 0.0114)
Report: TK0147009 Study: TK0147009 Trial: T489 - Study to GLP - Study carried out in 2013	Barley (Bentley)	Canada (NAFTA/ Region 14)	49.5 (EC)	BBCH 14-15	61	Straw	0.0065, 0.0099	0.068, 0.0085	0.085 (0.0745, 0.0949)
Report: TK0147009 Study: TK0147009 Trial: T490 - Study to GLP - Study carried out in 2013	Barley (AC Metcalfe)	Canada (NAFTA/ Region 14)	54.6 (EC)	BBCH 58-59	61	Straw	0.11, 0.077	0.10, 0.10	0.194 (0.177, 0.21)

GLP and Trial Details	Crop (Variety)	Country (Region) (Postcode)	Application		DALA	Crop Part	Residue Found (Uncorrected, mg/kg)		
			Rate (g ai/ha) (Formulation)	Growth Stage			Bicyclopyrone eq. (SYN503780)	Bicyclopyrone eq. (CSCD686480)	Total Mean[a]
Report: TK0147009 Study: TK0147009 Trial: T491 - Study to GLP - Study carried out in 2013	Barley (AC Metcalfe)	Canada (NAFTA/ Region 14)	49.5 (EC)	BBCH 51-59	59	Straw	0.023, 0.026	0.067, 0.072	0.094 (0.090, 0.098)
Report: TK0147009 Study: TK0147009 Trial: T492 - Study to GLP - Study carried out in 2013	Barley (AC Metcalfe)	Canada (NAFTA/ Region 14)	54.7 (EC)	BBCH 51-52	63	Straw	0.092, 0.084	0.11, 0.11	0.198 (0.202, 0.194)
Report: TK0147009 Study: TK0147009 Trial: T493 - Study to GLP - Study carried out in 2013	Barley (Coalition)	Canada (NAFTA/ Region 14)	53.2 (EC)	BBCH 45-51	60	Straw	0.014, 0.015	0.032, 0.033	0.047 (0.046, 0.048)
Report: TK0147009 Study: TK0147009 Trial: T494 - Study to GLP - Study carried out in 2013	Barley (Bentley)	Canada (NAFTA/ Region 14)	50 (EC)	BBCH 13-14 (majority 14)	61	Straw	< 0.0050, < 0.0050	< 0.0054, < 0.0054	0.010 (< 0.0104, < 0.0104)
					65	Straw	< 0.0050	< 0.0054	< 0.0104
					70	Straw	< 0.0050	< 0.0054	< 0.0104
Report: TK0147009 Study: TK0147009 Trial: T495 - Study to GLP - Study carried out in 2013	Barley (Coalition)	Canada (NAFTA/ Region 14)	52.3 (EC)	BBCH 13-14 (majority 14)	61	Straw	0.018, 0.019	0.037, 0.037	0.056 (0.055, 0.056)
					65	Straw	0.023	0.045	0.068
					70	Straw	0.020	0.037	0.057

[a] Determined as the sum of common moieties SYN503780 (expressed as bicyclopyrone equivalents) and CSCD686480 (expressed as bicyclopyrone equivalents).

The limit of quantification (LOQ) was 0.0050 mg/kg for bicyclopyrone equivalents from SYN503780 and 0.0054 mg/kg for bicyclopyrone equivalents from CSCD686480 in the Canadian study and 0.005 mg/kg for both analytes in the USA study.

DBH = Days Before Harvest

Residues in All Untreated Samples (controls) were <LOQ (< 0.005 mg/kg for SYN503780 and CSCD686480 expressed as bicyclopyrone equivalents).

Total Residues = Sum of SYN503780 and CSCD686480 expressed as bicyclopyrone equivalents (LOQ = 0.01 mg/kg).

Corn (sweetcorn and maize) fodder and forage

Residue data have been collected from 26 field trials located in the USA in which samples of green plant material corresponding to the definition of forage were collected, whole plants harvested at approximately BBCH growth stage 39 (milk stage). The SL formulation was applied once as

broadcast foliar application. The application was made in the trials pre-emergence. Method GRM030.05A was used for residues analysis bicyclopyrone (as SYN503780) and CSAA915194 (as CSCD686480) in the corn (sweet corn and maize) matrices. Separation and quantitation were accomplished with HPLC-MS/MS with a limit of quantitation of 0.01 mg/kg expressed as bicyclopyrone equivalents.

Four trials in maize were conducted in Brazil. Method POPIT MET.117 was used for residues analysis bicyclopyrone (as SYN503780) and CSAA915194 (as CSCD686480) in maize quantifying the analytes by HPLC/MS/MS with a limit of quantitation of 0.01 mg/kg expressed as bicyclopyrone equivalents.

Twenty-nine trials in sweetcorn and maize were conducted in the USA. The SL formulation was applied to the plots as broadcast foliar application at rate of 50 g ai/h. Method GRM030.05A was used for residues analysis bicyclopyrone (as SYN503780) and CSAA915194 (as CSCD686480) in the corn (sweet corn and maize) matrices. Separation and quantitation were accomplished with HPLC-MS/MS with a limit of quantitation of 0.01 mg/kg expressed as bicyclopyrone equivalents.

Table 122 Bicyclopyrone residues on corn forage (sweetcorn and maize) from supervised trails conducted in USA and Brazil

GLP and Trial Details	Crop (Variety)	Country (Region) (Postcode)	Application		DALA)	Crop Part	Residue Found (Uncorrected, mg/kg)		
			Rate (g ai/ha) (Formulation)	Growth Stage			Bicyclopyrone eq. (SYN503780)	Bicyclopyrone eq. (CSCD686480)	Total Mean[a]
GAP	Sweetcorn/ maize	Uruguay	200	Pre-emergence	Defined by application timing				
Report: M09107 Study: M09107 Trial: M09107-JJB - Study to GLP - Study carried out in 2009	Maize (Impacto)	Brazil (Uberlandia-MG)	200 (A16003)	BBCH 00	91	Plants	< 0.01	<0.01	<0.02
			100 100 (A16003)	BBCH 14 BBCH 18	56	Plants	< 0.01	0.021	0.031
Report: M09107 Study: M09107 Trial: M09107-LZF - Study to GLP - Study carried out in 2009	Maize (BR 106)	Brazil (Holambra-SP)	200 (A16003)	BBCH 00	98	Plants	< 0.01	<0.01	<0.02
			100 100 (A16003)	BBCH 14 BBCH 18	45	Plants	< 0.01	0.020	0.03
Report: M09107 Study: M09107 Trial: M09107-MFG - Study to GLP - Study carried out in 2009	Maize (Impacto)	Brazil (Goiania- GO)	200 (A16003)	BBCH 00	99	Plants	< 0.01	<0.01	<0.02
			100 100 (A16003)	BBCH 14 BBCH 18	67	Plants	< 0.01	<0.01	<0.02
Report: M09107 Study: M09107 Trial: M09107-DMO - Study to GLP - Study carried out in 2009	Maize (Sprint)	Brazil (Itabera-SP)	200 (A16003)	BBCH 00	94	Plants	< 0.01	<0.01	<0.02
			100 100 (A16003)	BBCH 14 BBCH 18	60	Plants	< 0.01	<0.01	<0.02
GAP	Sweetcorn/ Maize	USA	50	V8/8-leaf stage	45 (for forage)				

GLP and Trial Details	Crop (Variety)	Country (Region) (Postcode)	Application		DALA)	Crop Part	Residue Found (Uncorrected, mg/kg)		
			Rate (g ai/ha) (Formulation)	Growth Stage			Bicyclopyrone eq. (SYN503780)	Bicyclopyrone eq. (CSCD686480)	Total Mean[a]
Report: TK0112879 Study: TK0112879 Trial: TK0112879-01 - Study to GLP - Study carried out in 2012	Maize (Pioneer 34F07)	USA (EPA/Region 1)	51.5 (A16003)	BBCH 17-19 30"corn/V8	39	Whole plant	< 0.01	0.207	0.24 (0.217, 0.258)
							< 0.01	0.248	
					42	Whole plant	< 0.01	0.132	0.14 (0.142, 0.139)
							< 0.01	0.129	
Report: TK0112879 Study: TK0112879 Trial: TK0112879-02 - Study to GLP - Study carried out in 2012	Maize (DKC66-96)	USA (EPA/Region 2)	50.4 (A16003)	BBCH 18-19 30"corn/V8	37	Whole plant	< 0.01	0.024	0.042 (0.034, 0.05)
							< 0.01	0.040	
					47	Whole plant	< 0.01	0.027	0.04 (0.037, 0.0430)
							< 0.01	0.033	
Report: TK0112879 Study: TK0112879 Trial: TK0112879-03 - Study to GLP - Study carried out in 2012	Maize (A1022967/ A1027871)	USA (EPA/Region 5)	51.5 (A16003)	BBCH 17-19 30"corn/V8	54	Whole plant	< 0.01	0.118	0.11 (0.128, 0.099)
							< 0.01	0.089	
					45	Whole plant	< 0.01	0.044	0.07 (0.054, 0.087)
							< 0.01	0.077	
Report: TK0112879 Study: TK0112879 Trial: TK0112879-04 - Study to GLP - Study carried out in 2012	Maize (33Z74)	USA (EPA/Region 5)	50.4 (A16003)	BBCH 17-19 30"corn/V8	40	Whole plant	< 0.01	0.072	0.09 (0.082, 0.097)
							< 0.01	0.087	
					45	Whole plant	< 0.01	0.075	0.083 (0.085, 0.08)
							< 0.01	0.070	
Report: TK0112879 Study: TK0112879 Trial: TK0112879-05 - Study to GLP - Study carried out in 2012	Maize (Pioneer P1948)	USA (EPA/Region 5)	50.4 (A16003)	BBCH 17-19 30"corn/V8	40	Whole plant	< 0.01	< 0.01	<0.02 (< 0.02,< 0.02)
							< 0.01	< 0.01	
					47	Whole plant	< 0.01	< 0.01	<0.02 (< 0.02, < 0.02)
							< 0.01	< 0.01	
Report: TK0112879 Study: TK0112879 Trial: TK0112879-06 - Study to GLP - Study carried out in 2012	Maize (DKC 33-54)	USA (EPA/Region 5)	50.4 (A16003)	BBCH 18 30"corn/V8	39	Whole plant	< 0.01	0.147	0.147 (0.157, 0.137)
							< 0.01	0.127	
					47	Whole plant	< 0.01	0.135	0.134 (0.145, 0.122)
							< 0.01	0.112	
Report: TK0112879 Study: TK0112879 Trial: TK0112879-07 - Study to GLP - Study carried out in 2012	Maize (P1151HR)	USA (EPA/Region 5)	50.4 (A16003)	BBCH 16-17 30"corn/V8	42	Whole plant	< 0.01	0.046	0.059 (0.056, 0.061)
							< 0.01	0.051	
					45	Whole plant	< 0.01	0.067	0.079 (0.077, 0.081)
							< 0.01	0.071	

GLP and Trial Details	Crop (Variety)	Country (Region) (Postcode)	Application		DALA)	Crop Part	Residue Found (Uncorrected, mg/kg)		
			Rate (g ai/ha) (Formulation)	Growth Stage			Bicyclopyrone eq. (SYN503780)	Bicyclopyrone eq. (CSCD686480)	Total Mean[a]
Report: TK0112879 Study: TK0112879 Trial: TK0112879-09 - Study to GLP - Study carried out in 2012	Sweet corn (Super Sweet Jubilee Plus)	USA (EPA/Region 3)	49.3 (A16003)	BBCH 38 30”corn/V8	26	Whole plant	< 0.01 0.017	0.080 0.154	0.13 (0.09, 0.171)
Report: TK0112879 Study: TK0112879 Trial: TK0112879-10 - Study to GLP - Study carried out in 2012	Sweet corn (Legion)	USA (EPA/Region 1)	49.3 (A16003)	BBCH 18 30”corn/V8	43	Whole plant	< 0.01 < 0.01	0.098 0.130	0.12 (0.108, 0.14)
Report: TK0112879 Study: TK0112879 Trial: TK0112879-14 - Study to GLP - Study carried out in 2012	Maize (Pioneer Brand)	USA (EPA/Region 5)	51.5 (A16003)	BBCH 17-19 30”corn/V8	44	Whole plant	< 0.01 < 0.01	0.069 0.102	0.096 (0.079, 0.112)
Report: TK0112879 Study: TK0112879 Trial: TK0112879-15 - Study to GLP - Study carried out in 2012	Maize (DKC 45-51 RIB)	USA (EPA/Region 5)	49.3 (A16003)	BBCH 17-19 30”corn/V8	44	Whole plant	< 0.01 < 0.01	0.126 0.118	0.132 (0.136, 0.128)
Report: TK0112879 Study: TK0112879 Trial: TK0112879-16 - Study to GLP - Study carried out in 2012	Maize (DKC 45-51 RIB)	USA (EPA/Region 5)	51.5 (A16003)	BBCH 17-19 30”corn/V8	44	Whole plant	< 0.01 < 0.01	0.167 0.124	0.16 (0.177, 0.134)
Report: TK0112879 Study: TK0112879 Trial: TK0112879-17 - Study to GLP - Study carried out in 2012	Sweet corn (SS Garrison)	USA (EPA/Region 5)	50.4 (A16003)	BBCH 17-18 30”corn/V8	25	Whole plant	< 0.01 < 0.01	0.217 0.162	0.2 (0.227, 0.172)
Report: TK0112879 Study: TK0112879 Trial: TK0112879-18 - Study to GLP - Study carried out in 2012	Maize (8066846)	USA (EPA/Region)	50.4 (A16003)	BBCH 18 30”corn/V8	46	Whole plant	< 0.01 < 0.01	0.042 0.017	0.04 (0.052, 0.027)

GLP and Trial Details	Crop (Variety)	Country (Region) (Postcode)	Application		DALA)	Crop Part	Residue Found (Uncorrected, mg/kg)		
			Rate (g ai/ha) (Formulation)	Growth Stage			Bicyclopyrone eq. (SYN503780)	Bicyclopyrone eq. (CSCD686480)	Total Mean[a]
Report: TK0112879 Study: TK0112879 Trial: TK0112879-19 - Study to GLP - Study carried out in 2012	Maize (8066846)	USA (EPA/Region 5)	50.4 (A16003)	BBCH 18 30"corn/V8	46	Whole plant	< 0.01 < 0.01	0.071 0.130	0.11 (0.081, 0.140)
Report: TK0112879 Study: TK0112879 Trial: TK0112879-20 - Study to GLP - Study carried out in 2012	Maize (P1360HR)	USA (EPA/Region 5)	50.4 (A16003)	BBCH 18 30"corn/V8	41	Whole plant	< 0.01 < 0.01	0.067 0.073	0.08 (0.077, 0.083)
Report: TK0112879 Study: TK0112879 Trial: TK0112879-21 - Study to GLP - Study carried out in 2012	Maize (Pioneer P9675)	USA (EPA/Region 5)	51.5 (A16003)	BBCH 19 30"corn/V8	46	Whole plant	< 0.01 < 0.01	0.082 0.124	0.11 (0.092, 0.134)
Report: TK0112879 Study: TK0112879 Trial: TK0112879-22 - Study to GLP - Study carried out in 2012	Maize (N77H-3000Gt)	USA (EPA/Region5)	51.5 (A16003)	BBCH 17-18 30"corn/V8	47	Whole plant	< 0.01 < 0.01	0.156 0.104	0.14 (0.166, 0.114)
Report: TK0112879 Study: TK0112879 Trial: TK0112879-23 - Study to GLP - Study carried out in 2012	Maize (PB878RRCB)	USA (EPA/Region 5)	50.4 (A16003)	BBCH 18 30"corn/V8	44	Whole plant	< 0.01 < 0.01	0.161 0.168	0.17 (0.171, 0.178)
Report: TK0112879 Study: TK0112879 Trial: TK0112879-24 - Study to GLP - Study carried out in 2012	Maize (89T43-3000GT)	USA (EPA/Region 5)	50.4 (A16003)	BBCH 18 30"corn/V8	45	Whole plant	< 0.01 < 0.01	0.094 0.088	0.1 (0.104, 0.098)
Report: TK0112879 Study: TK0112879 Trial: TK0112879-25 - Study to GLP - Study carried out in 2012	Maize (DKC52-59 (VT3))	USA (EPA/Region 5)	51.5 (A16003)	BBCH 17-18 30"corn/V8	46	Whole plant	< 0.01 < 0.01	0.095 0.072	0.09 (0.105, 0.082)

GLP and Trial Details	Crop (Variety)	Country (Region) (Postcode)	Application		DALA)	Crop Part	Residue Found (Uncorrected, mg/kg)		
			Rate (g ai/ha) (Formulation)	Growth Stage			Bicyclopyrone eq. (SYN503780)	Bicyclopyrone eq. (CSCD686480)	Total Mean[a]
Report: TK0112879 Study: TK0112879 Trial: TK0112879-26 - Study to GLP - Study carried out in 2012	Maize (33Z74)	USA (EPA/Region 5)	51.5 (A16003)	BBCH 17-19 30"corn/V8	45	Whole plant	< 0.01 < 0.01	0.228 0.122	0.18 (0.238, 0.132)
Report: TK0112879 Study: TK0112879 Trial: TK0112879-27 - Study to GLP - Study carried out in 2012	Sweet corn (Golden Beauty SU)	USA (EPA/Region 7)	51.5 (A16003)	BBCH 18-19 30"corn/V8	34	Whole plant	< 0.01 < 0.01	0.146 0.132	0.15 (0.156, 0.142)
Report: TK0112879 Study: TK0112879 Trial: TK0112879-28 - Study to GLP - Study carried out in 2012	Sweet corn (BSS0982)	USA (EPA/Region 10)	54.9 (A16003)	BBCH 33-34 30"corn/V8	38	Whole plant	< 0.01 0.011	0.157 0.280	0.23 (0.167, 0.291)
Report: TK0112879 Study: TK0112879 Trial: TK0112879-29 - Study to GLP - Study carried out in 2012	Sweet corn (Ambrosia)	USA (EPA/Region 11)	52.6 (A16003)	BBCH 18 30"corn/V8	45	Whole plant	< 0.01 < 0.01	0.043 0.028	0.05 (0.053, 0.038)
Report: TK0112879 Study: TK0112879 Trial: TK0112879-30 - Study to GLP - Study carried out in 2012	Sweet corn (Jubilee)	USA (EPA/Region 12)	50.4 (A16003)	BBCH 17-19 30"corn/V8	51	Whole plant	< 0.01 < 0.01	0.150 □□□□□	0.155 (0.16, 0.15)

[a] Determined as the sum of common moieties SYN503780 (expressed as bicyclopyrone equivalents) and CSCD686480 (expressed as bicyclopyrone equivalents).

Table 123 Bicyclopyrone residues on corn (sweetcorn and maize) fodder from supervised trails conducted in USA.

GLP and Trial Details	Crop (Variety)	Country (Region) (Postcode)	Application Rate (g ai/ha) (Formulation)	Growth Stage at Application	PHI (days)	Crop Part	Residue Found (Uncorrected, mg/kg)		
							Bicyclopyrone eq. (SYN503780)	Bicyclopyrone eq. (CSCD686480)	Total Mean[a]
GAP	Sweetcorn/ Maize	USA	50	V8/8-leaf stage	45 (for forage)				
Report: TK0112879 Study: TK0112879 Trial: TK0112879-01 - Study to GLP - Study carried out in 2012	Maize (Pioneer 34F07)	USA (EPA/Region 1)	51.5 (A16003)	BBCH 17-19 30"corn/V8	100	Remaining plant	< 0.01 < 0.01	< 0.01 < 0.01	< 0.02 (< 0.02, < 0.02)

GLP and Trial Details	Crop (Variety)	Country (Region) (Postcode)	Application Rate (g ai/ha) (Formulation)	Growth Stage at Application	PHI (days)	Crop Part	Residue Found (Uncorrected, mg/kg)		
							Bicyclopyrone eq. (SYN503780)	Bicyclopyrone eq. (CSCD686480)	Total Mean[a]
Report: TK0112879 Study: TK0112879 Trial: TK0112879-02 - Study to GLP - Study carried out in 2012	Maize (DKC66-96)	USA (EPA/Region 2)	50.4 (A16003)	BBCH 18-19 30”corn/V8	94	Remaining plant	< 0.01 < 0.01	< 0.01 < 0.01	< 0.02 (< 0.02, < 0.02)
Report: TK0112879 Study: TK0112879 Trial: TK0112879-03 - Study to GLP - Study carried out in 2012	Maize (A1022967/ A1027871)	USA (EPA/Region 5)	51.5 (A16003)	BBCH 17-19 30”corn/V8	90	Remaining plant	< 0.01 < 0.01	0.059 0.025	0.052 (0.069, 0.0354)
Report: TK0112879 Study: TK0112879 Trial: TK0112879-04 - Study to GLP - Study carried out in 2012	Maize (33Z74)	USA (EPA/Region 5)	50.4 (A16003)	BBCH 17-19 30”corn/V8	110	Remaining plant	< 0.01 < 0.01	0.031 0.016	0.034 (0.041, 0.026)
Report: TK0112879 Study: TK0112879 Trial: TK0112879-05 - Study to GLP - Study carried out in 2012	Maize (Pioneer P1948)	USA (EPA/Region 5)	50.4 (A16003)	BBCH 17-19 30”corn/V8	92	Remaining plant	< 0.01 < 0.01	0.12 0.119	0.13 (0.13, 0.129)
Report: TK0112879 Study: TK0112879 Trial: TK0112879-06 - Study to GLP - Study carried out in 2012	Maize (DKC 33-54)	USA (EPA/Region 5)	50.4 (A16003)	BBCH 18 30”corn/V8	109	Remaining plant	< 0.01 < 0.01	0.122 0.151	0.147 (0.132, 0.161)
Report: TK0112879 Study: TK0112879 Trial: TK0112879-07 - Study to GLP - Study carried out in 2012	Maize (P1151HR)	USA (EPA/Region 5)	50.4 (A16003)	BBCH 16-17 30”corn/V8	112	Remaining plant	< 0.01 < 0.01	0.02 0.014	0.027 (0.03, 0.024)
Report: TK0112879 Study: TK0112879 Trial: TK0112879-09 - Study to GLP - Study carried out in 2012	Sweet corn (Super Sweet Jubilee Plus)	USA (EPA/Region 3)	49.8 (A16003)	BBCH 17-19 30”corn/V8	56	Remaining plant	< 0.01 < 0.01	0.026 0.013	0.03 (0.036, 0.023)

GLP and Trial Details	Crop (Variety)	Country (Region) (Postcode)	Application Rate (g ai/ha) (Formulation)	Growth Stage at Application	PHI (days)	Crop Part	Residue Found (Uncorrected, mg/kg)		
							Bicyclopyrone eq. (SYN503780)	Bicyclopyrone eq. (CSCD686480)	Total Mean[a]
Report: TK0112879 Study: TK0112879 Trial: TK0112879-10 - Study to GLP - Study carried out in 2012	Sweet corn (Legion)	USA (EPA/Region 1)	49.3 (A16003)	BBCH 18 30"corn/V8	50	Remaining plant	< 0.01 < 0.01	0.182 0.251	0.227 (0.192, 0.261)
Report: TK0112879 Study: TK0112879 Trial: TK0112879-11 - Study to GLP - Study carried out in 2012	Pop corn (997 Yellow F1)	USA (EPA/Region 5)	50.4 (A16003)	BBCH 18 30"corn/V8	100	Remaining plant	< 0.01 < 0.01	< 0.01 0.208	0.12 (0.02, 0.218)
Report: TK0112879 Study: TK0112879 Trial: TK0112879-12 - Study to GLP - Study carried out in 2012	Pop corn (997 Yellow F1)	USA (EPA/Region 5)	50.4 (A16003)	BBCH 18 30"corn/V8	100	Remaining plant	< 0.01 < 0.01	0.018 0.011	0.025 (0.028, 0.021)
Report: TK0112879 Study: TK0112879 Trial: TK0112879-13 - Study to GLP - Study carried out in 2012	Pop corn (Robust Yellow Popcorn)	USA (EPA/Region 5)	50.4 (A16003)	BBCH 16-17 30"corn/V8	98	Remaining plant	< 0.01 < 0.01	0.03 0.042	0.046 (0.04, 0.052)
Report: TK0112879 Study: TK0112879 Trial: TK0112879-14 - Study to GLP - Study carried out in 2012	Maize (Pioneer)	USA (EPA/Region 5)	51.5 (A16003)	BBCH 17-19 30"corn/V8	103	Remaining plant	< 0.01 < 0.01	0.046 0.029	0.048 (0.056, 0.039)
Report: TK0112879 Study: TK0112879 Trial: TK0112879-15 - Study to GLP - Study carried out in 2012	Maize (DKC 45-51 RIB)	USA (EPA/Region 5)	49.3 (A16003)	BBCH 17-19 30"corn/V8	100	Remaining plant	0.014 0.014	0.204 0.205	0.219 (0.218, 0.219)
Report: TK0112879 Study: TK0112879 Trial: TK0112879-16 - Study to GLP - Study carried out in 2012	Maize (DKC 45-51 RIB)	USA (EPA/Region 5)	51.5 (A16003)	BBCH 17-19 30"corn/V8	100	Remaining plant	< 0.01 < 0.01	0.131 0.127	0.139 (0.141, 0.137)

