REGISTRATION REPORT

Part B
Section 2: Methods of analysis

Detailed summary of the risk assessment

TRANSFORM (GF-2372)

500 g/Kg Sulfoxaflor

Southern Zone

Zonal Rapporteur Member State: France

CORE ASSESSMENT

Applicant: DOW AgroSciences

Date: October 2017

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IIIA 5 METHODS OF ANALYSIS

The active substance submission followed a zonal approach where the evaluation was shared by four Member States participating under a work-share umbrella as follows: Ireland - RMS, lead reviewer for the sections Toxicology, Residues and Metabolism along with coordination of the work-share project. France: Lead reviewer for the sections Identity/Physical-Chemical properties, Methods of Analysis and Efficacy/Biology. Poland: Lead reviewer for the section Environmental Fate. Czech Republic: Lead reviewer for the section Ecotoxicology.

The Draft Assessment Report (DAR) on sulfoxaflor was finalised and distributed by Ireland in November 2012, with a recommendation for approval of the active substance according to Regulation (EC) 1107/2009. The EFSA peer review process was conducted and the EFSA conclusion was published in May 2014.

Dow AgroSciences submitted an EU MRL dossier to the RMS, Ireland, in April 2011. The EU MRL evaluation was integrated with the active substance evaluation under 1107/2009. EU MRLs have been established (Reg (EU) 396/2005).

There were two representative formulations for the EU active approval submission. These were GF-2372 (500 g/kg WG) and GF-2626 (120 g/L SC).

This current submission is for one of these two formulations, GF-2372. This is the first submission for authorisation of plant protection products containing sulfoxaflor in EU Member States. The proposed zonal RMS for Central Zone and Southern Zone are Ireland and France respectively.

Where appropriate, this document refers to the conclusions of the EFSA review report (EFSA Journal 2014; 12(5):3692) of sulfoxaflor. This will be where: the active substance data are relied upon in the risk assessment of the formulation; or when the EU review concluded that additional data/information should be considered at national registration.

This Part B document only reviews data (active substance or plant protection product) and additional information that has not previously been considered within the EU review process, as part of the active approval decision. Studies for the active substance which have already been evaluated during the approval process are not summarised. New active substance data are only included if they are considered essential for the evaluation and a full study summary is provided.

Details of the active substance, the active approval Regulation and the Commission Review Report are provided in Table #-1.

Table #-1: Details for the active substance

Active Substance	Approval Regulation	EFSA Scientific Report
Sulfoxaflor	Regulation EU 2015/1295	EFSA Journal 2014; 12(5):3692

The active approval Regulation for sulfoxaflor provides specific provisions which need to be considered by the applicant in the preparation of their product submissions and by the Member States prior to granting an authorisation:

For sulfoxaflor, Member States shall pay particular attention to :

(a) the risk to bees and other non-target arthropods;

(b) the risk to bees and bumble bees released for pollination, when the substance is applied in glasshouses.

Conditions of use shall include risk mitigation measures, where appropriate.

The applicant shall submit confirmatory information as regards:

(a) the risk to honey bees via the different routes of exposure, in particular nectar, pollen, guttation fluid and dust;

(b) risk to honey bees foraging in nectar or pollen in succeeding crops and flowering weeds;

(c) the risk to pollinators other than honey bees;

(d) the risk to bee brood.

The applicant shall submit that information to the Commission, the Member States and the Authority by 18 August 2017.'

Appendix 1 of this document contains the list of references included in this document for support of the evaluation.
Appendix 2 of this document is the table of intended uses for GF-2372.

Information on the detailed composition of GF-2372 can be found in the confidential dossier of this submission (Registration Report - Part C).

NOTE

Sulfoxaflor is also referred to as manufacture's code numbers X11422208, XR-208, XDE-208 and DE-208 in the section.

IIIA 5.1 Analytical standards and samples

IIIA 5.1.1 Samples of the preparation

Samples will be provided upon request.

IIIA 5.1.2 Analytical standards for the pure active substance

Samples will be provided upon request.

IIIA 5.1.3 Analytical standards for the active substance as manufactured

Samples will be provided upon request.

IIIA 5.1.4 Analytical standards for relevant metabolites and all other compounds included in the residue definition

Samples will be provided upon request.

IIIA 5.1.5 Samples of reference substances for relevant impurities

Samples will be provided upon request.