GLP and Trial Details	Crop (Variety)	Country (Region) (Postcode)	Application Rate (g ai/ha) (Formulation)	Growth Stage at Application	PHI (days)	Crop Part	Residue Found (Uncorrected, mg/kg)		
							Bicyclopyrone eq. (SYN503780)	Bicyclopyrone eq. (CSCD686480)	Total Mean[a]
Report: TK0112879 Study: TK0112879 Trial: TK0112879-17 - Study to GLP - Study carried out in 2012	Sweet corn (SS Garrison)	USA (EPA/Region 5)	50.4 (A16003)	BBCH 17-18 30”corn/V8	58	Remaining plant	0.011 0.011	0.287 0.287	0.297 (0.297, 0.297)
Report: TK0112879 Study: TK0112879 Trial: TK0112879-18 - Study to GLP - Study carried out in 2012	Maize (8066846)	USA (EPA/Region)	50.4 (A16003)	BBCH 18 30”corn/V8	80	Remaining plant	< 0.01 < 0.01	0.046 0.042	0.054 (0.056, 0.052)
Report: TK0112879 Study: TK0112879 Trial: TK0112879-19 - Study to GLP - Study carried out in 2012	Maize (8066846)	USA (EPA/Region 5)	50.4 (A16003)	BBCH 18 30”corn/V8	80	Remaining plant	< 0.01 < 0.01	0.058 0.085	0.082 (0.068, 0.095)
Report: TK0112879 Study: TK0112879 Trial: TK0112879-20 - Study to GLP - Study carried out in 2012	Maize (P1360HR)	USA (EPA/Region 5)	50.4 (A16003)	BBCH 18 30”corn/V8	99	Remaining plant	< 0.01 < 0.01	< 0.01 < 0.01	<0.02 (< 0.02, < 0.02)
Report: TK0112879 Study: TK0112879 Trial: TK0112879-21 - Study to GLP - Study carried out in 2012	Maize (Pioneer P9675)	USA (EPA/Region 5)	51.5 (A16003)	BBCH 19 30”corn/V8	106	Remaining plant	< 0.01 < 0.01	0.04 0.047	0.054 (0.05, 0.057)
Report: TK0112879 Study: TK0112879 Trial: TK0112879-22 - Study to GLP - Study carried out in 2012	Maize (N77H-3000Gt)	USA (EPA/Region5)	51.5 (A16003)	BBCH 17-18 30”corn/V8	113	Remaining plant	< 0.01 < 0.01	0.044 0.041	0.053 (0.054, 0.051)
Report: TK0112879 Study: TK0112879 Trial: TK0112879-23 - Study to GLP - Study carried out in 2012	Maize (PB878RRCB)	USA (EPA/Region 5)	50.4 (A16003)	BBCH 18 30”corn/V8	98	Remaining plant	< 0.01 < 0.01	0.278 0.263	0.28 (0.288, 0.273)

GLP and Trial Details	Crop (Variety)	Country (Region) (Postcode)	Application Rate (g ai/ha) (Formulation)	Growth Stage at Application	PHI (days)	Crop Part	Residue Found (Uncorrected, mg/kg)		
							Bicyclopyrone eq. (SYN503780)	Bicyclopyrone eq. (CSCD686480)	Total Mean[a]
Report: TK0112879 Study: TK0112879 Trial: TK0112879-24 - Study to GLP - Study carried out in 2012	Maize (89T43-3000GT)	USA (EPA/Region 5)	50.4 (A16003)	BBCH 18 30"corn/V8	107	Remaining plant	< 0.01 < 0.01	0.103 0.099	0.111 (0.113, 0.109)
Report: TK0112879 Study: TK0112879 Trial: TK0112879-25 - Study to GLP - Study carried out in 2012	Maize (DKC52-59 (VT3))	USA (EPA/Region 5)	51.5 (A16003)	BBCH 17-18 30"corn/V8	109	Remaining plant	< 0.01 < 0.01	0.059 0.04	0.06 (0.069, 0.05)
Report: TK0112879 Study: TK0112879 Trial: TK0112879-26 - Study to GLP - Study carried out in 2012	Maize (33Z74)	USA (EPA/Region 5)	51.5 (A16003)	BBCH 17-19 30"corn/V8	96	Remaining plant	< 0.01 < 0.01	0.036 0.037	0.047 (0.046, 0.047)
Report: TK0112879 Study: TK0112879 Trial: TK0112879-27 - Study to GLP - Study carried out in 2012	Sweet corn (Golden Beauty SU)	USA (EPA/Region 7)	51.5 (A16003)	BBCH 18-19 30"corn/V8	78	Remaining plant	0.035 < 0.01	0.067 0.046	0.079 (0.102, 0.056)
Report: TK0112879 Study: TK0112879 Trial: TK0112879-28 - Study to GLP - Study carried out in 2012	Sweet corn (BSS0982)	USA (EPA/Region 10)	54.9 (A16003)	BBCH 33-34 30"corn/V8	48	Remaining plant	< 0.01 0.014	0.207 0.373	0.302 (0.217, 0.387)
Report: TK0112879 Study: TK0112879 Trial: TK0112879-29 - Study to GLP - Study carried out in 2012	Sweet corn (Ambrosia)	USA (EPA/Region 11)	52.6 (A16003)	BBCH 18 30"corn/V8	96	Remaining plant	< 0.01 < 0.01	0.023 0.01	0.027 (0.033, 0.02)
Report: TK0112879 Study: TK0112879 Trial: TK0112879-30 - Study to GLP - Study carried out in 2012	Sweet corn (Jubilee)	USA (EPA/Region 12)	50.4 (A16003)	BBCH 17-19 30"corn/V8	69	Remaining plant	< 0.01 < 0.01	0.071 0.066	0.079 (0.081, 0.076)

[a] Determined as the sum of common moieties SYN503780 (expressed as bicyclopyrone equivalents) and CSCD686480 (expressed as bicyclopyrone equivalents).

Thirty-two supervised residue trials on sweetcorn and maize were conducted in the USA in which samples corresponding to the definition of forage were collected but at GAPs more critical that

the US label. Bicyclopyrone was applied once or twice using the SL formulation at a rate of 200 g ai/ha. Applications were made to the soil surface pre-emergence of the crop and as a foliar spray post-emergence, or as a single post-emergence foliar spray. Samples were analysed by the common-moiety analytical method GRM030.05A, a common moiety method which includes hydrolysis of the bridge between the two rings of bicyclopyrone to release the structurally-related moieties SYN503780 and CSCD686480. In these studies, SYN503780 and CSCD686480 were corrected to bicyclopyrone equivalents. The limit of quantification (LOQ) was 0.01 mg/kg expressed as bicyclopyrone equivalents.

Table 124 Bicyclopyrone residues on corn forage (sweetcorn and maize) from supervised trails conducted in USA

GLP and Trial Details	Crop (Variety)	Country (Region) (Postcode)	Application		DALA	Crop Part	Residue Found (Uncorrected) (mg/kg)		
			Rate (g ai/ha) (Formulation)	Growth Stage			Bicyclopyrone eq. (SYN503780)	Bicyclopyrone eq. (CSCD686480)	Total Mean[a]
GAP	Sweetcorn/ Maize	USA	50	V8/8-leaf stage	PHI: 45 (for forage)				
Report: T019378-04 Study: 09SYN253A.REP Trial: E10NC081383 - Study to GLP - Study carried out in 2008	Field corn (Garst 8377YG1/RR)	USA (EPA Region 2)	200 + 200 (soil surface + post-emergence foliar) (EC)	Pre-plant	43	Plants without ears	0.027 0.033	0.250 0.270	0.29 (0.277, 0.303)
				BBCH 36 (V8)	45	Forage	0.020 0.022	0.022 0.291	0.177 (0.042, 0.303)
			200 (post-emergence foliar) (EC)	BBCH 36 (V8)	43	Plants without ears	0.013 0.020	0.114 0.187	0.167 (0.127, 0.207)
					45	Forage	0.011 0.011	0.135 0.114	0.135 (0.146, 0.125)
Report: T019378-04 Study: 09SYN253A.REP Trial: C19MO081385 - Study to GLP - Study carried out in 2008	Field corn (Pioneer 33D47)	USA (EPA Region 5)	200 + 200 (soil surface + post-emergence foliar) (EC)	Pre-plant	46	Forage	< 0.01 < 0.01	0.046 0.030	0.0479 (0.056, 0.040)
				BBCH 36 (V8)	49	Plants without ears	0.021 0.017	0.302 0.218	0.279 (0.323, 0.235)
			200 (post-emergence foliar) (EC)	BBCH 36 (V8)	46	Forage	< 0.01 < 0.01	0.022 0.187	0.114 (0.032, 0.197)
					49	Plants without ears	< 0.01 < 0.01	0.097 0.069	0.092 (0.107, 0.079)
Report: T019378-04 Study: 09SYN253A.REP Trial: C19KS081386 - Study to GLP - Study carried out in 2008	Field corn (DK 6019)	USA (EPA Region 5)	200 + 200 (soil surface + post-emergence foliar) (EC)	Pre-plant	45	Forage	0.011 < 0.01	0.104 0.062	0.093 (0.115, 0.072)
				BBCH 37 (V8)	50	Plants without ears	0.013 0.017	0.156 0.187	0.186 (0.169, 0.204)
			200 (post-emergence foliar) (EC)	BBCH 37 (V8)	45	Forage	< 0.01 < 0.01	0.046 0.042	0.053 (0.056, 0.052)
					50	Plants without ears	0.016 < 0.01	0.187 0.084	0.148 (0.203, 0.094)
Report: T019378-04 Study: 09SYN253A.REP Trial: C01MI081387 - Study to GLP - Study carried out in 2008	Field corn (Pioneer 38N85 RR)	USA (EPA Region 5)	200 + 200 (soil surface + post-emergence foliar) (EC)	Pre-plant	7	Forage	< 0.01	0.025	0.0174 (< 0.01, 0.025)
				BBCH 19 (V8)			Sample lost		
					50	Plants without ears	< 0.01 < 0.01	0.032 0.021	0.036 (0.042, 0.031)
			200 (post-emergence foliar)	BBCH 19 (V8)	7	Forage	< 0.01 < 0.01	0.040 0.038	0.049 (0.05, 0.048)
					50	Plants	< 0.01	0.029	0.030

GLP and Trial Details	Crop (Variety)	Country (Region) (Postcode)	Application		DALA	Crop Part	Residue Found (Uncorrected) (mg/kg)		
			Rate (g ai/ha) (Formulation)	Growth Stage			Bicyclopyrone eq. (SYN503780)	Bicyclopyrone eq. (CSCD686480)	Total Mean[a]
			(EC)			without ears	< 0.01	0.010	(0.039, 0.02)
Report: T019378-04 Study: 09SYN253A.REP Trial: C01OH081388 - Study to GLP - Study carried out in 2008	Field corn (691RR2)	USA (EPA Region 5)	200 + 200 (soil surface + post-emergence foliar) (EC)	Pre-plant BBCH 18 (V8)	47	Forage	< 0.01 < 0.01	0.023 0.029	0.036 (0.033, 0.039)
					47	Plants without ears	< 0.01 < 0.01	0.011 0.028	0.030 (0.021, 0.038)
			200 (post-emergence foliar) (EC)	BBCH 19 (V8)	47	Forage	< 0.01 < 0.01	0.038 0.058	0.058 (0.048, 0.068)
					47	Plants without ears	< 0.01 0.014	0.025 0.114	0.082 (0.035, 0.128)
Report: T019378-04 Study: 09SYN253A.REP Trial: C08WI081389 - Study to GLP - Study carried out in 2008	Field corn (Dekalb DK43-27 (VT3))	USA (EPA Region 5)	200 + 200 (soil surface + post-emergence foliar) (EC)	Pre-plant BBCH 18 (V8)	43	Plants without ears	< 0.01 < 0.01	0.078 0.086	0.092 (0.088, 0.096)
					49	Forage	< 0.01 < 0.01	0.070 0.086	0.088 (0.08, 0.096)
			200 (post-emergence foliar) (EC)	BBCH 18 (V8)	43	Plants without ears	< 0.01 < 0.01	0.094 0.072	0.093 (0.104, 0.082)
					49	Forage	0.014 0.012	0.125 0.114	0.133 (0.139, 0.126)
Report: T019378-04 Study: 09SYN253A.REP Trial: C08WI081390 - Study to GLP - Study carried out in 2008	Field corn (Pioneer 37Y12)	USA (EPA Region 5)	200 + 200 (soil surface + post-emergence foliar) (EC)	Pre-plant BBCH 18 (V8)	43	Forage	< 0.01 < 0.01	0.040 0.040	0.050 (0.048, 0.061)
			200 (post-emergence foliar) (EC)	BBCH 18 (V8)	43	Forage	< 0.01 < 0.01	0.053 0.041	0.057 (0.063, 0.051)
Report: T019378-04 Study: 09SYN253A.REP Trial: C08WI081391 - Study to GLP - Study carried out in 2008	Field corn (H-7151CB/LL/RW)	USA (EPA Region 5)	200 + 200 (soil surface + post-emergence foliar) (EC)	Pre-plant BBCH 18 (V8)	47	Forage	< 0.01 < 0.01	0.015 0.023	0.029 (0.025, 0.033)
			200 (post-emergence foliar) (EC)	BBCH 18 (V8)	47	Forage	< 0.01 < 0.01	0.017 0.024	0.0305 (0.027, 0.034)
Report: T019378-04 Study: 09SYN253A.REP Trial: C13ND081392 - Study to GLP - Study carried out in 2008	Field corn (238 RR2/BT)	USA (EPA Region 5)	200 + 200 (soil surface + post-emergence foliar) (EC)	Pre-plant BBCH 18 (V8)	24	Forage	0.020	0.187	0.205
					31		0.013	0.166	0.179
					38		0.021	0.229	0.32
					45		0.011 < 0.01	0.156 0.066	0.121 (0.167, 0.076)
					52		0.015	0.135	0.15
			200 (post-emergence foliar) (EC)	BBCH 18 (V8)	24	Forage	0.016	0.177	0.193
					31		< 0.01	0.046	0.056
					38		< 0.01	0.050	0.06
					45		< 0.01 < 0.01	0.064 0.089	0.086 (0.074, 0.099)
					52		< 0.01	0.073	0.083

GLP and Trial Details	Crop (Variety)	Country (Region) (Postcode)	Application		DALA	Crop Part	Residue Found (Uncorrected) (mg/kg)		
			Rate (g ai/ha) (Formulation)	Growth Stage			Bicyclopyrone eq. (SYN503780)	Bicyclopyrone eq. (CSCD686480)	Total Mean[a]
Report: T019378-04 Study: 09SYN253A.REP Trial: C13ND081393 - Study to GLP - Study carried out in 2008	Field corn (238 RR2/BT)	USA (EPA Region 5)	200 + 200 (soil surface + post-emergence foliar) (EC)	Pre-plant BBCH 18 (V8)	45	Forage	< 0.01 < 0.01	0.104 0.085	0.104 (0.114, 0.095)
			200 (post-emergence foliar) (EC)	BBCH 18 (V8)	45	Forage	< 0.01 0.013	0.052 0.146	0.107 (0.060, 0.153)
Report: T019378-04 Study: 09SYN253A.REP Trial: E19IA081395 - Study to GLP - Study carried out in 2008	Field corn (B0000948 Hybrid Seed Corn)	USA (EPA Region 5)	200 + 200 (soil surface + post-emergence foliar) (EC)	Pre-plant BBCH 18 (V8)	45	Forage	< 0.01 0.014	0.080 0.114	0.106 (0.087, 0.124
			200 (post-emergence foliar) (EC)	BBCH 18 (V8)	45	Forage	< 0.01 0.011	0.079 0.088	0.094 (0.09, 0.099)
Report: T019378-04 Study: 09SYN253A.REP Trial: E19IA081396 - Study to GLP - Study carried out in 2008	Field corn (B0000948 Hybrid Seed Corn)	USA (EPA Region 5)	200 + 200 (soil surface + post-emergence foliar) (EC)	Pre-plant BBCH 18 (V8)	45	Forage	< 0.01 < 0.01	0.025 0.035	0.04 (0.035, 0.045)
			200 (post-emergence foliar) (EC)	BBCH 18 (V8)	45	Forage	< 0.01 < 0.01	0.041 0.038	0.049 (0.051, 0.048)
Report: T019378-04 Study: 09SYN253A.REP Trial: E19IA081397 - Study to GLP - Study carried out in 2008	Field corn (B0000948 Hybrid Seed Corn)	USA (EPA Region 5)	200 + 200 (soil surface + post-emergence foliar) (EC)	Pre-plant BBCH 18 (V8)	45	Forage	0.013 < 0.01	0.125 0.095	0.121 (0.138, 0.105)
			200 (post-emergence foliar) (EC)	BBCH 18 (V8)	45	Forage	< 0.01 < 0.01	0.114 0.083	0.108 (0.124, 0.093)
Report: T019378-04 Study: 09SYN253A.REP Trial: E19IA081398 - Study to GLP - Study carried out in 2008	Maize (B0000948 Hybrid Seed Corn)	USA (EPA Region 5)	200 + 200 (soil surface + post-emergence foliar) (EC)	Pre-plant BBCH 18 (V8)	45	Forage	< 0.01 < 0.01	0.098 0.068	0.093 (0.108, 0.078)
			200 (post-emergence foliar) (EC)	BBCH 18 (V8)	45	Forage	< 0.01 < 0.01	0.059 0.076	0.077 (0.069, 0.086)
Report: T019378-04 Study: 09SYN253A.REP Trial: C30IA081399 - Study to GLP - Study carried out in 2008	Field corn (33H27)	USA (EPA Region 5)	200 + 200 (soil surface + post-emergence foliar) (EC)	Pre-plant BBCH 18 (V8)	45	Forage	< 0.01 < 0.01	0.036 0.071	0.063 (.046 0.081)
			200	BBCH	45	Forage	< 0.01	0.022	0.049

GLP and Trial Details	Crop (Variety)	Country (Region) (Postcode)	Application		DALA	Crop Part	Residue Found (Uncorrected) (mg/kg)		
			Rate (g ai/ha) (Formulation)	Growth Stage			Bicyclopyrone eq. (SYN503780)	Bicyclopyrone eq. (CSCD686480)	Total Mean[a]
			(post-emergence foliar) (EC)	18 (V8)			< 0.01	0.056	(0.032, 0.066)
Report: T019378-04 Study: 09SYN253A.REP Trial: C30IA081400 - Study to GLP - Study carried out in 2008	Field corn (FA5614R)	USA (EPA Region 5)	200 + 200 (soil surface + post-emergence foliar) (EC)	Pre-plant BBCH 18 (V8)	24	Forage	< 0.01	0.083	0.093
					31		< 0.01	0.068	0.078
					38		< 0.01	0.030	0.040
					45		< 0.01	0.043	0.06
							< 0.01	0.057	(0.053, 0.067)
					52		< 0.01	0.083	0.093
			200 (post-emergence foliar) (EC)	BBCH 18 (V8)	24	Forage	< 0.01	0.044	0.054
					31		< 0.01	0.047	0.057
					38		< 0.01	0.022	0.032
					45		< 0.01	0.027	0.0375
							< 0.01	0.028	(0.037, 0.038)
					52		< 0.01	0.036	0.046
Report: T019378-04 Study: 09SYN253A.REP Trial: C30IA081401 - Study to GLP - Study carried out in 2008	Field corn (Stine 903228VT3)	USA (EPA Region 5)	200 + 200 (soil surface + post-emergence foliar) (EC)	Pre-plant BBCH 18 (V8)	45	Forage	< 0.01	0.047	0.0815
							< 0.01	0.096	(0.057, 0.106)
			200 (post-emergence foliar) (EC)	BBCH 18 (V8)	45	Forage	< 0.01	0.057	0.0615
							< 0.01	0.046	(0.067, 0.056)
Report: T019378-04 Study: 09SYN253A.REP Trial: W07TX081402 - Study to GLP - Study carried out in 2008	Field corn (DKC69-44)	USA (EPA Region 6)	200 + 200 (soil surface + post-emergence foliar) (EC)	Pre-plant BBCH 18 (V8)	42	Forage	< 0.01	0.063	0.063
							< 0.01	0.043	(0.073, 0.053)
			200 (post-emergence foliar) (EC)	BBCH 18 (V8)	42	Forage	< 0.01	0.069	0.073
							< 0.01	0.058	(0.079, 0.068)
Report: T019378-04 Study: 09SYN253A.REP Trial: W32CA081404 - Study to GLP - Study carried out in 2008	Sweet corn (Bodacious)	USA (EPA Region 10)	200 + 200 (soil surface + post-emergence foliar) (EC)	Pre-plant BBCH 18 (V8)	24	Plants without ears	0.033	0.260	0.293
					31		0.028	0.260	0.288
					38		0.020	0.177	0.197
					45		0.014	0.177	0.255
							0.036	0.302	(0.191, 0.338)
					52		0.017	0.135	0.152
			200 (post-emergence foliar) (EC)	BBCH 18 (V8)	24	Plants without ears	0.032	0.250	0.282
					31		0.024	0.187	0.211
					38		0.013	0.156	0.169
					45		< 0.01	0.077	0.116
							< 0.01	0.135	(0.087, 0.145)
					52		0.011	0.114	0.125
Report: T019378-04 Study: 09SYN253A.REP Trial: W15ID081405 - Study to GLP - Study carried out in 2008	Sweet corn (Honey 'N Pearl)	USA (EPA Region 11)	200 + 200 (soil surface + post-emergence foliar) (EC)	Pre-plant BBCH 18 (V8)	45	Plants without ears	< 0.01	0.037	0.044
							< 0.01	0.032	(0.047, 0.042)
			200	BBCH	45	Plants	< 0.01	0.026	0.030

GLP and Trial Details	Crop (Variety)	Country (Region) (Postcode)	Application		DALA	Crop Part	Residue Found (Uncorrected) (mg/kg)		
			Rate (g ai/ha) (Formulation)	Growth Stage			Bicyclopyrone eq. (SYN503780)	Bicyclopyrone eq. (CSCD686480)	Total Mean[a]
			(post-emergence foliar) (EC)	18 (V8)		without ears	< 0.01	0.015	(0.036, 0.025)
Report: T019378-04 Study: 09SYN253A.REP Trial: W21OR081406 - Study to GLP - Study carried out in 2008	Sweet corn (Honey and Pearls)	USA (EPA Region 12)	200 + 200 (soil surface + post-emergence foliar) (EC)	Pre-plant BBCH 22 (V8)	47	Plants without ears	0.013 0.031	0.084 0.135	0.131 (0.097, 0.166)
			200 (post-emergence foliar) (EC)	BBCH 22 (V8)	47	Plants without ears	< 0.011 0.01	0.047 0.046	0.057 (0.058, 0.056)
Report: T019378-04 Study: 09SYN253A.REP Trial: E19FL081407 - Study to GLP - Study carried out in 2008	Sweet corn (Awesome)	USA (EPA Region 3)	200 + 200 (soil surface + post-emergence foliar) (EC)	Pre-plant BBCH 18 (V8)	42	Plants without ears	0.018 0.030	0.114 0.187	0.174 (0.132, 0.217)
Report: T019378-04 Study: 09SYN253A.REP Trial: C13ND081408 - Study to GLP - Study carried out in 2008	Field corn (Croplan Genetics 9618888)	USA (EPA Region 5)	200 + 200 (soil surface + post-emergence foliar) (EC)	Pre-plant BBCH 37 (V8)	45	Forage	< 0.01 < 0.01	0.038 0.034	0.046 (0.048, 0.044)
			200 (post-emergence foliar) (EC)	BBCH 37 (V8)	45	Forage	< 0.01 < 0.01	0.052 0.043	0.057 (0.062, 0.053)
			200 + 200 (pre-plant + post-emergence foliar) (EC)	Pre-plant BBCH 37 (V8)	45	Forage	< 0.01 < 0.01	0.036 0.051	0.053 (0.046, 0.061)
Report: T019378-04 Study: 09SYN253A.REP Trial: E04PA081411 - Study to GLP - Study carried out in 2008	Field corn (Mycogen Hybrid Seed (Hybrid 2D324))	USA (EPA Region 1)	200 + 200 (soil surface + post-emergence foliar) (EC)	Pre-plant BBCH 18 (V8)	45	Plants without ears	0.015 0.012	0.218 0.187	0.216 (0.233, 0.199)
						Forage	< 0.01 < 0.01	0.125 0.218	0.181 (0.135, 0.228)
			200 (post-emergence foliar) (EC)	BBCH 18 (V8)	45	Plants without ears	0.018 0.017	0.281 0.239	0.277 (0.299, 0.256)
						Forage	0.010 0.011	0.208 0.208	0.218 (0.218, 0.219)
			200 + 200 (pre-plant + post-emergence foliar) (EC)	Pre-plant BBCH 35 (V8)	45	Plants without ears	0.027 0.036	0.385 0.458	0.453 (0.412, 0.494)
						Forage	0.016 < 0.01	0.218 0.208	0.226 (0.234, 0.218)

GLP and Trial Details	Crop (Variety)	Country (Region) (Postcode)	Application		DALA	Crop Part	Residue Found (Uncorrected) (mg/kg)		
			Rate (g ai/ha) (Formulation)	Growth Stage			Bicyclopyrone eq. (SYN503780)	Bicyclopyrone eq. (CSCD686480)	Total Mean[a]
Report: T019378-04 Study: 09SYN253A.REP Trial: E04PA081412 - Study to GLP - Study carried out in 2008	Sweet corn (Mirai 421 W Insect Guard F1)	USA (EPA Region 1)	200 + 200 (soil surface + post-emergence foliar) (EC)	Pre-plant BBCH 35 (V8)	45	Plants without ears	0.013 0.014	0.135 0.156	0.159 (0.148, 0.17)
			200 (post-emergence foliar) (EC)	BBCH 35 (V8)	45	Plants without ears	0.021 0.020	0.260 0.229	0.265 (0.281, 0.249)
			200 + 200 (pre-plant + post-emergence foliar) (EC)	Pre-plant BBCH 35 (V8)	45	Plants without ears	0.013 0.019	0.177 0.229	0.219 (0.19, 0.248)
Report: T019378-04 Study: 09SYN268A.REP Trial: E15-9451/FL - Study to GLP - Study carried out in 2009	Sweet corn (Hybrid Sweet Corn #274A)	USA (NAFTA Region 3)	200 + 200 (soil surface + post-emergence foliar) (EC)	Pre-plant BBCH 53 (V8)	30	Plants without ears	0.022 0.031	0.499 0.655	0.603 (0.521, 0.686)
			200 + 200 (pre-plant + post-emergence foliar) (EC)	Pre-plant BBCH 53 (V8)	30	Plants without ears	0.034 0.029	0.759 0.676	0.749 (0.793, 0.705)
Report: T019378-04 Study: 09SYN268A.REP Trial: C19-9452/MO - Study to GLP - Study carried out in 2009	Sweet corn (Bodacious)	USA (NAFTA Region 5)	200 + 200 (soil surface + post-emergence foliar) (EC)	Pre-plant BBCH 32 (V8)	46	Plants without ears	0.080 0.086	1.352 1.664	1.59 (1.432, 1.75)
			200 + 200 (pre-plant + post-emergence foliar) (EC)	Pre-plant BBCH 32 (V8)	46	Plants without ears	0.056 0.035	1.144 0.790	1.01 (1.2, 0.825)
Report: T019378-04 Study: 09SYN268A.REP Trial: C30-9453/IA - Study to GLP - Study carried out in 2009	Field corn (33D47)	USA (NAFTA Region 5)	200 + 200 (soil surface + post-emergence foliar) (EC)	Pre-plant BBCH 31 (V8)	45	Forage	< 0.01 < 0.01	0.146 0.114	0.14 (0.156, 0.124)
						Plants without ears	< 0.01 < 0.01	0.156 0.098	0.137 (0.166, 0.108)
			200 + 200 (pre-plant + post-emergence foliar) (EC)	Pre-plant BBCH 31 (V8)	45	Forage	0.023 0.020	0.239 0.198	0.24 (0.262, 0.218)
						Plants without ears	0.016 0.043	0.177 0.624	0.43 (0.193, 0.667)
Report: T019378-04 Study: 09SYN268A.REP Trial: C13-9454/ND - Study to GLP - Study carried out in 2009	Field corn (9618888)	USA (NAFTA Region 5)	200 + 200 (soil surface + post-emergence foliar) (EC)	Pre-plant BBCH 37 (V8)	39	Forage	< 0.01 < 0.01	0.156 0.156	0.166 (0.166, 0.166)
					45	Plants without ears	< 0.01 0.011	0.302 0.322	0.322 (0.312, 0.333)
			200 + 200	Pre-	39	Forage	< 0.01	0.177	0.187

GLP and Trial Details	Crop (Variety)	Country (Region) (Postcode)	Application		DALA	Crop Part	Residue Found (Uncorrected) (mg/kg)		
			Rate (g ai/ha) (Formulation)	Growth Stage			Bicyclopyrone eq. (SYN503780)	Bicyclopyrone eq. (CSCD686480)	Total Mean[a]
			(pre-plant + post-emergence foliar) (EC)	plant			0.011	0.177	(0.187, 0.188)
				BBCH 37 (V8)	45	Plants without ears	0.022 0.031	0.343 0.437	0.416 (0.365, 0.468)
Report: T019378-04 Study: 09SYN268A.REP Trial: C19-9455/MO - Study to GLP - Study carried out in 2009	Field corn (Pioneer 33T56)	USA (NAFTA Region 5)	200 + 200 (soil surface + post-emergence foliar) (EC)	Pre-plant BBCH 37 (V8)	40	Plants without ears	0.041 0.016	0.811 0.312	0.59 (0.852, 0.328
					47	Forage	0.038 < 0.01	0.707 0.146	0.45 (0.745, 0.156)
			200 + 200 (pre-plant + post-emergence foliar) (EC)	Pre-plant BBCH 37 (V8)	40	Plants without ears	0.016 0.041	0.333 0.728	0.559 (0.349, 0.769)
					47	Forage	0.015 0.025	0.312 0.510	0.421 (0.327, 0.515)
Report: T019378-04 Study: 09SYN268A.REP Trial: C12-9456/ND - Study to GLP - Study carried out in 2009	Field corn (INT65D85R)	USA (NAFTA Region 5)	200 + 200 (soil surface + post-emergence foliar) (EC)	Pre-plant BBCH 18 (V8)	45	Forage	< 0.01 < 0.01	0.082 0.067	0.081 (0.089, 0.074)
			200 + 200 (pre-plant + post-emergence foliar) (EC)	Pre-plant BBCH 18 (V8)	45	Forage	< 0.01 < 0.01	0.125 0.075	0.110 (0.135, 0.085)
Report: T019378-04 Study: 09SYN268A.REP Trial: C12-9457/ND - Study to GLP - Study carried out in 2009	Field corn (INT65D85R)	USA (NAFTA Region 5)	200 + 200 (soil surface + post-emergence foliar) (EC)	Pre-plant BBCH 18 (V8)	44	Forage	< 0.01 0.011	0.064 0.114	0.099 (0.074, 0.125)
			200 + 200 (pre-plant + post-emergence foliar) (EC)	Pre-plant BBCH 18 (V8)	44	Forage	< 0.01 < 0.01	0.069 0.044	0.066 (0.079, 0.054)

[a] Determined as the sum of common moieties SYN503780 (expressed as bicyclopyrone equivalents) and CSCD686480 (expressed as bicyclopyrone equivalents). LOQ – Limit of quantification-The limit of quantification (LOQ) was 0.01 mg/kg for bicyclopyrone equivalents from SYN503780 and for bicyclopyrone equivalents from CSCD686480

Thirty-three supervised residue trials on sweetcorn and maize were conducted in the USA in which samples corresponding to the definition of fodder were collected but at GAPs more critical that the US label. Bicyclopyrone was applied once or twice using the SL formulation at a rate of 200 g ai/ha. Applications were made to the soil surface pre-emergence of the crop and as a foliar spray post-emergence, or as a single post-emergence foliar spray. Samples were analysed by the common-moiety analytical method GRM030.05A, a common moiety method which includes hydrolysis of the bridge between the two rings of bicyclopyrone to release the structurally-related moieties SYN503780 and CSCD686480. In these studies, SYN503780 and CSCD686480 were corrected to bicyclopyrone equivalents. The limit of quantification (LOQ) was 0.01 mg/kg expressed as bicyclopyrone equivalents.

Table 125: Bicyclopyrone residues on corn fodder (sweetcorn and maize) from supervised trails conducted in USA

GLP and Trial Details	Crop (Variety)	Country (Region) (Postcode)	Application		DALA	Crop Part	Residue Found (Uncorrected) (mg/kg)		
			Rate (g ai/ha) (Formulation)	Growth Stage			Bicyclopyrone eq. (SYN503780)	Bicyclopyrone eq. (CSCD686480)	Total Mean[a]
GAP	Sweetcorn/ Maize	USA	50	V8/8-leaf stage	PHI: 45 (for forage)				
Report: T019378-04 Study: 09SYN253A.REP Trial: E10NC081383 - Study to GLP - Study carried out in 2008	Field corn (Garst 8377YG1/RR)	USA (EPA Region 2)	200 + 200 (soil surface + post-emergence foliar) (EC)	Pre-plant BBCH 36 (V8)	96	Stover	< 0.01 < 0.01	0.020 0.015	0.03 (0.03, 0.025)
			200 (post-emergence foliar) (EC)	BBCH 36 (V8)	96	Stover	< 0.01 < 0.01	< 0.01 < 0.01	< 0.02
Report: T019378-04 Study: 09SYN253A.REP Trial: C19MO081385 - Study to GLP - Study carried out in 2008	Field corn (Pioneer 33D47)	USA (EPA Region 5)	200 + 200 (soil surface + post-emergence foliar) (EC)	Pre-plant BBCH 36 (V8)	111	Stover	< 0.01 < 0.01	< 0.01 < 0.01	< 0.02
			200 (post-emergence foliar) (EC)	BBCH 36 (V8)	111	Stover	< 0.01 < 0.01	0.012 0.017	0.024 (0.022, 0.027)
Report: T019378-04 Study: 09SYN253A.REP Trial: C19KS081386 - Study to GLP - Study carried out in 2008	Field corn (DK 6019)	USA (EPA Region 5)	200 + 200 (soil surface + post-emergence foliar) (EC)	Pre-plant BBCH 37 (V8)	109	Stover	< 0.01 < 0.01	0.027 0.021	0.033 (0.037, 0.031)
			200 (post-emergence foliar) (EC)	BBCH 37 (V8)	109	Stover	< 0.01 < 0.01	0.016 0.024	0.029 (0.026, 0.034)
Report: T019378-04 Study: 09SYN253A.REP Trial: C01MI081387 - Study to GLP - Study carried out in 2008	Field corn (Pioneer 38N85 RR)	USA (EPA Region 5)	200 + 200 (soil surface + post-emergence foliar) (EC)	Pre-plant BBCH 19 (V8)	114	Stover	< 0.01 < 0.01	0.011 < 0.01	0.021 (0.021, 0.02)
			200 (post-emergence foliar) (EC)	BBCH 19 (V8)	114		< 0.01 < 0.01	0.018 0.017	0.027 (0.028, 0.027)
Report: T019378-04 Study: 09SYN253A.REP Trial: C01OH081388 - Study to GLP - Study carried out in 2008	Field corn (691RR2)	USA (EPA Region 5)	200 + 200 (soil surface + post-emergence foliar) (EC)	Pre-plant BBCH 18 (V8)	112	Stover	< 0.01 < 0.01	< 0.01 0.019	0.0245 (0.02, 0.029)
			200 (post-emergence foliar) (EC)	BBCH 19 (V8)	112		< 0.01 < 0.01	0.022 0.016	0.029 (0.032, 0.026)

GLP and Trial Details	Crop (Variety)	Country (Region) (Postcode)	Application		DALA	Crop Part	Residue Found (Uncorrected) (mg/kg)		
			Rate (g ai/ha) (Formulation)	Growth Stage			Bicyclopyrone eq. (SYN503780)	Bicyclopyrone eq. (CSCD686480)	Total Mean[a]
Report: T019378-04 Study: 09SYN253A.REP Trial: C08WI081389 - Study to GLP - Study carried out in 2008	Field corn (Dekalb DK43-27 (VT3))	USA (EPA Region 5)	200 + 200 (soil surface + post-emergence foliar) (EC)	Pre-plant BBCH 18 (V8)	115	Stover	< 0.01 < 0.01	0.071 0.034	0.062 (0.081, 0.044)
			200 (post-emergence foliar) (EC)	BBCH 18 (V8)	115		< 0.01 < 0.01	0.029 0.074	0.061 (0.039, 0.084)
Report: T019378-04 Study: 09SYN253A.REP Trial: C08WI081390 - Study to GLP - Study carried out in 2008	Field corn (Pioneer 37Y12)	USA (EPA Region 5)	200 + 200 (soil surface + post-emergence foliar) (EC)	Pre-plant BBCH 18 (V8)	109	Stover	< 0.01 < 0.01	0.017 0.015	0.026 (0.027, 0.025)
			200 (post-emergence foliar) (EC)	BBCH 18 (V8)	109	Stover	< 0.01 < 0.01	< 0.01 0.014	0.023 (0.02, 0.024)
Report: T019378-04 Study: 09SYN253A.REP Trial: C08WI081391 - Study to GLP - Study carried out in 2008	Field corn (H-7151CB/LL/RW)	USA (EPA Region 5)	200 + 200 (soil surface + post-emergence foliar) (EC)	Pre-plant BBCH 18 (V8)	119	Stover	< 0.01 < 0.01	< 0.01 < 0.01	0.02
			200 (post-emergence foliar) (EC)	BBCH 18 (V8)	119	Stover	< 0.01 < 0.01	0.015 0.032	0.0335 (0.025, 0.042)
Report: T019378-04 Study: 09SYN253A.REP Trial: C13ND081392 - Study to GLP - Study carried out in 2008	Field corn (238 RR2/BT)	USA (EPA Region 5)	200 + 200 (soil surface + post-emergence foliar) (EC)	Pre-plant BBCH 18 (V8)	99 107 113 120 (Maturity) 127	Stover	< 0.01 < 0.01 < 0.01 < 0.01 < 0.01 < 0.01	0.093 0.058 0.014 0.022 0.022 0.035	0.103 0.068 0.014 0.032 (0.032, 0.032) 0.045
			200 (post-emergence foliar) (EC)	BBCH 18 (V8)	99 107 113 120 (Maturity) 127	Stover	< 0.01 < 0.01 < 0.01 < 0.01 < 0.01 < 0.01	0.061 0.043 0.014 0.022 0.017 0.029	0.071 0.053 0.024 0.029 (0.032, 0.027) 0.039
Report: T019378-04 Study: 09SYN253A.REP Trial: C13ND081393 - Study to GLP - Study carried out in 2008	Field corn (238 RR2/BT)	USA (EPA Region 5)	200 + 200 (soil surface + post-emergence foliar) (EC)	Pre-plant BBCH 18 (V8)	110	Stover	< 0.01 < 0.01	0.061 0.055	0.068 (0.071, 0.065)
			200 (post-emergence foliar) (EC)	BBCH 18 (V8)	110	Stover	0.015 0.011	0.218 0.156	0.2 (0.233, 0.167)
Report: T019378-04 Study: 09SYN253A.REP Trial: E19IA081395 - Study to GLP	Field corn (B0000948 Hybrid Seed Corn)	USA (EPA Region 5)	200 + 200 (soil surface + post-emergence foliar) (EC)	Pre-plant BBCH 37 (V8)	80	Stover	< 0.01 < 0.01	0.054 0.062	0.068 (0.064, 0.072)

GLP and Trial Details	Crop (Variety)	Country (Region) (Postcode)	Application		DALA	Crop Part	Residue Found (Uncorrected) (mg/kg)		
			Rate (g ai/ha) (Formulation)	Growth Stage			Bicyclopyrone eq. (SYN503780)	Bicyclopyrone eq. (CSCD686480)	Total Mean[a]
- Study carried out in 2008			200 (post-emergence foliar) (EC)	BBCH 37 (V8)	80	Stover	< 0.01	0.055	0.0625 (0.065, 0.060)
							< 0.01	0.050	
Report: T019378-04 Study: 09SYN253A.REP Trial: E19IA081396 - Study to GLP - Study carried out in 2008	Field corn (B0000948 Hybrid Seed Corn)	USA (EPA Region 5)	200 + 200 (soil surface + post-emergence foliar) (EC)	Pre-plant BBCH 37 (V8)	88	Stover	< 0.01	0.021	0.033 (0.031, 0.035)
							< 0.01	0.025	
			200 (post-emergence foliar) (EC)	BBCH 37 (V8)	88	Stover	< 0.01	0.023	0.026 (0.033, 0.02)
							< 0.01	< 0.01	
Report: T019378-04 Study: 09SYN253A.REP Trial: E19IA081397 - Study to GLP - Study carried out in 2008	Field corn (B0000948 Hybrid Seed Corn)	USA (EPA Region 5)	200 + 200 (soil surface + post-emergence foliar) (EC)	Pre-plant BBCH 37 (V8)	87	Stover	0.012	0.042	0.043 (0.054, 0.032)
							< 0.01	0.022	
			200 (post-emergence foliar) (EC)	BBCH 37 (V8)	87	Stover	< 0.01	0.019	0.033 (0.029, 0.038)
							< 0.01	0.028	
Report: T019378-04 Study: 09SYN253A.REP Trial: E19IA081398 - Study to GLP - Study carried out in 2008	Field corn (B0000948 Hybrid Seed Corn)	USA (EPA Region 5)	200 + 200 (soil surface + post-emergence foliar) (EC)	Pre-plant BBCH 37 (V8)	87	Stover	< 0.01	0.028	0.033 (0.038, 0.029)
							< 0.01	0.019	
			200 (post-emergence foliar) (EC)	BBCH 37 (V8)	87	Stover	< 0.01	0.014	0.022 (0.024, 0.02)
							< 0.01	< 0.01	
Report: T019378-04 Study: 09SYN253A.REP Trial: C30IA081399 - Study to GLP - Study carried out in 2008	Field corn (33H27)	USA (EPA Region 5)	200 + 200 (soil surface + post-emergence foliar) (EC)	Pre-plant BBCH 18 (V8)	106	Stover	< 0.01	0.022	0.030 (0.032, 0.029)
							< 0.01	0.019	
			200 (post-emergence foliar) (EC)	BBCH 18 (V8)	106	Stover	< 0.01	0.011	0.021 (0.022, 0.02)
							< 0.01	< 0.01	
Report: T019378-04 Study: 09SYN253A.REP Trial: C30IA081400 - Study to GLP - Study carried out in 2008	Field corn (FA5614R)	USA (EPA Region 5)	200 + 200 (soil surface + post-emergence foliar) (EC)	Pre-plant BBCH 18 (V8)	76	Stover	< 0.01	0.075	0.085
					83		< 0.01	0.045	0.055
					90		< 0.01	0.250	0.260
					97 (Maturity)		< 0.01	0.031	0.036 (0.041, 0.031)
							< 0.01	0.021	
					104		< 0.01	0.022	0.032
			200 (post-emergence foliar) (EC)	BBCH 18 (V8)	76	Stover	< 0.01	0.051	0.061
					83		< 0.01	< 0.01	< 0.02
					90		< 0.01	0.034	0.044
					97 (Maturity)		< 0.01	0.023	0.027 (0.033, 0.021)
							< 0.01	0.011	
					104		< 0.01	0.020	0.03

GLP and Trial Details	Crop (Variety)	Country (Region) (Postcode)	Application		DALA	Crop Part	Residue Found (Uncorrected) (mg/kg)		
			Rate (g ai/ha) (Formulation)	Growth Stage			Bicyclopyrone eq. (SYN503780)	Bicyclopyrone eq. (CSCD686480)	Total Mean[a]
Report: T019378-04 Study: 09SYN253A.REP Trial: C30IA081401 - Study to GLP - Study carried out in 2008	Field corn (Stine 903228VT3)	USA (EPA Region 5)	200 + 200 (soil surface + post-emergence foliar) (EC)	Pre-plant BBCH 18 (V8)	83	Stover	< 0.01 < 0.01	0.025 0.022	0.033 (0.035, 0.032)
			200 (post-emergence foliar) (EC)	BBCH 18 (V8)	83	Stover	< 0.01 < 0.01	0.029 0.030	0.039 (0.039, 0.040)
Report: T019378-04 Study: 09SYN253A.REP Trial: W07TX081402 - Study to GLP - Study carried out in 2008	Field corn (DKC69-44)	USA (EPA Region 6)	200 + 200 (soil surface + post-emergence foliar) (EC)	Pre-plant BBCH 16 (V8)	115	Stover	< 0.01 < 0.01	0.101 0.024	0.072 (0.111, 0.034)
			200 (post-emergence foliar) (EC)	BBCH 16 (V8)	115	Stover	< 0.01 < 0.01	0.024 0.022	0.033 (0.034, 0.032)
Report: T019378-04 Study: 09SYN253A.REP Trial: E13TX081403 - Study to GLP - Study carried out in 2008	Popcorn (Robust 128YH F1)	USA (EPA Region 6)	200 + 200 (soil surface + post-emergence foliar) (EC)	Pre-plant BBCH 16 (V8)	124	Stover	< 0.01 < 0.01	< 0.01 < 0.01	< 0.02 (< 0.02, < 0.02)
			200 (post-emergence foliar) (EC)	BBCH 16 (V8)	124	Stover	< 0.01 < 0.01	< 0.01 < 0.01	< 0.02 (< 0.02, < 0.02)
Report: T019378-04 Study: 09SYN253A.REP Trial: W32CA081404 - Study to GLP - Study carried out in 2008	Sweet corn (Bodacious)	USA (EPA Region 10)	200 + 200 (soil surface + post-emergence foliar) (EC)	Pre-plant BBCH 18 (V8)	76	Stover	0.024	0.302	0.326
					83		< 0.01	0.125	0.135
					90		0.013	0.146	0.159
					97 (Maturity)		< 0.01 < 0.01	0.101 0.077	0.098 (0.111, 0.087)
					104		< 0.01	0.086	0.096
			200 (post-emergence foliar) (EC)	BBCH 18 (V8)	76	Stover	0.023	0.114	0.137
					83		0.019	0.114	0.133
					90		0.011	0.079	0.090
					97 (Maturity)		0.012 0.012	0.051 0.058	0.066 (0.063, 0.070)
					104		0.012	0.093	0.105
Report: T019378-04 Study: 09SYN253A.REP Trial: W15ID081405 - Study to GLP - Study carried out in 2008	Sweet corn (Honey 'N Pearl)	USA (EPA Region 11)	200 + 200 (soil surface + post-emergence foliar) (EC)	Pre-plant BBCH 18 (V8)	123	Stover	< 0.01 < 0.01	0.024 0.015	0.03 (0.034, 0.026)
			200 (post-emergence foliar) (EC)	BBCH 18 (V8)	123	Stover	< 0.01 < 0.01	< 0.01 < 0.01	< 0.02 (< 0.02, < 0.02)
Report: T019378-04 Study: 09SYN253A.REP Trial: W21OR081406 - Study to GLP	Sweet corn (Honey and Pearls)	USA (EPA Region 12)	200 + 200 (soil surface + post-emergence foliar) (EC)	Pre-plant BBCH 22 (V8)	81	Stover	< 0.01 0.017	0.094 0.114	0.117 (0.104, 0.131)

GLP and Trial Details	Crop (Variety)	Country (Region) (Postcode)	Application		DALA	Crop Part	Residue Found (Uncorrected) (mg/kg)		
			Rate (g ai/ha) (Formulation)	Growth Stage			Bicyclopyrone eq. (SYN503780)	Bicyclopyrone eq. (CSCD686480)	Total Mean[a]
- Study carried out in 2008			200 (post-emergence foliar) (EC)	BBCH 22 (V8)	81	Stover	< 0.01 < 0.01	0.010 0.042	0.036 (0.02, 0.052)
Report: T019378-04 Study: 09SYN253A.REP Trial: E19FL081407 - Study to GLP - Study carried out in 2008	Sweet corn (Awesome)	USA (EPA Region 3)	200 + 200 (soil surface + post-emergence foliar) (EC)	Pre-plant BBCH 18 (V8)	98	Stover	0.012 < 0.01	0.011 < 0.01	0.022 (0.023, 0.02)
Report: T019378-04 Study: 09SYN253A.REP Trial: C13ND081408 - Study to GLP - Study carried out in 2008	Field corn (Croplan Genetics 9618888)	USA (EPA Region 5)	200 + 200 (soil surface + post-emergence foliar) (EC)	Pre-plant BBCH 37 (V8)	110	Stover	< 0.01 < 0.01	< 0.01 0.011	0.021 (0.02,0.021)
			200 (post-emergence foliar) (EC)	BBCH 37 (V8)	110	Stover	< 0.01 < 0.01	0.010 < 0.01	0.01 (0.02, 0.02)
			200 + 200 (pre-plant + post-emergence foliar) (EC)	Pre-plant BBCH 37 (V8)	110	Stover	< 0.01 < 0.01	0.023 0.016	0.03 (0.033, 0.027)
Report: T019378-04 Study: 09SYN253A.REP Trial: E04PA081411 - Study to GLP - Study carried out in 2008	Field corn (Mycogen Hybrid Seed (Hybrid 2D324))	USA (EPA Region 1)	200 + 200 (soil surface + post-emergence foliar) (EC)	Pre-plant BBCH 37 (V8)	85	Stover	0.022 < 0.01	0.343 0.135	0.255 (0.365, 0.145)
			200 (post-emergence foliar) (EC)	BBCH 37 (V8)	85	Stover	< 0.01 0.015	0.198 0.260	0.241 (0.208, 0.275)
			200 + 200 (pre-plant + post-emergence foliar) (EC)	Pre-plant BBCH 37 (V8)	85	Stover	0.016 0.019	0.291 0.343	0.331 (0.301, 0.362)
Report: T019378-04 Study: 09SYN253A.REP Trial: E04PA081412 - Study to GLP - Study carried out in 2008	Sweet corn (Mirai 421 W Insect Guard F1)	USA (EPA Region 1)	200 + 200 (soil surface + post-emergence foliar) (EC)	Pre-plant BBCH 35 (V8)	85	Stover	< 0.01 < 0.01	0.057 0.038	0.057 (0.067, 0048)
			200 (post-emergence foliar) (EC)	BBCH 35 (V8)	85	Stover	< 0.01 < 0.01	0.064 0.057	0.070 (0.074, 0.067)
			200 + 200	Pre-	85	Stover	< 0.01	0.045	0.064

GLP and Trial Details	Crop (Variety)	Country (Region) (Postcode)	Application		DALA	Crop Part	Residue Found (Uncorrected) (mg/kg)		
			Rate (g ai/ha) (Formulation)	Growth Stage			Bicyclopyrone eq. (SYN503780)	Bicyclopyrone eq. (CSCD686480)	Total Mean[a]
			(pre-plant + post-emergence foliar) (EC)	plant BBCH 35 (V8)			< 0.01	0.063	(0.055, 0.073)
Report: T019378-04 Study: 09SYN268A.REP Trial: E15-9451/FL - Study to GLP - Study carried out in 2009	Sweet corn (Hybrid Sweet Corn #274A)	USA (NAFTA Region 3)	200 + 200 (soil surface + post-emergence foliar) (EC)	Pre-plant BBCH 53 (V8)	58	Stover	0.016 0.012	0.302 0.250	0.29 (0.308, 0.272)
			200 + 200 (pre-plant + post-emergence foliar) (EC)	Pre-plant BBCH 53 (V8)	58		< 0.01 < 0.01	0.187 0.067	0.137 (0.197, 0.077)
Report: T019378-04 Study: 09SYN268A.REP Trial: C19-9452/MO - Study to GLP - Study carried out in 2009	Sweet corn (Bodacious)	USA (NAFTA Region 5)	200 + 200 (soil surface + post-emergence foliar) (EC)	Pre-plant BBCH 32 (V8)	110	Stover	< 0.01 < 0.01	0.125 0.187	0.166 (0.135, 0.197)
			200 + 200 (pre-plant + post-emergence foliar) (EC)	Pre-plant BBCH 32 (V8)	110		< 0.01 < 0.01	< 0.01 0.086	0.058 (0.02, 0.096)
Report: T019378-04 Study: 09SYN268A.REP Trial: C30-9453/IA - Study to GLP - Study carried out in 2009	Field corn (33D47)	USA (NAFTA Region 5)	200 + 200 (soil surface + post-emergence foliar) (EC)	Pre-plant BBCH 31 (V8)	111	Stover	< 0.01 < 0.01	0.035 0.038	0.046 (0.045, 0.048)
			200 + 200 (pre-plant + post-emergence foliar) (EC)	Pre-plant BBCH 31 (V8)	111	Stover	< 0.01 < 0.01	0.052 0.045	0.058 (0.062, 0.055)
Report: T019378-04 Study: 09SYN268A.REP Trial: C13-9454/ND - Study to GLP - Study carried out in 2009	Field corn (9618888)	USA (NAFTA Region 5)	200 + 200 (soil surface + post-emergence foliar) (EC)	Pre-plant BBCH 37 (V8)	104	Stover	< 0.01 < 0.01	0.025 0.038	0.041 (0.035, 0.048)
			200 + 200 (pre-plant + post-emergence foliar) (EC)	Pre-plant BBCH 37 (V8)	104	Stover	< 0.01 < 0.01	0.096 0.098	0.107 (0.106, 0.108)
Report: T019378-04 Study: 09SYN268A.REP Trial: C19-9455/MO - Study to GLP	Field corn (Pioneer 33T56)	USA (NAFTA Region 5)	200 + 200 (soil surface + post-emergence foliar) (EC)	Pre-plant BBCH 37 (V8)	94	Stover	0.01 < 0.01	0.135 0.096	0.125 (0.145, 0.106)

GLP and Trial Details	Crop (Variety)	Country (Region) (Postcode)	Application		DALA	Crop Part	Residue Found (Uncorrected) (mg/kg)		
			Rate (g ai/ha) (Formulation)	Growth Stage			Bicyclopyrone eq. (SYN503780)	Bicyclopyrone eq. (CSCD686480)	Total Mean[a]
- Study carried out in 2009			200 + 200 (pre-plant + post-emergence foliar) (EC)	Pre-plant BBCH 37 (V8)	94	Stover	< 0.01 < 0.01	0.096 0.094	0.105 (0.106, 0.104)
Report: T019378-04 Study: 09SYN268A.REP Trial: C12-9456/ND - Study to GLP - Study carried out in 2009	Field corn (INT65D85R)	USA (NAFTA Region 5)	200 + 200 (soil surface + post-emergence foliar) (EC)	Pre-plant BBCH 18 (V8)	109	Stover	< 0.01 < 0.01	0.028 0.038	0.043 (0.038, 0.048)
			200 + 200 (pre-plant + post-emergence foliar) (EC)	Pre-plant BBCH 18 (V8)	109	Stover	< 0.01 < 0.01	0.031 0.035	0.043 (0.041, 0.045)
Report: T019378-04 Study: 09SYN268A.REP Trial: C12-9457/ND - Study to GLP - Study carried out in 2009	Field corn (INT65D85R)	USA (NAFTA Region 5)	200 + 200 (soil surface + post-emergence foliar) (EC)	Pre-plant BBCH 18 (V8)	105	Stover	< 0.01 < 0.01	0.090 0.104	0.107 (0.100, 0.114)
			200 + 200 (pre-plant + post-emergence foliar) (EC)	Pre-plant BBCH 18 (V8)	105	Stover	< 0.01 0.018	0.146 0.208	0.191 (0.156, 0.226)

[a] Determined as the sum of common moieties SYN503780 (expressed as bicyclopyrone equivalents) and CSCD686480 (expressed as bicyclopyrone equivalents). LOQ – Limit of quantification-The limit of quantification (LOQ) was 0.01 mg/kg for bicyclopyrone equivalents from SYN503780 and for bicyclopyrone equivalents from CSCD686480

Wheat forage, hay and straw

Thirty-three trials have been conducted on wheat in the USA and Canada. Each trial contained two treated plots. The EC formulation of bicyclopyrone, were applied once at a rate equivalent to 50 g ai/ha to each treated plot. One plot was treated 30 days before normal harvest of forage and hay and a second plot was treated 60 days before normal harvest of straw. The common moiety analytical method GRM030.05A (in the Canadian study, GRM030.05B was used only for the calculation of final residues expressed as bicyclopyrone) was used for the determination of residues of bicyclopyrone in wheat. The limit of quantification (LOQ) in the US study was 0.005 mg/kg for SYN503780 or CSCD686480 expressed as bicyclopyrone equivalents, whereas in the Canadian study the limits of quantification were 0.0050 mg/kg for SYN503780 and 0.0054 mg/kg for CSCD686480 expressed as bicyclopyrone equivalents.