IIIA 5.2 Methods of analysis of the plant protection product

Analytical methods for determination of sulfoxaflor and relevance of CIPAC methods in GF-2372 were evaluated as part of the EU review of sulfoxaflor active substance. There is currently no CIPAC method available for the determination of Sulfoxaflor.

IIIA 5.2.1 Description of the analytical methods for the determination of the active substance in the plant protection product

The following analytical method for the determination of the active substance in the plant protection product performed on GF-2372 **was assessed in the EU review**. The study was deemed acceptable but since this is a new substance a full summary of this report is also provided below for information only.

Report:	DAS-AM-G-09-19
Title:	Analytical Method and Validation for the Determination of XDE-208 in GF-2372 and GF-2032 End Use Products and in XDE-208 Technical Grade Active Ingredient
Document No:	NA
Guidelines:	SANCO 3030/99
GLP	Yes

Principle:
Sample preparation involves weighing an aliquot of the sample into a jar then adding 5.0 mL of internal standard (4-ethylphenol) solution using a volumetric pipet, followed by 45 mL of dilution solution added by bottle-top dispenser. The solutions are analyzed by LC using an agilent Zorbax SB-Phenyl 75 mm x 4.6 mm x 3.5 µm column and ultraviolet (UV) detector set at 260 nm. Quantitation is performed by internal standard calibration using peak areas. Principle of this method is similar to the one of method DAS-AM-G-11-1 evaluated above for the formulation GF-2626.

Validation data:
For the following validation data, the sum of peaks of both diastereoisomer has been used to found Sulfoxaflor contents.

Specificity:
Chromatograms were provided for blank formulation, formulation, for technical active substance and for a standard solution. Moreover, the absence of interference was checked changing the stationary phase and comparing the obtained chromatograms. The method is specific to the determination of active substance in the formulation GF-2372.

Linearity:
Linearity was investigated by the analysis of seven standard samples of different active substance concentrations. The method was found linear and validation data were reported in the table below.

Recovery:

The accuracy of the method was evaluated by the analysis sample containing different amounts of active substance (between 21 and 96 % SA added). Recoveries were found in the acceptable range and have been reported in the table below.

Precision:
The precision of the method was evaluated by the analysis of GF-2372 formulation, with five samples prepared in one day and five samples prepared another day. The overall RSD is found acceptable and have been reported in the table below.
The precision of the system was investigated by the analysis of five injections of the same prepared sample. The precision was found acceptable (RSD: 0.5 %)

Samples stability:
The solution stability of the formulation was determined by the analysis six days after the initial analysis of sample solutions prepared for the precision study. Mean content was found equal to 49.6 % instead of 49.3 % in the initial analysis. Acceptable.

Method of determination of active substance in GF-2372 - Validation data

Linearity		Recovery		Precision	
Range (mg/mL)	coefficient of determination r^2	Recovery range (Mean recovery) (%)	Overall RSD (%)	Mean content (% w/w)	RSD (%)
0.51 – 2.22 (25.5 – 111 %)	0.9999	98.8 – 99.7 (99.2)	0.3	49.3	0.5

Conclusion:
The analytical method DAS-AM-G-09-19 using HPLC-UV (260 nm) is fully validated for the determination of active substance in the formulation GF-2372.

IIIA 5.2.2 For preparations containing more than one active substance. Description of the method for determining each in the presence of the other

Not applicable; no other active substances are contained in this formulation. See IIIA 5.2.1 above.

IIIA 5.2.3 Applicability of existing CIPAC methods

See IIIA 5.2.1 above.

IIIA 5.2.4 Description of analytical methods for determination of relevant impurities

There are no relevant impurities in this formulation.

IIIA 5.2.5 Description of analytical methods for the determination of formulants

No methods are required as none of the co-formulants are defined as relevant for toxicity (environment, health).

IIIA 5.3 Description of analytical methods for the determination of residues

Analytical methods are active substance data and were provided in the EU review of sulfoxaflor and were considered adequate (EFSA Scientific Report (2014); 12(5):3692).

The notifier DOW is the notifier of the DAR 2012/addendum 2013 of the active substance sulfoxaflor.

The crop uses of Transform are claimed to be for cotton, oilseed rape and cereal (wheat, barley, oats, rye, spelt, triticale).