Table 126 Bicyclopyrone residue on wheat forage from supervised trails conducted in USA and Canada

GLP and Trial Details	Crop (Variety)	Country (Region) (Postcode)	Application Rate (g ai/ha) (Formulation)	Growth Stage at Application	PHI (days)	Crop Part	Residue Found (Uncorrected, mg/kg)		
							Bicyclopyrone eq. (SYN503780)	Bicyclopyrone eq. (CSCD686480)	Total Mean[s]
GAP	Wheat	USA	50	30 DBH	30	-	-	-	-
Report: TK0021323 Study: TK0021323 Trial: TK0021323-01 - Study to GLP - Study carried out in 2012	Wheat (Pioneer 26R12)	USA (NAFTA/Region 2)	50 (EC)	BBCH 24-26 30 DBH	30	Forage	< 0.005, < 0.005	< 0.005, < 0.005	< 0.01 (< 0.01, < 0.01)
Report: TK0021323 Study: TK0021323 Trial: TK0021323-02 - Study to GLP - Study carried out in 2012	Wheat (Oakes)	USA (NAFTA/Region 4)	52 (EC)	BBCH 28-30 30 DBH	27	Forage	0.0109, 0.0111	0.0661, 0.0634	0.076 (0.0769, 0.0746)
Report: TK0021323 Study: TK0021323 Trial: TK0021323-03 - Study to GLP - Study carried out in 2012	Wheat (Armour)	USA (NAFTA/Region 5)	50 (EC)	BBCH 1-15	28	Forage	0.0223, 0.0244	0.0653, 0.0661	0.089 (0.0876, 0.0905)
Report: TK0021323 Study: TK0021323 Trial: TK0021323-04 - Study to GLP - Study carried out in 2012	Wheat (Croplan 9201)	USA (NAFTA/Region 5)	52 (EC)	BBCH 28-30	21	Forage	0.0203, 0.0207	0.0312, 0.0309	0.0516, 0.0517
					25		0.0118, 0.0118	0.0191, 0.0191	0.0310, 0.0310
					30		0.0077, 0.0115	0.0115, 0.0177	0.024 (0.0192, 0.0292)
					35		0.0071, 0.0063	0.0109, 0.0092	0.0180, 0.0155
					39		0.0052, 0.0058	0.0065, 0.0070	0.0117, 0.0127
Report: TK0021323 Study: TK0021323 Trial: TK0021323-05 - Study to GLP - Study carried out in 2012	Wheat (Faller)	USA (NAFTA/Region 5)	50 (EC)	BBCH 13-30 30 DBH	31	Forage	< 0.005, < 0.005	< 0.005, < 0.005	< 0.01 (< 0.01, < 0.01)
Report: TK0021323 Study: TK0021323 Trial: TK0021323-06 - Study to GLP - Study carried out in 2012	Wheat (Beretta)	USA (NAFTA/Region 5)	50 (EC)	BBCH 27-30 30 DBH	27	Forage	0.0149, 0.0136	0.0306, 0.0303	0.045 (0.0455, 0.0439)
Report: TK0021323 Study: TK0021323 Trial: TK0021323-07 - Study to GLP - Study carried out in 2012	Wheat (Divide)	USA (NAFTA/Region 7)	52 (EC)	BBCH 20-21 30 DBH	20	Forage	0.00792, 0.00816	0.0316, 0.0369	0.0395, 0.0451
					24		< 0.005, < 0.005	0.0347, 0.0177	0.0396, 0.202
					29		< 0.005, < 0.005	0.0107, 0.0107	0.013 (0132, 0.0132)
					35		< 0.005, < 0.005	0.0138, < 0.005	0.0188, < 0.005
					40		< 0.005, < 0.005	0.0063, 0.0061	< 0.005, < 0.005

GLP and Trial Details	Crop (Variety)	Country (Region) (Postcode)	Application Rate (g ai/ha) (Formulation)	Growth Stage at Application	PHI (days)	Crop Part	Residue Found (Uncorrected, mg/kg)		
							Bicyclopyrone eq. (SYN503780)	Bicyclopyrone eq. (CSCD686480)	Total Mean[s]
Report: TK0021323 Study: TK0021323 Trial: TK0021323-08 - Study to GLP - Study carried out in 2012	Wheat (TAM 304)	USA (NAFTA/Region 6)	52 (EC)	BBCH 21-23 30 DBH	31	Forage	0.213, 0.184	0.151, 0.133	0.340 (0.363, 0.218)
Report: TK0021323 Study: TK0021323 Trial: TK0021323-09 - Study to GLP - Study carried out in 2012	Wheat (Traverse)	USA (NAFTA/Region 7)	50 (EC)	BBCH 30-31 30 DBH	30	Forage	< 0.005, < 0.005	0.00696, 0.00812	0.013 (0.0120, 0.0131)
Report: TK0021323 Study: TK0021323 Trial: TK0021323-10 - Study to GLP - Study carried out in 2012	Wheat (Glenn)	USA (NAFTA/Region 7)	50 (EC)	BBCH 20-21 30 DBH	29	Forage	< 0.005, < 0.005	0.0127, 0.0149	0.019 (0.0177, 0.0199)
Report: TK0021323 Study: TK0021323 Trial: TK0021323-11 - Study to GLP - Study carried out in 2012	Wheat (Faller)	USA (NAFTA/Region 7)	49 (EC)	BBCH 14 30 DBH	30	Forage	< 0.005, < 0.005	< 0.005, < 0.005	< 0.01 (< 0.01, < 0.01)
Report: TK0021323 Study: TK0021323 Trial: TK0021323-12 - Study to GLP - Study carried out in 2012	Wheat (Prosper)	USA (NAFTA/Region 7)	52 (EC)	BBCH 20-21 30 DBH	29	Forage	0.00502, < 0.005	0.00863, 0.00612	0.012 (0.0137, 0.0111)
Report: TK0021323 Study: TK0021323 Trial: TK0021323-13 - Study to GLP - Study carried out in 2012	Wheat (Duster)	USA (NAFTA/Region 8)	63 (EC)	BBCH 29-30 30 DBH	30	Forage	0.0191, 0.0216	0.0584, 0.0648	0.082 (0.0775, 0.0864)
Report: TK0021323 Study: TK0021323 Trial: TK0021323-14 - Study to GLP - Study carried out in 2012	Wheat (Duster)	USA (NAFTA/Region 8)	52 (EC)	BBCH 31-32	21	Forage	ND, 0.0243	0.0405, 0.0375	0.0429, 0.0617
					26		0.0142, 0.0165	0.0266, 0.0272	0.0408, 0.0437
					30		< 0.005, 0.00561	0.0200, 0.0198	0.025 (0.0250, 0.0254)
					25		< 0.005, < 0.005	0.0117, 0.0109	0.0167, 0.0159
					40		< 0.005, < 0.005	0.00664, 0.00570	0.0116, 0.0107

GLP and Trial Details	Crop (Variety)	Country (Region) (Postcode)	Application Rate (g ai/ha) (Formulation)	Growth Stage at Application	PHI (days)	Crop Part	Residue Found (Uncorrected, mg/kg)		
							Bicyclopyrone eq. (SYN503780)	Bicyclopyrone eq. (CSCD686480)	Total Mean[s]
Report: TK0021323 Study: TK0021323 Trial: TK0021323-15 - Study to GLP - Study carried out in 2012	Wheat (Blend)	USA (NAFTA/Region 8)	50 (EC)	BBCH 21-29 30 DBH	28	Forage	0.136, 0.125	0.162, 0.125	0.274 (0.298, 0.250)
Report: TK0021323 Study: TK0021323 Trial: TK0021323-16 - Study to GLP - Study carried out in 2012	Wheat (Tam 111 Hard Red Winter)	USA (NAFTA/Region 8)	52 (EC)	BBCH 24-30 30 DBH	30	Forage	< 0.005, 0.0197	< 0.005, 0.0252	0.025 (ND, 0.0449)
Report: TK0021323 Study: TK0021323 Trial: TK0021323-17 - Study to GLP - Study carried out in 2012	Wheat (Coronado)	USA (NAFTA/Region 8)	48 (EC)	BBCH 34-35 30 DBH	27	Forage	0.0761, 0.0669	0.110, 0.0952	0.174 (0.187, 0.162)
Report: TK0021323 Study: TK0021323 Trial: TK0021323-18 - Study to GLP - Study carried out in 2012	Wheat (Stephens)	USA (NAFTA/Region 11)	50 (EC)	BBCH 32-34 30 DBH	29	Forage	0.00741, 0.00735	0.0127, 0.0122	0.020 (0.0201, 0.0196)
Report: TK0021323 Study: TK0021323 Trial: TK0021323-19 - Study to GLP - Study carried out in 2012	Wheat (Willcross 748 SRW)	USA (NAFTA/Region 5)	52 (EC)	BBCH 31 30 DBH	30	Forage	0.00836, 0.0107	0.0131, 0.0170	0.025 (0.0215, 0.0276)
Report: TK0021323 Study: TK0021323 Trial: TK0021323-20 - Study to GLP - Study carried out in 2012	Wheat (Duster)	USA (NAFTA/Region 6)	49 (EC)	BBCH 28-30 30 DBH	31	Forage	0.00915, 0.00978	0.0508, 0.0570	0.063 (0.0600, 0.0668)
Report: TK0044065 Study: TK0044065 Trial: T474 - Study to GLP - Study carried out in 2013	Wheat (Shaw VB)	Canada (NAFTA/ Region 7)	49.3 (EC)	BBCH 23	31	Forage	< 0.0050, < 0.0050	< 0.0054, < 0.0054	0.01 (< 0.0104, < 0.0104)
Report: TK0044065 Study: TK0044065 Trial: T475 - Study to GLP - Study carried out in 2013	Wheat (Unity)	Canada (NAFTA/ Region 7)	51.2 (EC)	BBCH 23	31	Forage	0.0092, 0.0057	0.02, 0.013	0.024 (0.0292, 0.0187)

GLP and Trial Details	Crop (Variety)	Country (Region) (Postcode)	Application Rate (g ai/ha) (Formulation)	Growth Stage at Application	PHI (days)	Crop Part	Residue Found (Uncorrected, mg/kg)		
							Bicyclopyrone eq. (SYN503780)	Bicyclopyrone eq. (CSCD686480)	Total Mean[s]
Report: TK0044065 Study: TK0044065 Trial: T476 - Study to GLP - Study carried out in 2013	Wheat (AC Cranberry)	Canada (NAFTA/ Region 7A)	48.6 (EC)	BBCH 13-14	29	Forage	< 0.0050, < 0.0050	0.0062, < 0.0054	0.011 (< 0.0112, <LOQ)
Report: TK0044065 Study: TK0044065 Trial: T477 - Study to GLP - Study carried out in 2013	Wheat (Harvest)	Canada (NAFTA/ Region 14)	49.3 (EC)	BBCH 13	30	Forage	< 0.0050, < 0.0050	< 0.0054, < 0.0054	0.01 (< 0.0104, < 0.0104)
Report: TK0044065 Study: TK0044065 Trial: T478 - Study to GLP - Study carried out in 2013	Wheat (AC Cranberry)	Canada (NAFTA/ Region14)	51.0 (EC)	BBCH 13-22	31	Forage	< 0.0050, < 0.0050	0.0083, 0.0085	0.013 (0.0133, 0.0135)
Report: TK0044065 Study: TK0044065 Trial: T479 - Study to GLP - Study carried out in 2013	Wheat (Unity VB)	Canada (NAFTA/ Region 14)	51.0 (EC)	BBCH 13-14	31	Forage	< 0.0050, < 0.0050	< 0.0054, < 0.0054	0.01 (< 0.0104, < 0.0104)
Report: TK0044065 Study: TK0044065 Trial: T480 - Study to GLP - Study carried out in 2013	Wheat (Shaw)	Canada (NAFTA/ Region 14)	49.9 (EC)	BBCH 13-14	30	Forage	< 0.0050, < 0.0050	< 0.0054, < 0.0054	0.01 (< 0.0104, < 0.0104)
Report: TK0044065 Study: TK0044065 Trial: T481 - Study to GLP - Study carried out in 2013	Wheat (Shaw)	Canada (NAFTA/ Region 14)	52.5 (EC)	BBCH 12-13	30	Forage	< 0.0050, < 0.0050	< 0.0054, < 0.0054	0.01 (< 0.0104, < 0.0104)
Report: TK0044065 Study: TK0044065 Trial: T482 - Study to GLP - Study carried out in 2013	Wheat (Harvest)	Canada (NAFTA/ Region 14)	51.1 (EC)	BBCH 13-14	29	Forage	< 0.0050, < 0.0050	< 0.0054, < 0.0054	0.01 (< 0.0104, < 0.0104)
Report: TK0044065 Study: TK0044065 Trial: T483 - Study to GLP - Study carried out in 2013	Wheat (Harvest)	Canada (NAFTA/ Region 14)	52.1 (EC)	BBCH 12-14	29	Forage	< 0.0050, < 0.0050	< 0.0054, < 0.0054	0.01 (< 0.0104, < 0.0104)

GLP and Trial Details	Crop (Variety)	Country (Region) (Postcode)	Application Rate (g ai/ha) (Formulation)	Growth Stage at Application	PHI (days)	Crop Part	Residue Found (Uncorrected, mg/kg)		
							Bicyclopyrone eq. (SYN503780)	Bicyclopyrone eq. (CSCD686480)	Total Mean[s]
Report: TK0044065 Study: TK0044065 Trial: T484 - Study to GLP - Study carried out in 2013	Wheat (Harvest)	Canada (NAFTA/ Region 14)	51.6 (EC)	BBCH 12-14	31	Forage	< 0.0050, < 0.0050	< 0.0054, 0.0056	0.011 (< 0.0104, 0.0106)
Report: TK0044065 Study: TK0044065 Trial: T485 - Study to GLP - Study carried out in 2013	Wheat (Vesper VB)	Canada (NAFTA/ Region 14)	49.8 (EC)	BBCH 13-14	21	Forage	< 0.0050	0.0099	0.0149
					25		< 0.0050	0.0086	0.0136
					30		< 0.0050, < 0.0050	< 0.0054, 0.0056	0.011 (< 0.0104, 0.0106)
					35		< 0.0050	< 0.0054	< 0.0104
					39		< 0.0050	< 0.0054	< 0.0104
Report: TK0044065 Study: TK0044065 Trial: T486 - Study to GLP - Study carried out in 2013	Wheat (Unity VB)	Canada (NAFTA/ Region 14)	52.5 (EC)	BBCH 13-14 (majority 14)	20	Forage	< 0.0050	0.0092	0.0142
					25		< 0.0050	< 0.0054	< 0.0104
					30		< 0.0050, < 0.0050	< 0.0054, 0.0056	0.011 (< 0.0104, 0.0106)
					35		< 0.0050	< 0.0054	< 0.0104
					40		< 0.0050	< 0.0054	< 0.0104

[a] Determined as the sum of common moieties SYN503780 (expressed as bicyclopyrone equivalents) and CSCD686480 (expressed as bicyclopyrone equivalents).

LOQ – Limit of quantification-The limit of quantification (LOQ) was 0.0050 mg/kg for bicyclopyrone equivalents from SYN503780 and 0.0054 mg/kg for bicyclopyrone equivalents from CSCD686480 in the Canadian study and 0.005 mg/kg for both analytes in the USA study.

DBH = Days Before Harvest

Residues in All Untreated Samples (controls) were <LOQ (< 0.005 mg/kg for SYN503780 and CSCD686480 expressed as bicyclopyrone equivalents).

Total Residues = Sum of SYN503780 and CSCD686480 expressed as bicyclopyrone equivalents (LOQ = 0.01 mg/kg).

Table 127 Bicyclopyrone residues on wheat hay from supervised trails conducted in USA and Canada

GLP and Trial Details	Crop (Variety)	Country (Region) (Postcode)	Application		DALA	Crop Part	Residue Found (Uncorrected, mg/kg)		
			Rate (g ai/ha) (Formulation)	Growth Stage			Bicyclopyrone eq. (SYN503780)	Bicyclopyrone eq. (CSCD686480)	Total Mean[a]
GAP	Wheat	USA	50	30 DBH	PHI: 30	-	-	-	-
Report: TK0021323 Study: TK0021323 Trial: TK0021323-01 - Study to GLP - Study carried out in 2012	Wheat (Pioneer 26R12)	USA (NAFTA/Region 2)	50 (EC)	BBCH 24-26 30 DBH	29	Hay	0.00552, 0.00572	0.00612, 0.00677	0.012 (0.0116, 0.0125)
Report: TK0021323 Study: TK0021323 Trial: TK0021323-02 - Study to GLP - Study	Wheat (Oakes)	USA (NAFTA/Region 4)	52 (EC)	BBCH 28-30 30 DBH	27	Hay	0.0143, 0.0149	0.0787, 0.0758	0.092 (0.0930, 0.0906)

GLP and Trial Details	Crop (Variety)	Country (Region) (Postcode)	Application		DALA	Crop Part	Residue Found (Uncorrected, mg/kg)		
			Rate (g ai/ha) (Formulation)	Growth Stage			Bicyclopyrone eq. (SYN503780)	Bicyclopyrone eq. (CSCD686480)	Total Mean[a]
carried out in 2012									
Report: TK0021323 Study: TK0021323 Trial: TK0021323-03 - Study to GLP - Study carried out in 2012	Wheat (Armour)	USA (NAFTA/Region 5)	50 (EC)	BBCH 1-15	28	Hay	0.0375, 0.0450	0.152, 0.168	0.201 (0.190, 0.213)
Report: TK0021323 Study: TK0021323 Trial: TK0021323-04 - Study to GLP - Study carried out in 2012	Wheat (Croplan 9201)	USA (NAFTA/Region 5)	52 (EC)	BBCH 28-30	21 25 30 35 39	Hay	0.0285, 0.0295 0.0220, 0.0192 0.0187, 0.0163 0.0138, 0.0143 0.0116, 0.0124	0.0362, 0.0337 0.0273, 0.0217 0.0309, 0.0274 0.0236, 0.0212 0.0175, 0.0186	0.0647, 0.0632 0.0492, 0.0409 0.047 (0.0496, 0.0437) 0.0374, 0.0355 0.0291, 0.0310
Report: TK0021323 Study: TK0021323 Trial: TK0021323-05 - Study to GLP - Study carried out in 2012	Wheat (Faller)	USA (NAFTA/Region 5)	50 (EC)	BBCH 13-30 30 DBH	31	Hay	0.00511, 0.00598	<LOQ ,<LOQ	0.011 (0.0101, 0.0110)
Report: TK0021323 Study: TK0021323 Trial: TK0021323-06 - Study to GLP - Study carried out in 2012	Wheat (Beretta)	USA (NAFTA/Region 5)	50 (EC)	BBCH 27-30 30 DBH	27	Hay	0.0360, 0.0363	0.0779, 0.0759	0.113 (0.114, 0.112)
Report: TK0021323 Study: TK0021323 Trial: TK0021323-07 - Study to GLP - Study carried out in 2012	Wheat (Divide)	USA (NAFTA/Region 7)	52 (EC)	BBCH 20-21 30 DBH	20 24 29 35 40	Hay	NA, NA < 0.005, < 0.005 < 0.005, < 0.005 < 0.005, < 0.005 < 0.005, < 0.005	NA, NA 0.0497, 0.0645 0.0189, 0.0204 0.0156, 0.0168 0.0112, 0.0136	NA, NA 0.0547, 0.0695 0.025 (0.0239, 0.0254) 0.0206, 0.0218 0.0162, 0.0176
Report: TK0021323	Wheat	USA	52	BBCH 21-23	31	Hay	0.296, 0.282	0.226, 0.210	0.507

GLP and Trial Details	Crop (Variety)	Country (Region) (Postcode)	Application		DALA	Crop Part	Residue Found (Uncorrected, mg/kg)		
			Rate (g ai/ha) (Formulation)	Growth Stage			Bicyclopyrone eq. (SYN503780)	Bicyclopyrone eq. (CSCD686480)	Total Mean[a]
Study: TK0021323 Trial: TK0021323-08 - Study to GLP - Study carried out in 2012	(TAM 304)	(NAFTA/Region 6)	(EC)	30 DBH					(0.522, 0.492)
Report: TK0021323 Study: TK0021323 Trial: TK0021323-09 - Study to GLP - Study carried out in 2012	Wheat (Traverse)	USA (NAFTA/Region 7)	50 (EC)	BBCH 30-31 30 DBH	30	Hay	0.00689, 0.00730	0.0209, 0.0237	0.029 (0.0278, 0.0310)
Report: TK0021323 Study: TK0021323 Trial: TK0021323-10 - Study to GLP - Study carried out in 2012	Wheat (Glenn)	USA (NAFTA/Region 7)	50 (EC)	BBCH 20-21 30 DBH	29	Hay	0.00708, < 0.005	0.0324, 0.0246	0.035 (0.0395, 0.0296)
Report: TK0021323 Study: TK0021323 Trial: TK0021323-11 - Study to GLP - Study carried out in 2012	Wheat (Faller)	USA (NAFTA/Region 7)	49 (EC)	BBCH 14 30 DBH	30	Hay	< 0.005, < 0.005	0.0148, 0.0127	0.019 (0.0198, 0.0177)
Report: TK0021323 Study: TK0021323 Trial: TK0021323-12 - Study to GLP - Study carried out in 2012	Wheat (Prosper)	USA (NAFTA/Region 7)	52 (EC)	BBCH 20-21 30 DBH	29	Hay	0.00731, 0.00647	0.0152, 0.0110	0.02 (0.0225, 0.0175)
Report: TK0021323 Study: TK0021323 Trial: TK0021323-13 - Study to GLP - Study	Wheat (Duster)	USA (NAFTA/Region 8)	63 (EC)	BBCH 29-30 30 DBH	30	Hay	0.0439, 0.0493	0.122, 0.137	0.176 (0.166, 0.187)

GLP and Trial Details	Crop (Variety)	Country (Region) (Postcode)	Application		DALA	Crop Part	Residue Found (Uncorrected, mg/kg)		
			Rate (g ai/ha) (Formulation)	Growth Stage			Bicyclopyrone eq. (SYN503780)	Bicyclopyrone eq. (CSCD686480)	Total Mean[a]
carried out in 2012									
Report: TK0021323 Study: TK0021323 Trial: TK0021323-14 - Study to GLP - Study carried out in 2012	Wheat (Duster)	USA (NAFTA/Region 8)	52 (EC)	BBCH 31-32	21 26 30 25 40	Hay	0.0806, 0.0840 0.0437, 0.0325 0.0104, 0.0121 0.00658, 0.00725 0.00732, 0.0116	0.104, 0.113 0.0713, 0.0697 0.0494, 0.0537 0.0316, 0.0355 0.0290, 0.0351	0.184, 0.197 0.115, 0.102 0.063 (0.0598, 0.0657) 0.0382, 0.0428 0.0363, 0.0466
Report: TK0021323 Study: TK0021323 Trial: TK0021323-15 - Study to GLP - Study carried out in 2012	Wheat (Blend)	USA (NAFTA/Region 8)	50 (EC)	BBCH 21-29 30 DBH	28	Hay	0.294, 0.294	0.347, 0.389	0.662 (0.641, 0.684)
Report: TK0021323 Study: TK0021323 Trial: TK0021323-16 - Study to GLP - Study carried out in 2012	Wheat (Tam 111 Hard Red Winter)	USA (NAFTA/Region 8)	52 (EC)	BBCH 24-30 30 DBH	30	Hay	0.0306, 0.0334	0.0346, 0.0397	0.069 (0.0652, 0.0731)
Report: TK0021323 Study: TK0021323 Trial: TK0021323-17 - Study to GLP - Study carried out in 2012	Wheat (Coronado)	USA (NAFTA/Region 8)	48 (EC)	BBCH 34-35 30 DBH	27	Hay	0.161, 0.123	0.229, 0.189	0.351 (0.389, 0.312)
Report: TK0021323 Study: TK0021323 Trial: TK0021323-18 - Study to GLP - Study carried out in 2012	Wheat (Stephens)	USA (NAFTA/Region 11)	50 (EC)	BBCH 32-34 30 DBH	29	Hay	0.0209, 0.0226	0.0212, 0.0268	0.046 (0.0422, 0.0494)
Report: TK0021323 Study: TK0021323	Wheat (Willcross	USA (NAFTA/Region 5)	52	BBCH 31 30 DBH	30	Hay	0.0350, 0.0293	0.0458, 0.0373	0.074 (0.0807, 0.0667)

GLP and Trial Details	Crop (Variety)	Country (Region) (Postcode)	Application		DALA	Crop Part	Residue Found (Uncorrected, mg/kg)		
			Rate (g ai/ha) (Formulation)	Growth Stage			Bicyclopyrone eq. (SYN503780)	Bicyclopyrone eq. (CSCD686480)	Total Mean[a]
Trial: TK0021323-19 - Study to GLP - Study carried out in 2012	748 SRW)		(EC)						
Report: TK0021323 Study: TK0021323 Trial: TK0021323-20 - Study to GLP - Study carried out in 2012	Wheat (Duster)	USA (NAFTA/Region 6)	49 (EC)	BBCH 28-30 30 DBH	31	Hay	0.0145, 0.0149	0.0573, 0.0614	0.074 (0.0718, 0.0763)
Report: TK0044065 Study: TK0044065 Trial: T474 - Study to GLP - Study carried out in 2013	Wheat (Shaw VB)	Canada (NAFTA/ Region 7)	49.3 (EC)	BBCH 23	31	Hay	< 0.0050, < 0.0050	0.0076, 0.010	0.014 (0.0126, 0.015)
Report: TK0044065 Study: TK0044065 Trial: T475 - Study to GLP - Study carried out in 2013	Wheat (Unity)	Canada (NAFTA/ Region 7)	51.2 (EC)	BBCH 23	31	Hay	0.014, 0.012	0.027, 0.025	0.039 (0.041, 0.037)
Report: TK0044065 Study: TK0044065 Trial: T476 - Study to GLP - Study carried out in 2013	Wheat (AC Cranberry)	Canada (NAFTA/ Region 7A)	48.6 (EC)	BBCH 13-14	29	Hay	< 0.0050, < 0.0050	0.0062, < 0.0054	0.011 (0.0112, < 0.0104)
Report: TK0044065 Study: TK0044065 Trial: T477 - Study to GLP - Study carried out in 2013	Wheat (Harvest)	Canada (NAFTA/ Region 14)	49.3 (EC)	BBCH 13	30	Hay	< 0.0050, < 0.0050	0.0074, 0.0064	0.012 (0.0124, 0.0114)
Report: TK0044065 Study: TK0044065 Trial: T478 - Study to GLP - Study	Wheat (AC Cranberry)	Canada (NAFTA/ Region14)	51 (EC)	BBCH 13-22	31	Hay	< 0.0050, 0.0053	0.017, 0.019	0.023 (0.022, 0.0243)

GLP and Trial Details	Crop (Variety)	Country (Region) (Postcode)	Application		DALA	Crop Part	Residue Found (Uncorrected, mg/kg)		
			Rate (g ai/ha) (Formulation)	Growth Stage			Bicyclopyrone eq. (SYN503780)	Bicyclopyrone eq. (CSCD686480)	Total Mean[a]
carried out in 2013									
Report: TK0044065 Study: TK0044065 Trial: T479 - Study to GLP - Study carried out in 2013	Wheat (Unity VB)	Canada (NAFTA/ Region 14)	51 (EC)	BBCH 13-14	31	Hay	0.0066, 0.0054	0.012, 0.011	0.018 (0.0186, 0.0164)
Report: TK0044065 Study: TK0044065 Trial: T480 - Study to GLP - Study carried out in 2013	Wheat (Shaw)	Canada (NAFTA/ Region 14)	49.9 (EC)	BBCH 13-14	30	Hay	< 0.0050, 0.0051	0.0054, < 0.0054	0.011 (0.0105,< 0.0104)
Report: TK0044065 Study: TK0044065 Trial: T481 - Study to GLP - Study carried out in 2013	Wheat (Shaw)	Canada (NAFTA/ Region 14)	52.5 (EC)	BBCH 12-13	30	Hay	< 0.0050, < 0.0050	< 0.0054, < 0.0054	0.01 (< 0.0104, < 0.0104)
Report: TK0044065 Study: TK0044065 Trial: T482 - Study to GLP - Study carried out in 2013	Wheat (Harvest)	Canada (NAFTA/ Region 14)	51.1 (EC)	BBCH 13-14	29	Hay	0.0066, 0.0078	0.012, 0.015	0.021 (0.0186, 0.0228)
Report: TK0044065 Study: TK0044065 Trial: T483 - Study to GLP - Study carried out in 2013	Wheat (Harvest)	Canada (NAFTA/ Region 14)	52.1 (EC)	BBCH 12-14	29	Hay	0.0092, 0.0085	0.014, 0.014	0.023 (0.0232, 0.0225)
Report: TK0044065 Study: TK0044065 Trial: T484 - Study to GLP - Study carried out in 2013	Wheat (Harvest)	Canada (NAFTA/ Region 14)	51.6 (EC)	BBCH 12-14	31	Hay	0.0077, 0.0094	0.0097, 0.013	0.02 (0.0174, 0.0224)
Report: TK0044065 Study: TK0044065 Trial: T485 - Study to	Wheat (Vesper VB)	Canada (NAFTA/ Region 14)	49.8 (EC)	BBCH 13-14	21 25 30	Hay	0.017 0.0096 < 0.0050, < 0.0050	0.035 0.02 0.0088, 0.011	0.052 0.0296 0.015 (0.0138, 0.016)

GLP and Trial Details	Crop (Variety)	Country (Region) (Postcode)	Application Rate (g ai/ha) (Formulation)	Application Growth Stage	DALA	Crop Part	Residue Found (Uncorrected, mg/kg) Bicyclopyrone eq. (SYN503780)	Bicyclopyrone eq. (CSCD686480)	Total Mean[a]
GLP - Study carried out in 2013					35		< 0.0050	< 0.0054	< 0.0104
					39		< 0.0050	< 0.0054	< 0.0104
Report: TK0044065 Study: TK0044065 Trial: T486 - Study to GLP - Study carried out in 2013	Wheat (Unity VB)	Canada (NAFTA/ Region 14)	52.5 (EC)	BBCH 13-14 (majority 14)	20	Hay	0.011	0.031	0.042
					25		0.0063	0.016	0.223
					30		< 0.0050, < 0.0050	0.0086, 0.011	0.015 (0.0136, 0.016)
					35		< 0.0050	0.0064	0.0114
					40		< 0.0050	< 0.0054	< 0.0104

[a] Determined as the sum of common moieties SYN503780 (expressed as bicyclopyrone equivalents) and CSCD686480 (expressed as bicyclopyrone equivalents).

LOQ – Limit of quantification-The limit of quantification (LOQ) was 0.0050 mg/kg for bicyclopyrone equivalents from SYN503780 and 0.0054 mg/kg for bicyclopyrone equivalents from CSCD686480 in the Canadian study and 0.005 mg/kg for both analytes in the USA study.

DBH = Days Before Harvest

NA-Not analysed

Residues in All Untreated Samples (controls) were <LOQ (< 0.005 mg/kg for SYN503780 and CSCD686480 expressed as bicyclopyrone equivalents).

Total Residues = Sum of SYN503780 and CSCD686480 expressed as bicyclopyrone equivalents (LOQ = 0.01 mg/kg).

Table 128 Bicyclopyrone residue on wheat straw from supervised trails conducted in the USA and Canada

GLP and Trial Details	Crop (Variety)	Country (Region) (Postcode)	Application Rate (g ai/ha) (Formulation)	Growth Stage at Application	PHI (days)	Crop Part	Residue Found (Uncorrected) (bicyclopyrone equivalents, mg/kg) Bicyclopyrone eq. (SYN503780)	Bicyclopyrone eq. (CSCD686480)	Total Mean[a]
GAP	Wheat	USA	50	60 DBH	60	-	-	-	-
Report: TK0021323 Study: TK0021323 Trial: TK0021323-01 - Study to GLP - Study carried out in 2012	Wheat (Pioneer 26R12)	USA (NAFTA/Region 2)	50 (EC)	BBCH 32-.34 60 DBH	58	Straw	< 0.0050, < 0.0050	0.0472, 0.0412	0.049 0.0522, 0.0462
Report: TK0021323 Study: TK0021323 Trial: TK0021323-02 - Study to GLP - Study	Wheat (Oakes)	USA (NAFTA/Region 4)	52 (EC)	BBCH 30-32 60 DBH	60	Straw	0.0146, 0.0159	0.106, 0.117	0.127 (0.120, 0.133)

GLP and Trial Details	Crop (Variety)	Country (Region) (Postcode)	Application Rate (g ai/ha) (Formulation)	Growth Stage at Application	PHI (days)	Crop Part	Residue Found (Uncorrected) (bicyclopyrone equivalents, mg/kg)		
							Bicyclopyrone eq. (SYN503780)	Bicyclopyrone eq. (CSCD686480)	Total Mean[a]
carried out in 2012									
Report: TK0021323 Study: TK0021323 Trial: TK0021323-03 - Study to GLP - Study carried out in 2012	Wheat (Armour)	USA (NAFTA/Region 5)	49 (EC)	BBCH 31-32 60 DBH	57	Straw	0.0214, 0.0206	0.129, 0.123	0.147 (0.151, 0.144)
Report: TK0021323 Study: TK0021323 Trial: TK0021323-04 - Study to GLP - Study carried out in 2012	Wheat (Croplan 9201)	USA (NAFTA/Region 5)	52 (EC)	BBCH 45-47	49	Straw	0.0313, 0.0310	0.138, 0.137	0.169, 0.168
					54		0.0301, 0.0308	0.133, 0.143	0.163, 0.174
					58		0.0331, 0.0371	0.147, 0.177	0.198 (0.180, 0.215
					63		0.0364, 0.0328	0.184, 0.154	0.220, 0.187
					68		0.0247, 0.029	0.122, 0.127	0.147, 0.152
Report: TK0021323 Study: TK0021323 Trial: TK0021323-05 - Study to GLP - Study carried out in 2012	Wheat (Faller)	USA (NAFTA/Region 5)	50 (EC)	BBCH 45-47 60 DBH	60	Straw	0.0877, 0.0957	0.209, 0.227	0.31 (0.297, 0.323)
Report: TK0021323 Study: TK0021323 Trial: TK0021323-06 - Study to GLP - Study carried out in 2012	Wheat (Beretta)	USA (NAFTA/Region 5)	50 (EC)	BBCH 30-32 60 DBH	60	Straw	0.0155, 0.0126	0.0510, 0.0407	0.06 (0.0666, 0.0533)
Report: TK0021323 Study: TK0021323 Trial: TK0021323-07 - Study to GLP - Study carried out in 2012	Wheat (Divide)	USA (NAFTA/Region 7)	50 (EC)	BBCH 30-35	50	Straw	< 0.0050, < 0.0050	0.0344, 0.0248	0.0394, 0.0298
					55		0.00589, 0.00653	0.0614, 0.0760	0.0673, 0.0825
					59		0.00688, < 0.0050	0.112, 0.0696	0.097 (0.119, 0.0746)
					64		< 0.0050, 0.00683	0.0948, 0.110	0.0998, 0.117
					70		< 0.0050,	0.0681, 0.0585	0.0731, 0.0635

GLP and Trial Details	Crop (Variety)	Country (Region) (Postcode)	Application Rate (g ai/ha) (Formulation)	Growth Stage at Application	PHI (days)	Crop Part	Residue Found (Uncorrected) (bicyclopyrone equivalents, mg/kg)		
							Bicyclopyrone eq. (SYN503780)	Bicyclopyrone eq. (CSCD686480)	Total Mean[a]
							< 0.0050		
Report: TK0021323 Study: TK0021323 Trial: TK0021323-08 - Study to GLP - Study carried out in 2012	Wheat (TAM 304)	USA (NAFTA/Region 6)	53 (EC)	BBCH 37-51 60 DBH	60	Straw	0.0502, 0.0545	0.0832, 0.0829	0.135 (0.133, 0.137)
Report: TK0021323 Study: TK0021323 Trial: TK0021323-09 - Study to GLP - Study carried out in 2012	Wheat (Traverse)	USA (NAFTA/Region 7)	50 (EC)	BBCH 30-31 60 DBH	57	Straw	< 0.0050, < 0.0050	0.0102, 0.0108	0.016 (0.0152, 0.0158)
Report: TK0021323 Study: TK0021323 Trial: TK0021323-10 - Study to GLP - Study carried out in 2012	Wheat (Glenn)	USA (NAFTA/Region 7)	50 (EC)	BBCH 30-35 60 DBH	59	Straw	0.0276, 0.0284	0.187, 0.192	0.218 (0.215, 0.220)
Report: TK0021323 Study: TK0021323 Trial: TK0021323-11 - Study to GLP - Study carried out in 2012	Wheat (Faller)	USA (NAFTA/Region 7)	53 (EC)	BBCH 15-21 60 DBH	60	Straw	< 0.0050, < 0.0050	0.0276, 0.0239	0.031 (0.0326, 0.0289)
Report: TK0021323 Study: TK0021323 Trial: TK0021323-12 - Study to GLP - Study carried out in 2012	Wheat (Prosper)	USA (NAFTA/Region 7)	52 (EC)	BBCH 30-35 30 DBH	59	Straw	0.0211, 0.0238	0.0645, 0.0631	0.086 (0.0856, 0.0869)
Report: TK0021323	Wheat	USA	53	BBCH 32-33	62	Straw	0.0359, 0.0422	0.147, 0.162	0.194

GLP and Trial Details	Crop (Variety)	Country (Region) (Postcode)	Application Rate (g ai/ha) (Formulation)	Growth Stage at Application	PHI (days)	Crop Part	Residue Found (Uncorrected) (bicyclopyrone equivalents, mg/kg)		
							Bicyclopyrone eq. (SYN503780)	Bicyclopyrone eq. (CSCD686480)	Total Mean[a]
Study: TK0021323 Trial: TK0021323-13 - Study to GLP - Study carried out in 2012	(Duster)	(NAFTA/Region 8)	(EC)	60 DBH					(0.183, 0.205)
Report: TK0021323 Study: TK0021323 Trial: TK0021323-14 - Study to GLP - Study carried out in 2012	Wheat (Duster)	USA (NAFTA/Region 8)	52 (EC)	BBCH 35	51	Straw	0.0146, 0.0123	0.0386, 0.0363	0.0532, 0.0486
					56		0.0166, 0.0203	0.0570, 0.0577	0.0737, 0.0780
					60		0.0214, 0.0224	0.0737, 0.0704	0.094 (0.0951, 0.0927)
					65		0.0212, 0.0213	0.0696, 0.0741	0.0908, 0.0953
					70		0.0169, 0.0197	0.0764, 0.0669	0.0933, 0.0866
Report: TK0021323 Study: TK0021323 Trial: TK0021323-15 - Study to GLP - Study carried out in 2012	Wheat (Blend)	USA (NAFTA/Region 8)	48 (EC)	BBCH 31-34 60 DBH	57	Straw	0.0498, 0.0529	0.172, 0.197	0.236 (0.222, 0.249)
Report: TK0021323 Study: TK0021323 Trial: TK0021323-16 - Study to GLP - Study carried out in 2012	Wheat (Tam 111 Hard Red Winter)	USA (NAFTA/Region 8)	52 (EC)	BBCH 43-47 60 DBH	60	Straw	0.0634, 0.0564	0.119, 0.112	0.175 (0.182, 0.168)
Report: TK0021323 Study: TK0021323 Trial: TK0021323-17 - Study to GLP - Study carried out in 2012	Wheat (Coronado)	USA (NAFTA/Region 8)	50 (EC)	BBCH 34-35 60 DBH	60	Straw	0.0451, 0.0482	0.0853, 0.0926	0.136 (0.130, 0.141)
Report: TK0021323 Study:	Wheat (Stephens)	USA (NAFTA/Region	50	BBCH 71-73 60 DBH	58	Straw	0.0388, 0.0385	0.0596, 0.0567	0.098 (0.0984, 0.0982)

GLP and Trial Details	Crop (Variety)	Country (Region) (Postcode)	Application Rate (g ai/ha) (Formulation)	Growth Stage at Application	PHI (days)	Crop Part	Residue Found (Uncorrected) (bicyclopyrone equivalents, mg/kg)		
							Bicyclopyrone eq. (SYN503780)	Bicyclopyrone eq. (CSCD686480)	Total Mean[a]
TK0021323 Trial: TK0021323-18 - Study to GLP - Study carried out in 2012		11)	(EC)						
Report: TK0021323 Study: TK0021323 Trial: TK0021323-19 - Study to GLP - Study carried out in 2012	Wheat (Willcross 748 SRW)	USA (NAFTA/Region 5)	50 (EC)	BBCH 71 60 DBH	61	Straw	0.0468, 0.0424	0.0701, 0.0681	0.114 (0.117, 0.111)
Report: TK0021323 Study: TK0021323 Trial: TK0021323-20 - Study to GLP - Study carried out in 2012	Wheat (Duster)	USA (NAFTA/Region 6)	47 (EC)	BBCH 31-32 60 DBH	63	Straw	< 0.0050, < 0.0050	0.124, 0.105	0.119 (0.129, 0.110)
Report: TK0044065 Study: TK0044065 Trial: T474 - Study to GLP - Study carried out in 2013	Wheat (Shaw VB)	Canada (NAFTA/ Region 7)	50 (EC)	BBCH 51-53	61	Straw	0.072, 0.063	0.13, 0.12	0.193 (0.202, 0.183)
Report: TK0044065 Study: TK0044065 Trial: T475 - Study to GLP - Study carried out in 2013	Wheat (Unity)	Canada (NAFTA/ Region 7)	50.8 (EC)	BBCH 55-57	60	Straw	0.13, 0.093	0.18, 0.14	0.272 (0.31, 0.233)
Report: TK0044065 Study: TK0044065 Trial: T476 - Study to GLP - Study carried out in 2013	Wheat (AC Cranberry)	Canada (NAFTA/ Region 7A)	49.6 (EC)	BBCH 34-37	60	Straw	0.035, 0.031	0.084, 0.076	0.113 (0.119, 0.107)

GLP and Trial Details	Crop (Variety)	Country (Region) (Postcode)	Application Rate (g ai/ha) (Formulation)	Growth Stage at Application	PHI (days)	Crop Part	Residue Found (Uncorrected) (bicyclopyrone equivalents, mg/kg)		
							Bicyclopyrone eq. (SYN503780)	Bicyclopyrone eq. (CSCD686480)	Total Mean[a]
Report: TK0044065 Study: TK0044065 Trial: T477 - Study to GLP - Study carried out in 2013	Wheat (Harvest)	Canada (NAFTA/ Region 14)	48.9 (EC)	BBCH 33-37	60	Straw	0.0059, 0.0056	0.028, 0.026	0.033 (0.0339, 0.0316)
Report: TK0044065 Study: TK0044065 Trial: T478 - Study to GLP - Study carried out in 2013	Wheat (AC Cranberry)	Canada (NAFTA/ Region14)	52.3 (EC)	BBCH 31-33	61	Straw	< 0.0050, 0.0050	0.011, 0.015	0.018 (0.016, 0.020)
Report: TK0044065 Study: TK0044065 Trial: T479 - Study to GLP - Study carried out in 2013	Wheat (Unity VB)	Canada (NAFTA/ Region 14)	51 (EC)	BBCH 34-37	60	Straw	0.043, 0.037	0.15, 0.14	0.185 (0.193, 0.177)
Report: TK0044065 Study: TK0044065 Trial: T480 - Study to GLP - Study carried out in 2013	Wheat (Shaw)	Canada (NAFTA/ Region 14)	52.3 (EC)	BBCH 59-61	61	Straw	0.13, 0.11	0.16, 0.14	0.27 (0.290, 0.250)
Report: TK0044065 Study: TK0044065 Trial: T481 - Study to GLP - Study carried out in 2013	Wheat (Shaw)	Canada (NAFTA/ Region 14)	51.2 (EC)	BBCH 51-59	59	Straw	0.039, 0.017	0.13, 0.067	0.127 (0.169, 0.084)
Report: TK0044065 Study: TK0044065 Trial: T482 - Study to GLP - Study carried out in 2013	Wheat (Harvest)	Canada (NAFTA/ Region 14)	49.1 (EC)	BBCH 39-41	59	Straw	0.030, 0.032	0.055, 0.070	0.094 (0.085, 0.102)
Report: TK0044065 Study:	Wheat (Harvest)	Canada (NAFTA/ Region	51.5	BBCH 29-43	61	Straw	0.046, 0.055	0.095, 0.12	0.158 (0.141, 0.175)

GLP and Trial Details	Crop (Variety)	Country (Region) (Postcode)	Application Rate (g ai/ha) (Formulation)	Growth Stage at Application	PHI (days)	Crop Part	Residue Found (Uncorrected) (bicyclopyrone equivalents, mg/kg)		
							Bicyclopyrone eq. (SYN503780)	Bicyclopyrone eq. (CSCD686480)	Total Mean[a]
TK0044065 Trial: T483 - Study to GLP - Study carried out in 2013		14)	(EC)						
Report: TK0044065 Study: TK0044065 Trial: T484 - Study to GLP - Study carried out in 2013	Wheat (Harvest)	Canada (NAFTA/ Region 14)	51.7 (EC)	BBCH 49-55	60	Straw	0.038, 0.038	0.076, 0.074	0.011 (0.0114 0.0112)
Report: TK0044065 Study: TK0044065 Trial: T485 - Study to GLP - Study carried out in 2013	Wheat (Vesper VB)	Canada (NAFTA/ Region 14)	50.6 (EC)	BBCH 16, 33-37	50	Straw	0.031	0.085	0.116
					56		0.034	0.14	0.174
					60		0.024, 0.024	0.14, 0.14	0.164 (0.164, 0.164)
					65		0.017	0.17	0.187
					71		0.012	0.14	0.152
Report: TK0044065 Study: TK0044065 Trial: T486 - Study to GLP - Study carried out in 2013	Wheat (Unity VB)	Canada (NAFTA/ Region 14)	52.5 (EC)	BBCH 32-33 (majority 14)	51	Straw	0.028	0.072	0.1
					56		0.019	0.063	0.082
					61		0.035, 0.030	0.12, 0.11	0.148 (0.155, 0.14)
					65		0.033	0.13	0.163
					70		0.029	0.13	0.159

[a] Determined as the sum of common moieties SYN503780 (expressed as bicyclopyrone equivalents) and CSCD686480 (expressed as bicyclopyrone equivalents).

LOQ – Limit of quantification-The limit of quantification (LOQ) was 0.0050 mg/kg for bicyclopyrone equivalents from SYN503780 and 0.0054 mg/kg for bicyclopyrone equivalents from CSCD686480 in the Canadian study and 0.005 mg/kg for both analytes in the USA study.

Residues in All Untreated Samples (controls) were <LOQ (< 0.005 mg/kg for SYN503780 and CSCD686480 expressed as bicyclopyrone equivalents).

Total Residues = Sum of SYN503780 and CSCD686480 expressed as bicyclopyrone equivalents (LOQ = 0.01 mg/kg).

FATE OF RESIDUES IN STORAGE AND PROCESSING

In stored products

Bicyclopyrone is not intended for use in stored products.

In processing

The Meeting received information on high temperature hydrolysis of bicyclopyrone and the fate of bicyclopyrone residues during the processing of maize grains and wheat grains.

High-temperature hydrolysis

The degradation of [^{14}C] bicyclopyrone was studied under hydrolytic conditions at high temperatures in sterile aqueous buffers at pH 4, 5 and 6 for periods of up to 60 minutes so as to simulate common processing practices (pasteurization, baking/brewing/boiling/, and sterilization) (McCorquodale, and Bell, 2010, NOA449280_11094). All test samples were shielded from light with aluminium foil to eliminate possible photolysis. The concentration of bicyclopyrone was approximately 1.0 mg/L. The hydrolysis tests were conducted with [^{14}C] bicyclopyrone, and samples were prepared in duplicate for each test system.

Samples were analysed immediately at time zero (these samples were not heated). Two additional samples at pH 4 ± 0.1 were placed in an oven and maintained at 90 °C for 20 minutes, another two samples at pH 5 were placed in an oven and maintained at 100 °C for 60 minutes, and two more samples at pH 6 were placed in an autoclave and maintained at sterilizing conditions (120 °C) for 20 minutes. Radiocarbon recoveries ranged from 97.1 to 100% for all samples. Radioactivity was determined by liquid scintillation counting (LSC). The samples were quantified by radio-HPLC. Co-chromatography with authentic reference standards using radio-TLC confirmed the identification of components.. The experiments showed that bicyclopyrone was stable under hydrolytic conditions at high temperatures. No degradates were detected at any of the investigated pH and temperature ranges.

Table 129 Hydrolysis recovery under the conditions for processing simulation, ^{14}C-pyridinyl label

pH	Incubation		Representative process	Bicyclopyrone found (%)	Unidentified (%)	Recovery after incubation (% of applied)
	Temperature [ºC]	Time [min]				
4	90	20	Pasteurization	97.71 98.24	2.29 1.76	100 100
5	100	60	Baking/brewing/boiling	98.27 98.65	1.73 1.35	100 100
6	120	20	Sterilization	98.71 98.93	1.29 1.07	100 100

Table 130 Hydrolysis recovery under the conditions for processing simulation, ^{14}C- bicyclooctenone label

pH	Incubation		Representative process	Bicyclopyrone found (%)	Unidentified (%)	Recovery after incubation (% of applied)
	Temperature [ºC]	Time [min]				
4	90	20	Pasteurization	99.17 99.14	0.83 0.86	100 100
5	100	60	Baking/brewing/boiling	100 100	ND ND	100 100
6	120	20	Sterilization	99.65 99.45	0.35 0.55	100 100

ND – Not detected

Maize (Corn)

A processing study was conducted on maize in the USA to determine the potential for concentration of residues of bicyclopyrone in maize processed fractions (Oakes, 2012, EC_50019). At the test location, a single broadcast foliar application of the EC formulation containing 250 g/L bicyclopyrone was made to maize targeting 1000.7 g ai/ha (5×) of bicyclopyrone. Grains for processing were

harvested at maturity and were later processed according to simulated commercial procedures into maize processed commodities aspirated grain fraction (AGF), distillates, flour, germ, gluten, grits, hulls, meal, oil, press cake, soap stock and starch.

The maize grain RAC and processed commodity samples were analysed for residues of bicyclopyrone and its metabolites using methods GRM030.03A and GRM030.05A. Method GRM030.09A was also used in analysing grain and processed fractions. The LOQ for all analytes in all sample matrices, including processed fractions, was 0.01 mg/kg.

Table 131 Bicyclopyrone and its metabolite residues in processed commodities of maize grain from supervised trails

Processed Fraction	Bicyclopyrone SYN503780 CSAA806573	CSCD686480					CSAA589691
		Trial 1393		Trial 1399		Mean Processing Factor [a]	
		Residue (mg/kg)	Process Factor[1]	Residue (mg/kg)	Process Factor [a]		
Pre-Process Grain	Residue levels in all samples < 0.01 mg/kg	0.03 0.03 0.03	-	0.013 <LOQ 0.014	-	-	Residue levels were similar in the control and treated samples, ranging from < 0.01 to 0.05 mg/kg
AGF		<LOQ 0.02	<1× <1×	<LOQ 0.02	<1× 1.7×	1.2 ×	
Flour		<LOQ 0.03	<1× <1×	<LOQ <LOQ	<1× <1×	<1×	
Germ		<LOQ 0.01	<1× <1×	Not generated in this trial		<1×	
Gluten		<LOQ 0.01	<1× <1×	Not generated in this trial		<1×	
Grits		<LOQ 0.01	<1× <1×	<LOQ <LOQ	<1× <1×	<1×	
Hulls		<LOQ 0.05	<1 × 1.7 ×	Not generated in this trial		1.4 X	
Meal		<LOQ 0.02	<1× <1×	<LOQ <LOQ	<1× <1×	<1×	
Oil [b]		<LOQ <LOQ	<1× <1×	<LOQ <LOQ	<1× <1×	<1×	
Presscake		<LOQ 0.02	<1× <1×	Not generated in this trial		<1×	
Soapstock		<LOQ 0.01	<1× <1×	Not generated in this trial		<1×	
Starch		<LOQ <LOQ	<1× <1×	<LOQ <LOQ	<1× <1×	<1×	

[a] Processing factor = Residue in processed commodity / residues in pre-process raw commodity (RAC).For < 0.01, a value of 0.01 was used for average processing factor calculation.

[b] Theoretical processing factor for maize oil (corn oil) = 25 (OPPTS 860.1520, Table 3, based on separation into components).

Wheat

A processing study was conducted on wheat in the USA to determine the potential for concentration of residues of bicyclopyrone in wheat processed fractions (Smith, 2015, TK0021323). At the test location, a single broadcast foliar application of the EC formulation containing 37.5 g/L bicyclopyrone was made to wheat targeting 150 g ai/ha (3×) of bicyclopyrone. Grains for processing were harvested at maturity and were later processed according to simulated commercial procedures into wheat processed commodities aspirated grain fraction (AGF), bran, flour, middlings, shorts and germ.

The wheat grain RAC and processed commodity samples were analysed for residues of bicyclopyrone and its metabolites using method GRM030.05A. The LOQ for all analytes in all sample matrices, including processed fractions, was 0.005 mg/kg.

Table 132 Bicyclopyrone and its metabolites residues its processed commodities of wheat grain from supervised trails

Trial id	Matrix	Bicyclopyrone eq. (as SYN503780)	Bicyclopyrone eq. (as CSCD686480)	Total mean residues	Processing factor
TK0021323-19	Grain (RAC)	0.0397, 0.0418, 0.0396, 0.0403, 0.0398, 0.0459	0.0508, 0.0521, 0.0507, 0.0502, 0.0515, 0.0590	0.094 (0.0905, 0.0939, 0.0903, 0.0905, 0.0913, 0.105)	-
	AGF	0.0586, 0.0611	0.101, 0.108	0.165 (0.160, 0.169)	1.8 ×
	Bran	0.122, 0.0127	0.122, 0.129	0.250 (0.244, 0.256)	2.7 ×
	Flour	0.00795, 0.00666	0.0185, 0.0138	0.024 (0.0265, 0.0205)	0.26 ×
	Middlings	0.0308, 0.0319	0.0540, 0.0544	0.086 (0.0848, 0.0863)	0.91 ×
	Shorts	0.0370, 0.0354	0.0514, 0.0490	0.086 (0.0884, 0.0844)	0.91 ×
	Germ	0.0535, 0.0600	0.0664, 0.0693	0.125 (0.120, 0.129)	1.3 ×
TK0021323-20	Grain (RAC)	< 0.005, < 0.005, < 0.005, < 0.005, < 0.005, < 0.005	0.0393, 0.0430, 0.0387, 0.0404, 0.0344, 0.0333	0.043 (0.0443, 0.0480, 0.0437, 0.0454, 0.0394, 0.0383)	-
	AGF	0.00671, 0.00667	0.753, 0.756	0.762 (0.760, 0.763)	17.7 ×
	Bran	0.00741, 0.00786	0.0691, 0.0670	0.076 (0.0765, 0.0749)	1.8 ×
	Flour	< 0.005, < 0.005	0.00620, 0.00864	0.012 (0.0112, 0.0136)	0.28 ×
	Middlings	< 0.005, < 0.005	0.0149, 0.0164	0.021 (0.0199, 0.0214)	0.49 ×
	Shorts	< 0.005, < 0.005	0.0148, 0.0158	0.020 (0.0198, 0.0208)	0.47 ×
	Germ	0.00634, 0.00724	0.0561, 0.0563	0.063 (0.0624, 0.0635)	1.5 ×

In summary, the mean (or best estimated) concentration factors for bicyclopyrone (bicyclopyrone and its structurally-related metabolites determined as SYN503870 and CSCD686480 by a common moiety method) in maize aspirated grain fractions and maize hulls were 1.2 and 1.4 and in wheat aspirated grain fractions, wheat bran and wheat germ were 17.7, 2.3 and 1.4, respectively. Bicyclopyrone residues did not concentrate in any of the other processed fractions.

RESIDUES IN ANIMAL COMMODITIES

Farm animal feeding studies

The Meeting received information on lactating cow feeding study.

Lactating cows

Farm animal feeding studies are available for lactating cows. In this study by Simmons *et al*. (2012, NOA449280_50303) lactating cows (3 cows per treatment group, 1 control cow) were administered daily doses of bicyclopyrone via gelatine capsule. The dose levels of the animals were 0.15 ppm (0.5×), 0.90 ppm (3×) and 3.00 ppm (10×), over 28 consecutive days. The control cow received capsules containing no bicyclopyrone. The animal body weightS were between 1000 to 1300 kg per animal. The amounts of milk per day varied between the animals from 14 to 20 kg, with an average of 15–18 kg per day and animal.

For CSCD686480 by method GRM030.08A, the limit of quantification (LOQ) was 0.01 mg/kg (expressed as bicyclopyrone) or 0.007 mg/kg as SYN503780 or CSCD686480 in milk and

livestock Milk samples were collected twice daily and a daily composite sample made from each cow. Within 22–26 hours of the final dose all animals were sacrificed and samples of fat (composite of subcutaneous, perirenal and mesenteric), kidney, liver, and muscle (composite of loin and hind-leg) were taken. All samples were analysed for residues of bicyclopyrone, SYN503780 and tissues.

Table 133 Residue of bicyclopyrone and its metabolites in dairy cow milk and tissues

Matrix	Nominal Dose Level	Sample Event (days after start of dosing)	Bicyclopyrone [d] (mg/kg)	SYN503780[a] (mg/kg)	CSCD686480[a] (mg/kg)
Milk	Non-Treated	10	<LOQ	<LOQ	<LOQ
	10×	-1, 1, 3, 7, 10, 14, 17, 21, 24, 28	<LOQ	<LOQ	<LOQ
	3×	-1, 1, 3, 7, 10, 14, 17, 21, 24, 28	Not Analysed	Not Analysed	Not Analysed
	0.5×	-1, 1, 3, 7, 10, 14, 17, 21, 24, 28	Not Analysed	Not Analysed	Not Analysed
Fat[b]	Non-Treated	28	<LOQ	<LOQ	<LOQ
	10×	28	<LOQ	<LOQ	<LOQ
	3×	28	Not Analysed	Not Analysed	Not Analysed
	0.5×	28	Not Analysed	Not Analysed	Not Analysed
Muscle[c]	Non-Treated	28	<LOQ	<LOQ	<LOQ
	10×	28	<LOQ	<LOQ	<LOQ
	3×	28	Not Analysed	Not Analysed	Not Analysed
	0.5×	28	Not Analysed	Not Analysed	Not Analysed
Liver	Non-Treated	28	<LOQ	<LOQ	<LOQ
	10×	28	1.19	1.17	0.19
	3×	28	1.67	1.40	0.19
	0.5×	28	0.76	0.79	0.11
Kidney	Non-Treated	28	<LOQ	<LOQ	<LOQ
	10×	28	0.31	0.34	0.03
	3×	28	0.34	0.35	0.02
	0.5×	28	0.27	0.28	0.01

[a] Uncorrected SYN503780 and CSCD686480

[b] Composite of subcutaneous, perirenal and mesenteric

[c] Composite of loin and hind-leg

[d] Bicyclopyrone was analysed directly, but because analysis of the common moieties SYN5037801 and CSCD686480 is inclusive of parent material, only these moiety residue values are required for estimation of residues for risk assessment purposes.

The proposed definition of the residue in animal commodities is bicyclopyrone and its structurally-related metabolites determined as the sum of the common moieties SYN503780 and CSCD686480 (expressed as bicyclopyrone). Bicyclopyrone was analysed directly, but because analysis of the common moieties SYN5037801 and CSCD686480 is inclusive of parent material, only these moiety residue values are required for estimation of residues for risk assessment purposes. Consequently, the total bicyclopyrone equivalent residue and a transfer factor can be calculated for each tissue; these are summarised in the following table.

Table 134 Mean total bicyclopyrone residue in dairy cow milk and tissues

Matrix	Mean Dose Level (mg/kg DM Feed)	days	SYN503780 Residue (mg/kg)		CSCD686480 Residue (mg/kg)		Total Bicyclopyrone Equivalents (mg/kg)
			Measured	Bicyclopyrone Equivalents [a]	Measured	Bicyclopyrone Equivalents [b]	
Milk	3.0	-1, 1, 3, 7, 10, 14, 17, 21, 24, 28	< 0.01	< 0.01	< 0.01	< 0.01	< 0.02
Fat	3.0	28	< 0.01	< 0.01	< 0.01	< 0.01	< 0.02
Muscle	3.0	28	< 0.01	< 0.01	< 0.01	< 0.01	< 0.02

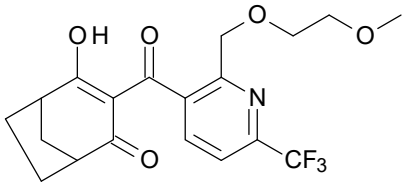
Matrix	Mean Dose Level (mg/kg DM Feed)	days	SYN503780 Residue (mg/kg)		CSCD686480 Residue (mg/kg)		Total Bicyclopyrone Equivalents (mg/kg)
			Measured	Bicyclopyrone Equivalents [a]	Measured	Bicyclopyrone Equivalents [b]	
Liver	3.0	28	0.36	0.51	0.03	0.05	0.56
	3.0	28	1.18	1.68	0.27	0.41	2.09
	3.0	28	1.98	2.83	0.28	0.42	3.25
	mean	28	1.17	1.67	0.19	0.29	1.96
	0.92	28	1.15	1.64	0.16	0.24	1.88
	0.92	28	1.49	2.13	0.17	0.26	2.38
	0.92	28	1.56	2.23	0.23	0.35	2.57
	mean	28	1.40	2.00	0.19	0.29	2.29
	0.15	28	0.66	0.94	0.09	0.13	1.08
	0.15	28	0.84	1.20	0.10	0.15	1.35
	0.15	28	0.88	1.25	0.13	0.19	1.45
	mean	28	0.79	1.13	0.11	0.17	1.30
Kidney	3.0	28	0.32	0.45	0.02	0.03	0.49
	3.0	28	0.33	0.47	0.03	0.04	0.52
	3.0	28	0.37	0.52	0.03	0.04	0.57
	mean	28	0.34	0.49	0.03	0.04	0.53
	0.92	28	0.28	0.40	0.02	0.03	0.43
	0.92	28	0.34	0.49	0.02	0.03	0.52
	0.92	28	0.42	0.60	0.03	0.04	0.65
	mean	28	0.35	0.50	0.02	0.03	0.53
	0.15	28	0.24	0.34	0.01	0.02	0.36
	0.15	28	0.27	0.39	0.01	0.02	0.40
	0.15	28	0.33	0.47	0.02	0.03	0.50
	mean	28	0.28	0.51	0.01	0.02	0.42

[a] CF for SYN503780 to bicyclopyrone = 1.43

[b] CF for CSCD686480 to bicyclopyrone = 1.51

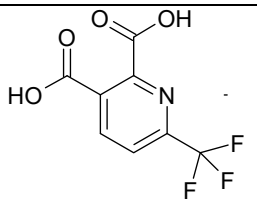
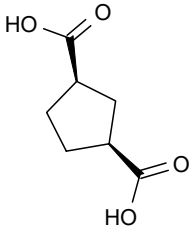
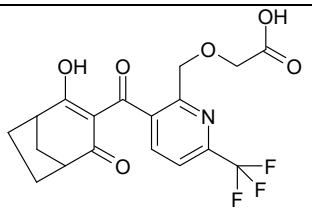
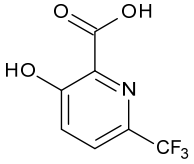
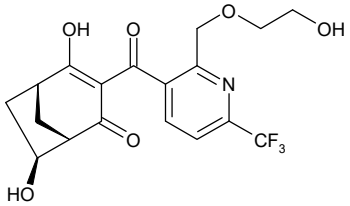
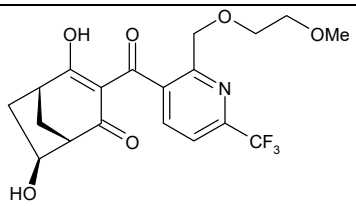
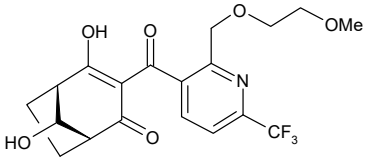
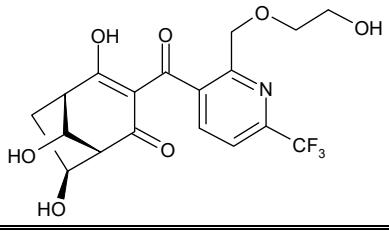
APPRAISAL

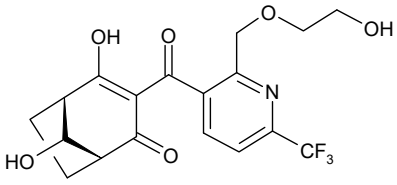
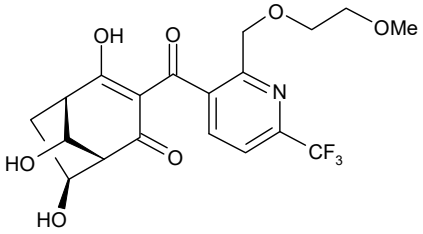
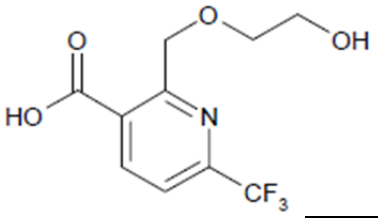
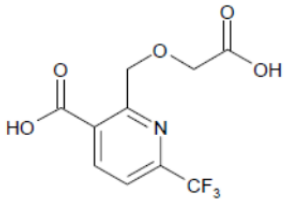
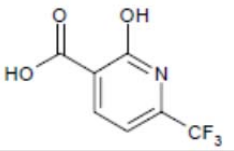
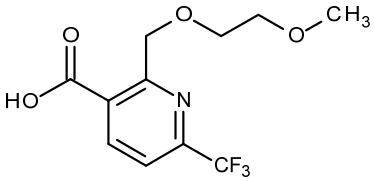
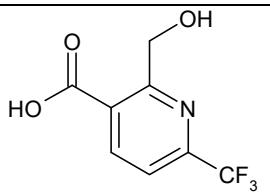
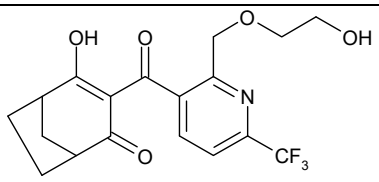
Bicyclopyrone is a selective herbicide developed for the control of broadleaf weeds and perennial grasses in corn, wheat, barley and sugar cane and is registered in a number of countries. At the 48th Session of the CCPR (2016), it was scheduled for toxicological and residue evaluation as a new compound by 2017 JMPR.



Information on the physical and chemical properties, animal and plant metabolism, environmental fate, analytical methods, storage stability, use patterns, supervised trials, processing and farm animal feeding was received by the present Meeting.

The following abbreviated names were used for the metabolites discussed below.

Compound Name/Code	Chemical name (IUPAC)	Structure	Occurrence in metabolism studies
CSCC163768 SYN504810	6-(trifluoromethyl)pyridine-2,3-dicarboxylic acid		Plants Soil Aqueous photolysis
CSAA589691 (NOA412101)	(1S,3R)-cyclopentane-1,3-dicarboxylic acid		Plants Soil Aqueous photolysis Rat cage wash
CSCD642512 (SYN545859)	2-[[3-(2-hydroxy-4-oxo-bicyclo[3.2.1]oct-2-ene-3-carbonyl)-6-(trifluoromethyl)-2-pyridyl]methoxy]acetic acid		Plants Soil
CSCD656832 (SYN545680)	3-hydroxy-6-(trifluoromethyl)pyridine-2-carboxylic acid		Plants Soil
CSCD675162	*rac*-(1R,5S,6S)-2,6-dihydroxy-3-[2-(2-hydroxyethoxymethyl)-6-(trifluoromethyl)pyridine-3-carbonyl]bicyclo[3.2.1]oct-2-en4-one		Plants Rat Goat Hen
CSCD675164	*rac*-(1R,5S,6S)-2,6-dihydroxy-3-[2-(2-methoxyethoxymethyl)-6-(trifluoromethyl)pyridine-3-carbonyl]bicyclo[3.2.1]oct-2-en-4-one		Plants Rat Goat Hen
CSCD677306	*rac*-(1S,5R)-2,8-dihydroxy-3-[2-(2-methoxyethoxymethyl)-6-(trifluoromethyl)pyridine-3-carbonyl]bicyclo[3.2.1]oct-2-en-4-one		Plants Rat Goat Hen
CSCD677692	*rac*-(1S,5R,6S)-2,6,8-trihydroxy-3-[2-(2-hydroxyethoxymethyl)-6-(trifluoromethyl)pyridine-3-carbonyl]bicyclo[3.2.1]oct-2-en-4-one		Plants Rat

Compound Name/Code	Chemical name (IUPAC)	Structure	Occurrence in metabolism studies
CSCD677693	*rac*-(1S,5R)-2,8-dihydroxy-3-[2-(2-hydroxyethoxymethyl)-6-(trifluoromethyl)pyridine-3-carbonyl]bicyclo[3.2.1]oct-2-en-4-one		Plants Rats Goat Hen
CSCD677694	*rac*-(1S,5R,6S)-2,6,8-trihydroxy-3-[2-(2-methoxyethoxymethyl)-6-(trifluoromethyl)pyridine-3-carbonyl]bicyclo[3.2.1]oct-2-en-4-one		Plants
CSCD686480 (SYN545910)	2-(2-hydroxyethoxymethyl)-6-(trifluoromethyl)pyridine-3-carboxylic acid		Plants Goat
CSCD686481 (SYN545911)	2-(carboxymethyloxymethyl)-6-(trifluoromethyl)pyridine-3-carboxylic acid		Plants
CSAA757083 (SYN510579)	2-hydroxy-6-(trifluoromethyl)pyridine-3-carboxylic acid		Plants Soil
CSAA794148 (SYN503780)	2-(2-methoxyethoxymethyl)-6-(trifluoromethyl)pyridine-3-carboxylic acid		Rat Soil Aqueous photolysis
CSAA806573 (NOA451778)	2-(hydroxymethyl)-6-(trifluoromethyl)pyridine-3-carboxylic acid		Plants Rat Soil Aqueous photolysis
CSAA915194 NOA454598	2-hydroxy-3-[2-(2-hydroxyethoxymethyl)-6-(trifluoromethyl)pyridine-3-carbonyl]bicyclo[3.2.1]oct-2-en-4-one		Plants Rat Goat Hen

Plant metabolism

The Meeting received information on the fate of bicyclopyrone in maize, sugar cane and soya bean.

Maize study

Field grown maize (*Zea mays*) received either a single pre-emergent treatment of 200 g ai/ha or a pre-emergence treatment of 200 g ai/ha followed by a post emergence treatment at 200 g ai/ha at the 8 to 9 leaf stage. Samples were taken from each treatment at three timings: early foliage (28 days after the post emergence application; foliage only), forage (BBCH 75–79; foliage immature cobs and immature grain) and crop maturity (BBCH 89; stover, cobs and grain).

The TRR in early foliage, forage and stover receiving only the pre-emergence application were 0.033, 0.023 and 0.032 mg eq/kg, respectively, for the [bicyclooctenone-6,7-^{14}C2]-labelled experiment and 0.042, 0.083 and 0.077 mg eq/kg, respectively, for the [pyridine-3-^{14}C]-labelled experiment. Values in immature cobs, immature grain, mature cobs and mature grain were ≤ 0.003 mg eq/kg for the [bicyclooctenone-6,7-^{14}C2]-labelled experiment and ≤ 0.005 mg eq/kg for the [pyridine-3-^{14}C]-labelled experiment.

The TRR in early foliage, forage and stover from the combined pre- and post-emergence application regime were 0.35, 0.46 and 0.46 mg eq/kg, respectively, for the [bicyclooctenone-6,7-^{14}C2]-labelled experiment and 0.44, 0.92 and 0.76 mg eq/kg, respectively, for the [pyridine-3-^{14}C]-labelled experiment. Values in immature cobs, immature grain, mature cobs and mature grain were 0.029, 0.037, 0.036 and 0.058 mg eq/kg, respectively, for the [bicyclooctenone-6,7-^{14}C2]-labelled experiment and 0.033, 0.020, 0.018 and 0.025 mg eq/kg, respectively, for the [pyridine-3-^{14}C]-labelled experiment.

Analysis of forage, stover and grain samples from the combined applications showed that bicyclopyrone is extensively metabolised and that no or only very minor residues of bicyclopyrone were present (≤ 4.3% TRR; ≤ 0.009 mg eq/kg). At least four desmethyl dihydroxylated bicyclopyrone isomers were shown to be present which collectively accounted for up to 36% TRR (0.33 mg eq/kg; all in the free metabolite form) and individually up to 21% TRR (CSCD677692: 0.19 mg/kg). Two desmethyl monohydroxy isomers of bicyclopyrone were shown to be present which collectively accounted for up to 22% TRR (0.200 mg eq/kg) and individually up to 8% TRR (CSCD677693: 0.07 mg eq/kg; as the free metabolite) or up to 14% TRR (CSCD675162: 0.13 mg eq/kg; total for the free and glycoside conjugated forms). CSAA589691, was shown to be present in immature and mature grain at levels up to 49% TRR (0.024 mg eq/kg).

Sugar cane study

The metabolism of bicyclopyrone in sugar cane was investigated using a single post-emergent treatment of 300 g ai/ha applied to cane plants at the 7–8 leaf stage (BBCH 17–18). Samples of immature foliage were collected 42 days after treatment (BBCH 23–24). Mature foliage (all leaves) and cane were collected 301 days after treatment (BBCH 39).

The TRR in sugar cane foliage, sampled 42 days after treatment, were 0.78 mg eq/kg and 0.89 mg eq/kg for the [bicyclooctenone-6,7-^{14}C2] and [pyridine-3-^{14}C]-bicyclopyrone labelled experiments, respectively. Residues in foliage at maturity were 0.004 mg eq/kg and 0.003 mg eq/kg respectively. The TRRs in the cane harvested at maturity were 0.002 mg eq/kg and 0.004 mg eq/kg for the [bicyclooctenone-6,7-^{14}C2] and [pyridine-3-^{14}C]-bicyclopyrone labelled experiments respectively.

Extractable residues in immature foliage represented 85% and 88% TRR for the [bicyclooctenone-6,7-^{14}C2]-bicyclopyrone and [pyridine-3-^{14}C]-bicyclopyrone labelled experiments respectively. The mature cane and foliage were not extracted since residues were below 0.01 mg eq/kg.

Bicyclopyrone was not detected in immature foliage. The most significant metabolite detected was the desmethyl monohydroxy metabolite CSCD677693 which was present as both the free form (17 to 18% TRR, 0.14 to 0.16 mg eq/kg) and as a glycoside conjugate (5.6 to 7.1% TRR, 0.05–0.055 mg eq/kg). Two other demethylated metabolites of bicyclopyrone were present, the desmethyl monohydroxy metabolite CSCD675162 (9.9 to 13% TRR, 0.088 to 0.098 mg eq/kg) and the desmethyl dihydroxy metabolite CSCD677692 (5.5 to 6.5% TRR, 0.043 to 0.058 mg eq/kg).

CSCD677306, the monohydroxy metabolite of bicyclopyrone, was present in both the free form and conjugated as the glycoside (4.6 to 5.7% TRR, 0.036 to 0.051 mg eq/kg and 11 to 13% TRR, 0.095 to 0.10 mg eq/kg respectively). Two other glycosides of monohydroxylated bicyclopyrone; including the glycoside of CSCD675164, were detected (2 to 4.2% TRR, 0.018 to 0.033 mg eq/kg and 2.3 to 3.5% TRR, 0.02 to 0.027 mg eq/kg). The dihydroxy metabolite CSCD677694 (8.1 to 9.3% TRR, 0.072 mg/kg) was also observed.

Detected metabolites that contained only the pyridine ring of bicyclopyrone were identified as CSCD686480, which was present in both the free form (2.7% TRR, 0.024 mg eq/kg) and as a glycoside (17% TRR, 0.15 mg eq/kg) and CSCD686481 (6.4% TRR, 0.057 mg eq/kg).

The unextracted residues remaining after the initial solvent extraction were further investigated by sequential extraction with 0.1 M and 1M HCl at 40 ºC and 90 ºC respectively after rehydration with water. The water released 0.5–0.7% TRR (0.004 to 0.0005 mg eq/kg), the mild acid 0.6% TRR (0.005 mg eq/kg) and the stronger acid conditions 2.6 to 4.3% TRR (0.023 to 0.03 mg eq/kg). A further 7.8 to 8.9% TRR, corresponding to 0.069 mg eq/kg in each debris fraction, remained unextracted.

Soya bean study

Bicyclopyrone metabolism in greenhouse grown investigated following a single pre-emergent application, at a rate of 186.1 g ai/ha.

Harvesting of forage occurred 35 to 36 days after treatment (DAT) at BBCH 16–21, of hay 62–63 DAT at BBCH 65–74 and of mature beans 113–114 DAT at BBCH 89. The TRRs in the beans were 0.19 mg eq/kg and 0.21 mg eq/kg for the [bicyclooctenone-6,7-$^{14}C_2$] and [pyridine-3-^{14}C] labelled experiments, respectively, while the residue in the corresponding hay samples reached 0.15 mg eq/kg and 0.19 mg eq/kg. The TRR in the forage samples were significantly lower, reaching only 0.02 mg eq/kg and 0.031 mg eq/kg for the [bicyclooctenone-6,7-$^{14}C_2$] and [pyridine-3-^{14}C] labelled experiments, respectively.

In mature beans, bicyclopyrone was detected at 15% TRR (0.029 mg eq/kg) and 13% TRR (0.026 mg eq/kg) in the [bicyclooctenone-6,7-$^{14}C_2$] and [pyridine-3-^{14}C] experiments, respectively. The most significant metabolites detected were the monohydroxy metabolite CSCD675164 (14–18% TRR; 0.028–0.034 mg eq/kg) and the demethylated metabolite of bicyclopyrone, CSAA915194 at 7.6–8.5% TRR (0.015– 0.018 mg eq/kg).

The desmethyl monohydroxy and dihydroxy metabolites CSCD677306, CSCD677694, CSCD675162, CSCD677693, CSCD642512, CSCD686480, CSCD656832 and CSCC163768 were also present but at low levels.

In bean hay, bicyclopyrone was detected at low levels of 3.3 and 3.9% TRR for the [pyridine-3-^{14}C] and [bicyclooctenone-6, 7-$^{14}C_2$] respectively with both corresponding to a residue of 0.006 mg eq/kg. The most significant metabolite detected was the desmethyl monohydroxy metabolite CSCD675162 (14.0–15% TRR; 0.023–0.027 mg eq/kg). A second desmethyl monohydroxy metabolite CSCD677693 was also present (5.6–6.7% TRR; 0.01– 0.011 mg eq/kg) along with the desmethyl metabolite CSAA915194 (4.7–6.2% TRR; 0.009 mg eq/kg). Two monohydroxy metabolites were also observed, CSCD675164 (7.2–9.2% TRR; 0.0014 mg eq/kg).

The metabolites CSCD677306, CSAA915194 and CSCD677694 was also present but at low levels. Metabolites that contained only the pyridine ring of bicyclopyrone were identified as CSCD686480 (14.2% TRR; 0.027 mg eq/kg) and CSCD656832 (1.2% TRR; 0.002 mg eq/kg). There were no bicyclooctenone specific metabolites.

In bean forage, residues was detected at low levels from both the radiolabelled experiments (0.02 and 0.031 mg eq/kg for the [bicyclooctenone-6,7-$^{14}C_2$] and [pyridine-3-^{14}C] experiments respectively). In the forage treated with [bicyclooctenone-6,7-$^{14}C_2$]-bicyclopyrone, bicyclopyrone was detected at levels of 10% TRR (0.002 mg eq/kg). The remaining residue consisted of at least four distinct radioactive components none of which exceeded 6.8% TRR (0.001 mg eq/kg). In the

[pyridine-3-^{14}C] experiment, bicyclopyrone was also detected at very low levels (9.2% TRR; 0.003 mg eq/kg) and the remainder of the radioactive residue was shown to consist of at least 10 distinct radioactive components none exceeding 11% (0.003 mg eq/kg).

Generally in all investigated plants, the metabolic pathways are similar but with low residues in all soya bean commodities. Unchanged bicyclopyrone was found in corn forage, soya bean seed and hay and was absent in all other samples examined. The majority of the metabolites were formed by hydroxylation on one or more sites on the bicyclic ring or demethylation of the methoxyethoxymethyl side chain followed by hydroxylation. Some glycoside conjugation of the hydroxyl derivatives and some cleavage between the two ring systems was observed. CSAA589691, was found in mature grain at levels up to 42% TRR.

Animal metabolism

The Meeting received information on the fate of orally-dosed bicyclopyrone in rat, lactating goats and laying hens. In metabolism studies, total radioactive residues are expressed in mg/kg bicyclopyrone equivalents unless otherwise stated.

Rat

Metabolism studies on laboratory animals including rats were reviewed in the framework of toxicological evaluation by the current JMPR.

Lactating goats

Lactating goats were orally dosed with [Pyridine-3-^{14}C]-bicyclopyrone or [Bicyclooctenone-6,7-^{14}C2]-bicyclopyrone, equivalent to 34 ppm in the feed for 7 consecutive days. The majority of the administered dose was recovered in urine (60% [pyridinyl label] and 62% [bicyclooctenone label], with moderate amounts recovered in the faeces, 6.5% and 6.2% for the pyridinyl and bicyclooctenone labels, respectively.

Highest TRR levels were found in the liver (2.7 mg eq/kg and 3 mg eq/kg for pyridinyl and bicyclooctenone labels, respectively). Residue levels in other commodities such as kidney, muscle and fat were 1.39 mg eq/kg and 1.35 mg eq/kg for pyridinyl and bicyclooctenone labels, respectively.

TRR levels in milk (mean for a 24 hour period) reached a plateau of about 0.008 mg eq/kg for both radiolabels at approximately 2 to 3 days.

Extractability of radioactivity from milk with hexane was high, greater than 95%. In other tissues extractability with solvents (e.g. acetonitrile, acetonitrile:water (4:1, v/v), acetonitrile:water (3:7, v/v) and water) ranged from 86 to 98%, with the exception of renal fat (63 to 71%), where very low levels of residues were found (< 0.016 mg eq/kg). Unextracted residues were either < 10% TRR or < 0.05 mg eq/kg.

Unchanged bicyclopyrone was identified in all samples. The lowest levels of bicyclopyrone were found in the liver (pyridinyl label 16% TRR, 0.44 mg eq/kg), and the highest in kidney (bicyclooctenone label 50% TRR, 0.64 mg eq/kg).

The most abundant metabolite detected in all commodities was CSAA915194. This compound was the principal component of the residue in liver and milk (maximum 70% TRR, 1.92 mg eq/kg (pyridinyl label) and 59% TRR, 0.01 mg eq/kg (bicyclooctenone label) respectively for the two commodities).

Laying hens

Laying hens were orally dosed with [Pyridine-3-^{14}C]-bicyclopyrone and [Bicyclooctenone-6,7-^{14}C2]-bicyclopyrone, at a dose equivalent to 24 or 22 ppm in feed for 10 consecutive days. The majority of the administered dose was recovered in excreta76% of both labels.

More than 84% of radioactivity in tissue samples was extracted by solvents (e.g. acetonitrile, acetonitrile:water (4:1, v/v), acetonitrile:water (3:7, v/v) and water). The majority of tissue-bound

radioactivity was found in liver (1.75 mg eq/kg and 1.77 mg eq/kg for pyridinyl and bicyclooctenone labels respectively) and accounted for only ca. 0.3% of the administered dose. Residue levels in other commodities such as egg yolk, egg white, peritoneal fat and skin and subcutaneous fat were 0.78–0.93 mg eq/kg.

Radioactive residues in eggs (mean for a 24 hour period) reached a plateau of 0.1 mg eq/kg for both labels at approximately 6 to 8 days. Eggs contributed a minor route of excretion of radioactivity, with daily recoveries not exceeding 0.017% of dose, equivalent to 0.14 mg eq/kg.

Radioactive residues in edible tissues predominantly consisted of parent bicyclopyrone (> 73% TRR). The metabolite CSAA915194 was detected at up to 3% TRR in egg yolk, egg white, liver, muscle and peritoneal fat and CSCD677306 were detected at very low levels in liver (1.6% TRR, 0.029 mg eq/kg and 2% TRR, 0.035 mg eq/kg respectively) from the bicyclooctenone label.

The metabolite CSCD677692 was detected in liver and excreta but at levels too low to quantify. CSCD675162 was detected at low levels in peritoneal fat (5.4% TRR, 0.01 mg eq/kg) from the bicyclooctenone label and in egg yolk (2.2% TRR, 0.002 mg eq/kg) from the pyridinyl label. CSCD677693 was detected in excreta only. All other metabolites detected for both labels were ≤ 0.009 mg eq/kg irrespective of detection method or label.

In summary, the primary metabolic processes observed include O-demethylation, oxidation on one or more sites of the bicyclooctenone ring, a minor amount of bridge cleavage between the rings, and conjugation to some extent. The tissue residues in both animals consisted primarily of parent bicyclopyrone (hen and goat) and CSAA915194 (desmethyl parent) (goat) and several very minor metabolites found in the liver for the goat and several samples for the laying hen. The major metabolites observed in lactating goat and hen were also observed in rats.

Environmental fate

The Meeting received information on aerobic degradation in soil, photolysis on soil, and confined and field rotational crop studies.

Aerobic degradation in soil

Aerobic degradation of [bicyclooctenone] and [pyridine]-^{14}C-bicyclopyrone under laboratory conditions was studied at 20 °C in various soil types treated at 0.27 mg /kg dry soil (200 g ai/ha).

Although the rate of transformation of bicyclopyrone differed between soils, the same transformation products were observed in each soil indicating a similar route of transformation. Bicyclopyrone was extensively mineralised to carbon dioxide. The major metabolites identified in soils were SYN503780, and CSCD642512. The three minor metabolites identified in the tested soil were, CSCD656832, CSCD163768 and CSAA757083

The half-life for bicyclopyrone was estimated at 108 days for clay loam soils, 141–331 days for loamy sand soils, 59–357 days for sandy loam soils, 89 days for silt clay soils, 69 days for silt loam soils, 159 days for silt clay loam soils and 19.8–59 days for loamy soils.

The Meeting concluded that bicyclopyrone is moderately persistent to persistent in soil.

Aerobic degradation of the major metabolites SYN503780 was investigated in three European soils. There were three extractable metabolites present at ≥ 5% of applied radioactivity (CSCD656832, CSCC163768 and CSAA757083). The half-lives for the metabolite SYN503780 were in range 4–9 days.

The Meeting concluded the metabolite SYN503780 is not persistent in soil.

Soil photolysis

Photolysis of bicyclopyrone was studied in dry and moist soils irradiated with artificial sunlight for the equivalent to 30 summer days.

Dry layer tests

There was no degradation in samples incubated in the dark. In irradiated samples there was only one degradate present at ≥ 5% of applied radioactivity, namely SYN503780 (maximum 17.2% at 12 DAT). The two minor degradates were CSAA589691 (bicyclo label) and CSCC163768 (pyridinyl label). Calculated photodegradation DT_{50} values for bicyclopyrone were 50–64 days (dry soil).

Moist layer tests

Degradation was more significant in irradiated and dark moist soil samples In addition to parent, four known degradates were identified from the pyridinyl label, one of which was present at ≥ 10% of applied radioactivity, namely SYN503780 (maximum 25%); CSCC163768, CSCD656832 and CSCD642512 were minor degradates. Calculated photodegradation DT_{50} values for bicyclopyrone were 24–25 days (moist soil).

In addition, the photolysis of bicyclopyrone was investigated in moist soil taken from three sites in the US. Under continuous irradiation, photolytic DT_{50} values for bicyclopyrone in the three moist soils were in the range 2–5.7 days. When adjusted to equivalent summer days at latitudes 30–50 °N, the DT_{50} values ranged from 3.9 to 11 days. Degradation involved cleavage of the bridge between the two ring systems and the main photodegradation product was SYN503780.

In summary, the major metabolites identified in soils were SYN503780 (up to 25%), and CSCD642512. In soil photolysis, SYN503780 was present at ≥ 10% of applied radioactivity.

Hydrolysis

Bicyclopyrone was stable to hydrolysis at pH values ranging from 4 to 9. Based on hydrolysis results, the DT_{50} was extrapolated to be > 1 year at 25 °C.

Aqueous Photolysis

Bicyclopyrone was extensively degraded under simulated sunlight. Degradation was pH-dependent in the order pH 5 > pH 7/natural water > pH 9. The two main photodegradation products at pH 5 were CSAA589691 from the bicyclo ring system and CSCC163768 from the pyridine ring system. Based on aqueous photolysis results, the DT_{50} values ranged from 10 to 50 days.

Residues in succeeding crops

A confined rotational crop study was conducted to examine the nature and level of residues of bicyclopyrone in succeeding crops. [^{14}C]-bicyclopyrone was applied to the soil of a planting container by spray application at a nominal rates of 200 g ai/ha or 350 g ai/ha.

Rotational crops (wheat, spinach and turnips) were sown at plant back intervals of 30, 120 and 270 days after application. Due to phytotoxicity of the test item to spinach and turnip, further sowings of both were made at 60 DAA and of spinach only at 180 DAA.

Low levels of bicyclopyrone were detectable in wheat (up to 5.8% TRR and 0.026 mg eq/kg) and turnip foliage (up to 3.8% TRR and 0.001 mg eq/kg). Higher residues were determined in spinach plants exhibiting phytotoxicity (up to 70% TRR and 0.03 mg eq/kg).

Two monohydroxy bicyclopyrone isomers, shown to be present in wheat in both the free and glycoside conjugated metabolite forms, collectively accounted for up to 29% TRR and 0.093 mg/kg. Individually these isomers accounted for up to 24% TRR and 0.082 mg eq/kg (CSCD677306) and up to 25% TRR and 0.082 mg eq/kg (CSCD675164). The free metabolites were also found to be present in early rotation turnip foliage but at much lower absolute residue levels, accounted for up to 11% TRR and 0.002 mg eq/kg (CSCD677306) and up to 34% TRR and 0.007 mg eq/kg(CSCD675164).

Two desmethyl monohydroxy-bicyclopyrone isomers, shown to be present in wheat in only the free metabolite form, collectively accounted up to 27% TRR and 0.11 mg/kg. Individually these metabolites accounted for up to 13% TRR and 0.057 mg eq/kg (CSCD677693) and up to 19% TRR and 0.053 mg eq/kg (CSCD675162).

Two metabolites present in wheat, with structures that retained only the pyridine ring of bicyclopyrone, both of which were found in the free and glycoside conjugated metabolite forms, accounted for up to 21% TRR and 0.10 mg/kg (CSCD686480) and up to 41% TRR and 0.064 mg eq/kg (CSCD656832). CSCD656832 was also present in turnip foliage but at much lower absolute residue levels, accounted for up to 71% TRR and 0.012 mg eq/kg.

A dihydroxy-bicyclopyrone metabolite (CSCD677694), shown to be present in wheat in the free form, accounted for up to 13% TRR and 0.057 mg eq/kg. Significant proportions of the residue in wheat grain (up to 37% TRR) were shown to be attributable to naturally incorporated radioactivity.

CSAA757083, a known soil metabolite was found at very low levels (2% TRR, 0.004 mg eq/kg) in wheat hay from the 120-day plant-back interval. Quantitatively, metabolites resulting from bridge cleavage were more prevalent in the rotational crops than the primary crops and were formed to a larger extent in the later plant-back intervals compared with the crops at the 30 day interval.

In a field rotational crop study with nine trials, bare ground was treated with bicyclopyrone formulated as an emulsifiable concentrate (EC) at a rate of 200 g ai/ha. Radish (root and tuber vegetable), spinach (leafy vegetable) and wheat (cereals) were planted 90, 150, 187, and 270 days after the application of the test substance and harvested at typical intervals reflecting normal farming practice.

No residues of bicyclopyrone or SYN503780 (Method GRM030.03A) were found for any sample at any time interval. The only detectable residues found were either SYN503780 or CSCS686480 (Common Moiety Method – GRM030.05A).

Second study was conducted to determine possible uptake levels in wheat commodities. Bicyclopyrone was applied to bare-ground at a rate of 200 g ai/ha. Winter wheat was planted 90 days after application and spring wheat 270 days after application. The rotational wheat was harvested at normal maturity to provide samples of forage (autumn and/or spring), hay, grain, and straw.

The only residues found above the limit of quantification were of bicyclopyrone, analysed directly using method GRM030.03A, and of common moiety SYN503780, analysed via method GRM030.05A, in autumn forage (45 DAP). In the decline trials, these residues decreased with longer intervals to harvest. All other residues were <LOQ in all matrices, including processed fractions.

In summary, bicyclopyrone related residues in soil could contribute to residues observed in rotational and primary crops.

Methods of analysis

The Meeting received description and validation data for analytical methods of bicyclopyrone related residues in plant and animal commodities.

The metabolism of bicyclopyrone in crops and livestock resulted in numerous different metabolites in the various crop fractions. Most of these metabolites fell into two groups. The first group (compounds structurally related to SYN503780) produce SYN503780 on base hydrolysis and the second group (compounds structurally related to CSC686480) produce CSC686480 on base hydrolysis.

Most of the methods developed to quantify bicyclopyrone residues in plants and animal commodities involve a hydrolysis step to convert bicyclopyrone and its metabolites to either SYN503780 or CSC686480. Any non-metabolised parent bicyclopyrone that might be present would be captured by this method as SYN503780. The analytes SYN503780 and CSC686480 are quantified and expressed in bicyclopyrone equivalents and then added to give a total bicyclopyrone residue.

All of the methods extract residues with acetonitrile/water. The common moiety methods hydrolyse residues with aqueous hydrogen peroxide/sodium hydroxide. Method provided for analysis of bicyclopyrone, SYN503780 and CSCD686480, as single compound, exclude the hydrolysis step. For all methods, final quantification is achieved using LC-MS/MS, with an LOQ of 0.01 mg/kg for

each analyte in high -water and high-starch crops and in animal commodities (for an LOQ of 0.02 mg/kg total bicyclopyrone.

Representative compounds that generate SYN503780 and CSCD686480 on base hydrolysis were used as reference materials for fortification and method validation.

The methods are suitable for the analysis of bicyclopyrone and related metabolites in plants and animal matrices.

Multi-residue methods are currently not available for bicyclopyrone and its metabolites.

Stability of pesticide residues in stored analytical samples

The Meeting received data on storage stability for bicyclopyrone and its metabolites in plant and animal matrices.

Storage stability studies, where bicyclopyrone and SYN503780 were analysed individually, demonstrated that residues were stable for at least 24 months at -18 °C in crop commodities representative of high water, high acid, high oil, high protein, high starch and dry commodity groups. The two compounds were stable for at least 12 months in processed commodities derived from maize, sugarcane and soya beans.

Storage stability studies using common moiety methods, demonstrated that the common moieties SYN503780 and CSCD686480 were stable for at least 26 months at -18 °C in sugar cane commodities, when bicyclopyrone, SYN503780, CSCD686480 or CSAA915914 were added to the samples.

Storage stability studies using common moiety methods demonstrated that total residues captured by the common moieties SYN503780 and CSCD 686480 were stable for at least 13 months at -18 °C in bovine tissues and milk.

The demonstrated periods of stability are sufficient to cover the periods for which samples have been stored during residues analyses.

Definition of the residue

Following application of bicyclopyrone to crops (maize, soya bean and sugar cane) a large number of structurally similar metabolites were detected. The majority of these metabolites were either desmethyl dihydoxylated bicyclopyrone isomers or desmethyl monohydroxylated bicyclopyrone isomers (free and glycoside conjugated forms)). In both cases these metabolites are structurally related to bicyclopyrone.

In maize grain the significant residues were CSAA589691 (up to 49% TRR, 0.024 mg eq/kg), CSCD675162 (up to 23% TRR, 0.006 mg eq/kg) and monohydroxy NO449280 (18% TRR, 0.004 mg eq/kg).

In soya bean seeds bicyclopyrone accounted for up to 15% TRR (0.029 mg eq/kg) and the only other major metabolite was CSCD675164 (up to 18% TRR, 0.034 mg eq/kg).

Residues in sugar cane stalks were < 0.01 mg eq/kg.

In animal feed items the major residues were CSCD677692 (up to 21% TRR, 0.19 mg eq/kg, maize forage), CSCD675162 (up to 15% TRR, 0.023 mg eq/kg, soya bean hay), CSCD677693 (up to 18.4% TRR, 0.163 mg eq/kg, cane forage), CSCD677306 glycoside (13.5% TRR, 0.105 mg eq/kg, cane forage) and bicyclopyrone (10.2% TRR, 0.002 mg eq/kg, soya bean forage).

In rotational crops bicyclopyrone was a significant part of the residue in spinach (19% of TRR, 0.002 mg eq/kg). The metabolite CSCD656832 was found in spinach (up to 71% TRR, 0.012 mg eq/kg). The metabolite CSCD675164 was found in turnip tubers (33% TRR, 0.005 mg eq/kg) and turnip foliage (34 %, 0.007 mg eq/kg).

The same desmethyl dihydoxylated bicyclopyrone isomers and desmethyl monohydroxylated bicyclopyrone isomers (free and glycoside conjugated forms) were also found in significant levels in

rotated crop fractions that are animal feed items. In addition a number of metabolites containing the pyridine ring only were found at significant levels; CSCD656832 (includes conjugates up to 41% TRR, 0.064 mg eq/kg in wheat hay; 16% TRR, 0.009 mg eq/kg in wheat grain) and CSCD686480 (includes conjugates, up to 19% TRR, 0.029 mg eq/kg in wheat hay).

Bicyclopyrone was found to be stable on processing.

Owing to the different metabolites found there is no obvious candidate compound for use as a residue definition for compliance nor is there a small group of compounds that could be usefully monitored to cover the range of metabolites found in the different crop fractions.

The meeting noted that the majority of the metabolites are structurally related to bicyclopyrone and fall into two groups:

The first group are compounds that can be hydrolysed to SYN503780 (bicyclopyrone, monohydroxy N0449280, CSCD675164, CSCD677306 glycoside, CSCD675164).

The second group covers compounds that can be hydrolysed to CSDC686480 (CSCD686480, CSCD675162, CSCD677692 and CSCD677693 and conjugates).

In addition, all crop fractions contained numerous other metabolites, all individually < 10% TRR, which would also belong to these groups.

Common moiety methods are available to cover these two groups of metabolites.

The meeting agreed that the residue definition for enforcement should be the *sum of bicyclopyrone and its structurally-related metabolites determined as sum of compounds hydrolysable with base to SYN503780 (is 2-(2-methoxyethoxymethyl)-6-(trifluoromethyl) pyridine-3-carboxylic acid) and CSCD686480 (2-(2-hydroxyethoxymethyl)-6-(trifluoromethyl)pyridine-3-carboxylic acid), expressed as bicyclopyrone.*

For risk assessment it was concluded that the structurally related compounds to bicyclopyrone (determined as either SYN503780 or CSCD686480) were likely to have a toxicity no greater than bicyclopyrone. Therefore all the metabolites quantified are covered by the toxicological endpoints for bicyclopyrone.

The only other metabolites that need to be considered for inclusion in the residue definition for risk assessment are CSAA589691 and CSCD656832.

Metabolite CSA589691was found in immature and mature maize grain at a level of 0.024 mg eq/kg. The meeting noted that the maize metabolism study was conducted at a rate of 200 g ai/ha applied pre-emergence followed by an application of 200 g ai/ha applied post-emergence. This represents an exaggerated rate compared to the critical GAP for cereals (pre-emergence treatment: maximum application of 200 g ai/ha or pre-emergence/post emergence treatment: maximum application of 50 g ai/ha). The meeting concluded that at the GAP residues of CSAA589691 were likely to be < 0.01 mg/kg and the contribution to the diet would be insignificant.

The metabolite CSCD656832 was a significant residue in rotational crops. The highest levels were wheat forage (0.018 mg/kg), wheat hay (0.064 mg/kg), wheat straw (0.056 mg/kg), wheat grain (0.009 mg/kg) and spinach foliage (0.012 mg/kg). The rotational crop metabolism study was conducted at a rate of 350 g ai/ha to the bare soil. This represents 1.75× the maximum seasonal application rate of 200 g ai/ha. Residues in rotational crop fractions of grain and spinach at the GAP are expected to be < 0.01 mg/kg. Residues in animal feed commodities at the GAP will not contribute significantly to the livestock dietary burden. Consequently, metabolite CSCD656832 does not need to be considered further.

The meeting concluded that the residue definition for risk assessment should be the *sum of bicyclopyrone and its structurally-related metabolites determined as sum of compounds hydrolysable with base to SYN503780 (2-(2-methoxyethoxymethyl)-6-(trifluoromethyl)pyridine-3-carboxylic acid) and CSCD686480 (2-(2-hydroxyethoxymethyl)-6-(trifluoromethyl)pyridine-3-carboxylic acid), expressed as bicyclopyrone.*

In livestock the major compounds identified were bicyclopyrone and CSAA915194. Bicyclopyrone was identified at levels ranging from 16% TRR to 94.8% TRR (0.12–0.44 mg eq/kg) in the different animal commodities. CSA915194 was identified at levels from 1–70% TRR (0.001–1.92 mg eq/kg) in the different animal commodities.

Trace levels of CSCD686480 were found in the goat metabolism study whereas in the dairy cow feeding study residues > 0.01 mg/kg were found in liver and kidney; the longer duration of the feeding study is likely to account for cleavage of the ring being more prominent.

A common moiety method is available that will determine bicyclopyrone and CSA915194. A common moiety method is also available for the determination of CSCD686480 and structurally related compounds.

The meeting agreed that based on the livestock metabolism and feeding studies the residue definition for enforcement and monitoring should be;

The *sum of bicyclopyrone and its structurally-related metabolites determined as sum of compounds hydrolysable with base to SYN503780 (is 2-(2-methoxyethoxymethyl)-6-(trifluoromethyl)pyridine-3-carboxylic acid) and CSCD686480 (2-(2-hydroxyethoxymethyl)-6-(trifluoromethyl)pyridine-3-carboxylic acid), expressed as bicyclopyrone.*

For risk assessment no additional metabolites were identified at significant levels in any animal tissues. Therefore the meeting concluded that the residue definition for monitoring should apply for risk assessment.

The meeting recommended the following residue definitions for bicyclopyrone:

Definition of the residue for compliance with the MRL and for dietary risk assessment for plant and animal commodities: *sum of bicyclopyrone and its structurally-related metabolites determined as sum of compounds hydrolysable with base to SYN503780 (is 2-(2-methoxyethoxymethyl)-6-(trifluoromethyl)pyridine-3-carboxylic acid) and CSCD686480 (2-(2-hydroxyethoxymethyl)-6-(trifluoromethyl)pyridine-3-carboxylic acid), expressed as bicyclopyrone.*

Bicyclopyrone and the structurally related compounds were not found to accumulate in fat. The meeting concluded the residues is not fat soluble.

Results of supervised residue trials on crops

The Meeting received supervised trial data for the foliar application of bicyclopyrone on barley, maize, wheat, sugar cane and sweet corn. Residue trial data was made available from Belize, Canada, Uruguay and USA. Labels were available from Belize, Uruguay and USA describing the registered uses of bicyclopyrone.

Total bicyclopyrone residues are calculated as the sum of two common moieties (SYN503780 and CSCD686480) expressed as bicyclopyrone equivalents. Where residues have been measured in duplicate samples, a mean total value is presented. Residues and application rates have been reported as provided in the study reports except for finite values below the LOQ, where these have been reported as < 0.01 mg/kg.

The results from trials used for the estimation of maximum residue levels (underlined) have been rounded to two significant digits (or if close to the LOQ, rounded to one significant digit).

Where a residue of both common moieties has been detected, the sum of the two values is used. Where both values are reported as < 0.01 mg/kg, the total bicyclopyrone equivalent residue is reported as < 0.02 mg/kg and where both values are reported as < 0.005 mg/kg, the total bicyclopyrone equivalent residue is reported as < 0.01 mg/kg.

The Meeting noted that some labels included both a latest growth stage for application and a PHI in the use instructions. In interpreting these use instructions, the Meeting decided that trial data reflecting application at the prescribed growth stage and with harvest no earlier than the PHI as suitable for making a recommendation.

Cereal grains

Sweetcorn

Data were available from supervised trials on sweetcorn in Brazil and the USA.

The critical GAP of bicyclopyrone on sweet corn of USA is a soil applied pre-plant pre-emergence application at a maximum rate of 50 g ai/ha with a PHI 45 days when used as pre-plant, pre emergence.

Total bicyclopyrone residue in sweetcorn from the USA trials matching USA GAP were (n=13): < 0.02 (12) and 0.023 mg/kg.

Based on the US trials for sweet corn, the Meeting estimated a maximum residue level of 0.03 mg/kg, STMR of 0.02 mg/kg and HR of 0.023 mg/kg for bicyclopyrone on sweetcorn (corn-on-the cob).

Barley

Data were available from supervised trials on barley in Canada and the USA following GAP of the USA.

The GAP of bicyclopyrone on barley of USA is as a foliar application at a maximum rate of 50 g ai/ha with the application timing at 2-leaf stage to pre-boot stage, and a PHI of 60 days.

Total bicyclopyrone residues in barley from trials in Canada and USA approximating GAP were (n=10): < 0.01 (4), < 0.011, 0.011, 0.013, 0.014, 0.021, 0.026 mg/kg.

Based on the trials for barley in Canada and USA, the Meeting estimated a maximum residue level of 0.04 mg/kg, a STMR of 0.011 mg/kg for bicyclopyrone on barley.

Maize

Field trials involving maize were performed in Brazil and the USA.

The GAP for maize in the Uruguay is as a single pre-emergence treatment at maximum rate of 200 g ai/ha. The pre-harvest interval is defined by application timings. In field trials from the Brazil matching Uruguay GAP, total residues for maize grains harvested at maturity were < 0.02 (3) mg/kg.

Bicyclopyrone can be applied to maize in the USA as either a pre-plant, pre-emergence or post-emergence treatment with a yearly maximum rate 50 g ai/ha. The critical US GAP in maize is a single early pre-emergence treatment at 50 g ai/ha applied to maize up 30 inches tall or up to the 8-leaf crop growth stage with PHI of 60-days. Results from 22 US trials conducted on maize, matching the critical GAP (a single application of 50 g ai/ha, PHI 79–113 days). The total bicyclopyrone residues for maize grains harvested at maturity were < 0.02 (22) mg/kg.

The Meeting noted that residues levels in three trials conducted in Brazil involving an application of bicyclopyrone at rate of 200 g ai/ha were < 0.02(3) mg/kg. In addition, the meeting noted that in 26 trials conducted in USA involving application of bicyclopyrone once or twice at a rate of 200g ai/ha, the residues levels were < 0.02 (26) mg/kg.

The Meeting estimated the maximum residue level and STMR of 0.02*and 0 mg/kg, respectively, for bicyclopyrone in maize.

Wheat

Data were available from supervised trials on wheat in Canada and the USA.

The GAP for wheat in the USA is a single treatment at maximum application rate of 50 g ai/ha applied between 2-leaf stage and pre-boot stage with a pre-harvest interval of 60 days.

In field trials from Canada and the USA matching GAP (1× 50 g ai/ha, PHI 57–63 days), total bicyclopyrone residues for wheat grains harvested at maturity were (n=20) < 0.01, 0.01(11), 0.011(4), 0.013, 0.014, 0.015, 0.016 (2), 0.022 mg/kg.

Based on the trials for wheat from Canada and USA, the Meeting estimated a maximum residue level of 0.04 mg/kg, and STMR of 0.01 mg/kg for bicyclopyrone on wheat grain.

Grasses for sugar or syrup production

Sugar cane

Data were available from supervised trials on sugar cane in Australia and Brazil. The GAP for sugar cane in Belize (South America) is as a pre-emergent treatment, BBCH 00 to BBCH 08 or early post-emergence from BBCH 11 (one true leaf or whorls unfolded) to BBCH 14 (four true leaves or whorls unfolded) treatment at 262.5 g ai/ha. The pre-harvest interval is defined by application timings, i.e. crop growth stage.

In field trials data from Brazil matching the GAP for bicyclopyrone on sugarcane in Belize, total bicyclopyrone residues for sugar cane were < 0.02 (17) mg/kg. Bicyclopyrone residues in sugar cane from data in Brazil at exaggerated rate of 900 g ai/ha (3 × GAP rate) were < 0.02 mg/kg and 1500 g ai/ha (5 × GAP rate) were < 0.02 mg/kg.

Total bicyclopyrone residues in sugar cane from trials in Australia with a GAP of up to two applications at a rate of 300 g ai/ha, or one application at 600 g ai/ha applied at a later growth stage (just before row closure, or "out-of-hand" stage) were < 0.02(8) mg/kg.

Based on the available information, the Meeting estimated a maximum residue level, STMR and HR at 0.02*, 0 and 0 mg/kg for bicyclopyrone in sugarcane, respectively.

Animal feedstuffs

Barley, wheat hay and straw

Data were available from supervised trials on barley and wheat (hay and straw) in Canada and the USA.

Trials from Canada on barley hay and straw were reported following the foliar application of an EC formulation (GAP: a post-emergent treatment at plant stage BBCH 12–37 with a maximum rate of 37.5 g ai/ha, and a PHI 30 days for hay and 60 days for straw).

Trials from the USA on barley hay and straw were reported following a foliar application of an EC formulation (GAP: a post-emergent application at plant stage 2-leaf to pre-boot at a maximum rate of 50 g ai/ha, , and a PHI of 30 days for hay and 60 days for straw).

Trials from Canada and the USA on wheat were reported following a foliar application of a EC formulation (GAP: single application at a rate of 50 g ai/ha, from the 2-leaf stage to pre-boot stage, PHI 30 days for forage and hay, 60 days for straw).

Barley and wheat straw and fodder, dry

Total bicyclopyrone residues in barley hay from trials in Canada and USA matching the USA GAP were (n=19): 0.012, 0.013, 0.015, 0.017, 0.018, 0.024(2), 0.026, 0.031, 0.035, 0.036, 0.039, 0.047, 0.048, 0.057, 0.066, 0.081, 0.082, 0.16 mg/kg.

Total bicyclopyrone residues in wheat hay from trials in Canada and USA matching the USA GAP were (n=32): 0.01, 0.011 (3), 0.012 (2), 0.014, 0.015 (2), 0.018, 0.019, 0.02 (2), 0.021, 0.023 (2), 0.025, 0.029, 0.035, 0.039, 0.046, 0.047, 0.063, 0.069, 0.074 (2), 0.092, 0.11, 0.18, 0.35, 0.51 and 0.66 mg/kg.

Total bicyclopyrone residues in barley straw from trials in Canada and USA matching the USA GAP were (n=15): 0.010, 0.012, 0.014, 0.016, 0.025 (2), 0.029 (2), 0.056(3), 0.061 (2), 0.085, 0.19 mg/kg as received basis.

Bicyclopyrone residues in wheat straw from trials in Canada and USA matching the USA GAP were (n=33): 0.016, 0.018 (2), 0.031, 0.033, 0.036, 0.049, 0.060, 0.094(2), 0.097, 0.12, 0.13, 0.14, 0.15(2), 0.16(2) 0.19, 0.22 and 0.24 mg/kg (as received).

The Meeting noted that the residues were higher in hay than in straw. Based on the residues in wheat hay from trials in Canada and the USA, the Meeting estimated maximum residue levels of 0.8 mg/kg (dw) for barley straw and fodder, dry and wheat straw and fodder, dry based on a dry matter content of 88%.

Based on the wheat hay data , the Meeting estimated a median residue value and a highest residue value for bicyclopyrone in barley hay and wheat hay of 0.024 and 0.68 (individual value) mg/kg respectively (as received).

Based on the residues in wheat straw from trials in Canada and the USA, the Meeting estimated a median residue value and a highest residue value for bicyclopyrone in barley and wheat straw of 0.097 and 0.25 (individual value) mg/kg, respectively.

Corn (maize and sweet corn) forage

Data for forage were available from supervised trials on corn crops (sweet corn and maize, including popcorn) in Brazil and the USA.

Trials from the USA on sweet corn forage and maize forage were reported for the application of a SL formulation (200 g/L) (GAP: a maximum rate of 50 g ai/ ha pre-emergence (sweet corn) and up to 30 inches tall or up to the 8-leaf growth stage of the crop (maize), PHI 60 days).

Total bicyclopyrone residues in maize forage from data in the USA matching the critical USA GAP were (n=21) < 0.02, 0.04, 0.042, 0.079, 0.08, 0.09(2), 0.096, 0.1, 0.11(3), 0.13, 0.132, 0.14, 0.15, 0.16, 0.17, 0.18, 0.2, 0.24 mg/kg (as received).

Total bicyclopyrone residues in sweet corn forage from trials in the USA matching GAP (n=4) were 0.05, 0.12 (2), 0.23 mg/kg (as received).

The Meeting noted that residues from maize forage and sweetcorn forage from the USA are from similar populations (Mann-Whitney test). As the residues from the USA trials (maize forage and sweetcorn forage) were considered similar, the Meeting decided that the data could be combined, < 0.02, 0.04, 0.042, 0.05, 0.079, 0.08, 0.09(2), 0.096, 0.1, 0.11(3), 0.120 (2), 0.13, 0.132, 0.14, 0.15, 0.16, 0.17, 0.18, 0.2, 0.23, 0.24 mg/kg.

The Meeting estimated median and highest residue for total bicyclopyrone in corn forage of 0.11 and 0.26 (individual value) mg/kg.

Corn (maize and sweet corn) fodder

Data for fodder were available from supervised trials on corn crops (sweet corn and maize, including popcorn) in the USA.

Trials from the USA on sweet corn fodder and maize fodder were reported following the foliar application (GAP: a single application at a rate of 50 g ai/ ha up to V8/8-leaf stage growth stage of the crop, PHI 45 days).

Nineteen trials were available from USA on maize fodder matching US GAP with total bicyclopyrone residues of < 0.02 (3), 0.034, 0.047, 0.048, 0.052, 0.053, 0.054(2), 0.06, 0.082, 0.11, 0.12, 0.13, 0.14, 0.15, 0.22 and 0.28 mg/kg (as received).

Seven trials were available from USA on sweet corn fodder matching US GAP with total bicyclopyrone residues of 0.027(2), 0.03, 0.079(2) , 0.30(2) mg/kg (as received).

Three trials were available from USA on popcorn fodder matching US GAP with total bicyclopyrone residues of 0.025, 0.046, 0.23 mg/kg (as received).

As the residues from the USA trials (maize fodder, popcorn fodder and sweetcorn fodder) were considered similar, the Meeting decided to combine the data ; < 0.02 (3), 0.025, 0.027(2), 0.03, 0.034, 0.046, 0.047, 0.048, 0.052, 0.053, 0.054(2), 0.06, 0.079(2), 0.082, 0.11, 0.12, 0.13, 0.14, 0.15, 0.22, 0.23, 0.28 and 0.30(2) mg/kg.

The Meeting estimated a median of 0.054 mg/kg, and highest residue 0.39 mg/kg (individual value). The Meeting estimated a maximum residue level of 0.5 mg/kg (dw) based on a dry matter content of 83% for sweet corn fodder, dry and maize fodder, dry.

Wheat forage

Data were available from supervised trials on wheat in Canada and the USA.

Trials from Canada and the USA on wheat were reported following a foliar application (GAP: single application at a rate of 50g ai/ha, from the 2-leaf stage to pre-boot stage, PHI 30 days for forage).

Total bicyclopyrone residues in wheat forage from trials in Canada and USA matching the USA GAP were (n=32): < 0.01(3), 0.01(6), 0.011(4), 0.012, 0.013(3), 0.019, 0.02, 0.024(2), 0.025(3), 0.045, 0.063, 0.076, 0.082, 0.089, 0.17, 0.27 and 0.34 mg/kg. Based on the residues in wheat forage from trials in Canada and the USA, the Meeting estimated a median residue value and a highest residue value for bicyclopyrone in wheat forage of 0.013 and 0.36 (individual value) mg/kg respectively (as received basis).

Fate of residues during processing

High temperature hydrolysis

The degradation of [^{14}C] bicyclopyrone was studied under hydrolytic conditions at high temperatures in sterile aqueous buffers at pH 4, 5 and 6 for periods of up to 60 minutes so as to simulate common processing practice (pasteurization, baking/brewing/boiling, and sterilization). No degradates were detected at any of the investigated pH and temperature ranges. Bicyclopyrone is stable under hydrolytic conditions at high temperatures.

Residues in processed commodities

The fate of total bicyclopyrone residues has been examined in maize and wheat processing studies.

Based on the results of processing studies conducted in the USA in combination with the residues from supervised trials, the estimated processing factors and the derived STMR-Ps are summarized in the Table below.

Processing factors, STMR-P and HR-P for food and feed

Crop	Residue value (mg/kg) in raw commodity			Processed Commodity	Calculated PF	PF (Mean or best estimated)*	Residue value (mg/kg) in processed commodity		
	MRL	STMR	HR				MRL**	STMR-P	HR-P
Wheat	0.04	0.01	0.023	AGF	1.8, 17.7	17.7	-	0.177	0.407
				Bran	2.7, 1.8	2.3	0.09	0.023	0.053
				Flour	0.26, 28	0.27	-		
				Middlings	0.91, 0.49	0.7	-		
				Shorts	0.91, 0.47	0.69	-		
				Germ	1.5, 1.3	1.4	0.06	0.014	0.032

*The factor is the ratio of the total residue in processed commodity divided by the total residue in the RAC.

** MRLs in processed commodities are only proposed where they are higher than the MRL in the raw grain.

The mean concentration factors for total bicyclopyrone (bicyclopyrone and its structurally-related metabolites determined as SYN503870 and CSCD686480 by a common moiety method) in wheat aspirated grain fractions, wheat bran and wheat germ were 17.7, 2.3 and 1.4, respectively. Bicyclopyrone residues did not concentrate in any of the other processed fractions.

The Meeting estimated a maximum residue level of 0.1 mg/kg for wheat bran (0.04×2.3= 0.092 mg/kg).

The Meeting decided to extrapolate the processing factor for wheat bran to estimate a maximum residue level, STMR-P and HR-P for barley bran. The Meeting estimated a maximum residue level of 0.1 mg/kg (0.04×2.3= 0.092 mg/kg), STMR-P of 0.0253 mg/kg (0.011×2.3= 0.0253 mg/kg) and HR-P of 0.06 mg/kg (0.026×2.3= 0.059 mg/kg) for barley bran.

Residue in animal commodities

Farm animal dietary burden

The Meeting estimated the dietary burden of bicyclopyrone in farm animals on the basis of the diets listed in Appendix IX of the FAO Manual 2016. Calculation from highest residue, STMR (some bulk commodities) and STMR-P values provides levels in feed suitable for estimating MRLs, while calculation from STMR and STMR-P values for feed is suitable for estimating STMR values for animal commodities. The percentage dry matter is taken as 100% when the highest residue levels and STMRs are already expressed on a dry weight basis.

Estimated maximum and mean dietary burdens of farm animals

Dietary burden calculations for beef cattle, dairy cattle, broilers and laying poultry are provided in Appendix IX of the FAO manual of 2016. The calculations were made according to the animal diets from US-Canada, EU, Australia and Japan in the Table (Appendix IX of the FAO manual).

Region	Livestock dietary burden, bicyclopyrone, ppm of dry matter diet							
	US-Canada		EU		Australia		Japan	
	Maximum	Mean	Maximum	Mean	Maximum	Mean	Maximum	Mean
Beef cattle	0.133	0.058	0.683	0.222	1.45[a]	0.24[b]	0.009	0.009
Dairy cattle	0.46	0.129	0.555	0.17	1.0[c]	0.223[d]	0.33	0.143
Broiler poultry	0.009	0.009	0.009	0.009	0.002	0.002	0.001	0.001
Laying poultry	0.009	0.009	0.16[e]	0.039[f]	0.001	0.002	-	-

[a] suitable for estimating maximum residue levels for meat, fat and edible offal of cattle.

[b] suitable for estimating STMR for meat, fat and edible offal of cattle.

[c] suitable for estimating maximum residue levels for Milk.

[d] suitable for STMR levels for Milk.

[e] suitable for estimating maximum residue levels for poultry meat, offal and eggs.

[f] suitable for STMR levels for poultry meat, offal and eggs.

Livestock feeding studies

The Meeting received a lactating dairy cow feeding studies using bicyclopyrone, which provided information on residues resulting in animal commodities and milk from bicyclopyrone residues in the animal diet.

Lactating dairy cows

Lactating dairy cows were dosed with bicyclopyrone for 28 days at the dose equivalent to 0.15, 0.90 and 3.0 ppm in the diet.

Total bicyclopyrone residues were less than the LOQ (< 0.01 mg/kg) in milk, fat and muscle at any of feeding levels. The residues found in kidney and liver were not linearly-related to the dose

administered. The highest residues of total bicyclopyrone equivalents occurred in liver were 3.2, 2.6 and 1.4 mg/kg from the 3, 0.9 and 0.15 ppm dose groups, respectively. The highest residues of total bicyclopyrone equivalents occurred in kidney were 0.54, 0.53 and 0.42 mg/kg from the 3.0, 0.9 and 0.15 ppm dose groups, respectively, and did not seen to be dose dependent.

Poultry

A poultry feeding study was not available.

Residues in animal commodities

Cattle-STMR, HR and MRLs

For maximum residue level estimation, the high residues in the cattle tissues were calculated by interpolating the maximum dietary burden for beef cattle (1.45 ppm) between the relevant feeding levels (0.92 and 3.0 ppm) in the dairy cow feeding study and using the highest tissue concentrations from individual animals within those feeding groups. For maximum residue level estimation, the high residues in the cattle milk were calculated by interpolating the maximum dietary burden for dairy cattle (1.0 ppm) between the relevant feeding levels (0.92 and 3.0 ppm) in the dairy cow feeding study and using the highest mean milk concentrations from those feeding groups.

The STMR values for the tissues were calculated by interpolating the mean dietary burden for dairy cattle (0.24 ppm) with the 0.15 and 0.92 ppm feeding levels from the dairy cow feeding study and using the mean milk concentrations from those feeding groups. The STMR values for the milk were calculated by interpolating the mean dietary burden for dairy cattle (0.22 ppm) with the 0.15 and 0.92 ppm feeding levels from the dairy cow feeding study and using the mean milk concentrations from those feeding groups.

Bicyclopyrone feeding study	Feed level (ppm) for milk residues	Residues (mg/kg) in milk	Feed level (ppm) for tissue residues	Residues (mg/kg)			
				Muscle	Liver	Kidney	Fat
MRL beef or dairy cattle							
Feeding study	0.90	< 0.02	0.90	< 0.02	2.57	0.65*	< 0.02
	3.00	< 0.02	3.00	< 0.02	3.25		< 0.02
Dietary burden and high residue	1.00	< 0.02	1.45	< 0.02	2.748	0.65	< 0.02
STMR beef or dairy cattle							
Feeding study	0.15	< 0.02	0.15	< 0.02	1.30	0.5*	< 0.02
	0.90	< 0.02	0.90	< 0.02	2.29		< 0.02
Dietary burden and residue estimate	0.23	< 0.02	0.24	< 0.02	1.415	0.5	< 0.02

*Residue levels in kidney were not dose dependent; values are median calculated over all dose levels.

The Meeting estimated the following STMR values: milk 0.02 mg/kg; muscle 0.02 mg/kg; liver 1.415 mg/kg; kidney 0.5 mg/kg and fat 0.02 mg/kg.

The Meeting estimated the following HR values: milk 0.02 mg/kg; muscle 0.02 mg/kg; edible offal (based on liver) 2.75 mg/kg and fat 0.02 mg/kg.

The Meeting estimated the following maximum residue levels: milk 0.02* mg/kg; meat (mammalian except marine mammals) 0.02* mg/kg, edible offal 3 mg/kg and mammalian fats (except milk fats) 0.02* mg/kg.

Poultry-STMR, HR and MRLs

A poultry feeding study was not available. The Meeting used TRR levels from the poultry metabolism study to estimate maximum residue levels, STMRs, and HRs for poultry commodities. To all tissues except liver, TRRs were less than 1 mg eq/kg at a feeding level of approximately 20 ppm. When

scaled to the dietary burden of 0.16 ppm, the anticipated residue is 0.008 mg/kg. In liver, the TRR in the metabolism study was approximately 1.8 mg eq/kg, which scales to 0.014 mg/kg. For eggs, the TRR was 0.14 mg eq/kg, which scales to 0.0011 mg/kg.

On the basis of the anticipated residues, the Meeting estimated maximum residue levels of 0.01* mg/kg, STMRs, and HRs each at 0.01 mg/kg for all poultry commodities

RECOMMENDATIONS

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

Definition of the residue for compliance with the MRL and for dietary risk assessment for plant and animal commodities: sum of bicyclopyrone and its structurally-related metabolites determined as sum of compounds hydrolysable with base to SYN503780 (2-(2-methoxyethoxymethyl)-6-(trifluoromethyl)pyridine-3-carboxylic acid) and CSCD686480 (2-(2-hydroxyethoxymethyl)-6-(trifluoromethyl)pyridine-3-carboxylic acid), expressed as bicyclopyrone.

The residue is not fat soluble.

CCN	Commodity	Proposed MRL (mg/kg)	STMR or STMR-P (mg/kg)	HR or HR-P (mg/kg)
GC 0447	Sweet corn	0.03	0.02	0.02
GC 0640	Barley grain	0.04	0.011	-
GC 0645	Maize grain	0.02*	0	-
GC 0654	Wheat grain	0.04	0.01	-
GS 0659	Sugar cane	0.02*	0	0
MO 0105	Edible offal (mammalian)	3	Liver:1.415 Kidney: 0.5	Liver: 2.75 Kidney: 0.65
ML 0107	Milk of cattle, goats and sheep	0.02*	0.02	0.02
MF 0100	Mammalian fats (except milk fats)	0.02*	0.02	0.02
MM 0095	Meat (from mammals other than marine mammals)	0.02*	0.02	0.02
PE 0112	Eggs	0.01 *	0.01	0.01
PO 0111	Poultry edible offal	0.01*	0.01	0.01
PF 0111	Poultry fats	0.01*	0.01	0.01
PM 0110	Poultry meat	0.01*	0.01	0.01
CF 0654	Wheat bran, processed	0.1	0.023	0.053
CF 0640	Barley bran, processed	0.1	0.025	0.06
CF 1210	Wheat germ	0.06	0.014	0.032

Recommendation for feed commodities for calculation of the dietary burden

CCN	Commodity	Proposed MRL (mg/kg)	STMR (mg/kg)	HR(mg/kg)
AS 0640	Barley straw and fodder, Dry	0.8 (dw)	0.025 (hay) 0.115 (straw)	0.68 (hay) 0.25 (straw)
AF 0645	Maize forage	-	0.11	0.26
AS 0645	Maize fodder	0.5	0.054	0.36
-	Wheat forage	-	0.013	0.36
AS 0654	Wheat straw and fodder, Dry	0.8 (dw)	0.025 (hay) 0.115 (straw)	0.68 (hay) 0.25 (straw)

DIETARY RISK ASSESSMENT

Long-term dietary exposure

The International Estimated Daily Intakes (IEDI) for bicyclopyrone 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 3 to the 2017 Report.

The IEDI of the 17 GEMS/Food cluster diets, based on the estimated STMRs represented 3% to 20% of the maximum ADI of 0.003 mg/kg bw/day. The Meeting concluded that the long-term exposure to residues of bicyclopyrone from uses considered by the Meeting is unlikely to present a public health concern.

Short-term dietary exposure

The International Estimated Short-Term Intake (IESTI) for bicyclopyrone was calculated for all food commodities and their processed fractions for which maximum residue levels were estimated and for which consumption data were available. The results are shown in Annex 4 to the 2017 Report.

The current Meeting established an ARfD of 0.01 mg/kg bw for bicyclopyrone for women of child bearing age. The IESTIs represented 0–100% of the ARfD for the women of child bearing age. On the basis of the information provided to the Meeting, it was concluded that the short-term dietary exposure to residues of bicyclopyrone, resulting from the uses considered by the Meeting are unlikely to present a public health concern.

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Reference Number	Author(s)	Year	Study Title
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TK0147009	Sagan, K.	2015a	Bicyclopyrone/Bromoxynil EC (A19278A) – Residue Levels on Barley (Hay, Grain and Straw) in Canada During 2013. Report No TK0147009 GLP, not published Syngenta File No A19278A_50036
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TK0044065	Sagan, K.	2015b	Bicyclopyrone/Bromoxynil EC (A19278A) – Residue Levels on Wheat, (Forage, Hay, Grain, and Straw) in Canada During 2013. Report No TK0044065 GLP, not published Syngenta File No A19278A_50092
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M09183	Casallanovo, F.	2012b	A16003 – Magnitude of Residues of NOA449280 and SYN503780 in Sugarcane – Brazil, 2009-10 Report No. M09183 GLP, not published Syngenta File No. A16003E_10055
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Reference Number	Author(s)	Year	Study Title
T001953-09	Simmons, D. Weich, E.I. Walsh, K. Herczog, K.J.S.	2012	Magnitude of Residues in Milk and Tissues of Dairy Cows Following Multiple Oral Administrations of NOA44928 Ricerca Biosciences, LLC, Concord, United States Report No T001953-09 GLP, not published Syngenta File No NOA449280_50303