IIIA 5.3.1 Description of analytical methods for the determination of residues in crops

Crop and Animal Matrices

Sulfoxaflor is a new active substance which is currently undergoing evaluation for active substance approval in the EU. The Draft Assessment Report (DAR) on sulfoxaflor was finalised with a recommendation for approval of the active substance according to Regulation (EC) 1107/2009. The sulfoxaflor status on the EU database is pending so there is no residue definition in food/feed of plant origin and in food/feed of animal origin in the EU database during the evaluation of the preparation Closer.

According to EFSA Journal 2014;12(5):3692 revised March 2015, the residue definition in food/feed of plant origin and in food/feed of animal origin is sulfoxaflor only (provisional).

According to the Setting of MRLs for SULFOXAFLOR (XDE-208) evaluated by ANSES France in 2012, the residue definition proposed for monitoring purpose in food/feed of plant origin and in food/feed of animal origin is Sulfoxaflor.

Analytical methods are active substance data and were provided in the EU review of sulfoxaflor and were considered adequate (EFSA Scientific Report (2014); 12(5):3692). Details of the EU agreed methods for sulfoxaflor are provided below in Table 5.3.1-01.

Table 5.3.1-01: EU Conclusions: Analytical methods for residues of sulfoxaflor in crop/animal matrices

Crop/ Matrix	Study	EU Agreed Method[1]		
		Method	Analyte	LOQ (mg/kg)
Wet Crops Dry Crops Oily Crops Acidic Crops	Method	**Rodrigues junior, 2010** PTR number 10001643 Method 091116 and	Sulfoxaflor X11719474 X11721061	0.01

Crop/ Matrix	Study	EU Agreed Method[1]		
		Method	Analyte	LOQ (mg/kg)
		Rodrigues junior, 2010 PTR number 10001643 Method091031		
Wet Crops Dry Crops	ILV	**Seal, 2010** Study id: 101097 ILV method 091116	Sulfoxaflor X11719474 X11721061	0.01
Wet Crops Dry Crops Oily Crops Acidic Crops	Method	**Rawle 2010** Study Id CEMR-4295	Sulfoxaflor X11719474 X11721061	0.01
Muscle bovine poultry Kidney bovine Liver bovine poultry Fat bovine poultry Milk, whole Cream Egg	Method	**Wendelburg, 2010** Study 091188 Confirmation: **Merdian, 2010** study id 101095	Sulfoxaflor X11719474 X11721061	0.01
Liver bovine Milk, whole Egg	ILV	**Seal, 2010** study 101098 ILV 091188	Sulfoxaflor X11719474 X11721061	0.01

Crop/ Matrix	Study	EU Agreed Method[1]		
		Method	Analyte	LOQ (mg/kg)
Muscle bovine Kidney bovine Liver bovine Fat bovine Milk, whole Milk, skim Cream	Method	**Rawle, 2010** CEMR 4567	Sulfoxaflor X11719474 X11721061	0.01
Muscle poultry Liver poultry Fat poultry Eggs	Method	**Rawle, 2010** CEMR 4568	Sulfoxaflor X11719474 X11721061	0.01

[1] EFSA Scientific Report (2014); 12(5):3692

For monitoring purpose, and based on the actual definition of residue (sulfoxaflor only), an analytical method (Rodrigues junior, 2010 method 091116) using HPLC-MS/MS confirmed by validation for two mass transitions and its ILV (Seal, 2010 study 101097) have been provided and fully validated for the EU evaluation of sulfoxaflor for the determination of sulfoxaflor in plant with LOQ = 0.01 mg/kg for cereals and dry products, matrices with high water content, acidic matrices and fatty product.

For monitoring purpose, and based on the actual definition of residue (sulfoxaflor only), an analytical method (Wendelburg, 2010 method 091188) using HPLC-MS/MS and its ILV (Seal, 2010 study 101098) have been provided and fully validated for the determination of sulfoxaflor in foodstuff of animal origin with LOQ = 0.01 mg/kg for cream, eggs, milk, liver, fat, muscle and kidney. This method can be confirmed by the multi residue method DFG S19 (Merdian, 2010 report 101095) validated at the same LOQ. Moreover, the efficiency of the extraction step used in these methods has been validated.

IIIA 5.3.2 Storage stability of working solutions in analytical methodology

The storage stability of working solutions was provided in the EU review of sulfoxaflor and was considered adequate.

IIIA 5.4 Description of methods for the analysis of soil

According to EFSA Journal 2014;12(5):3692 revised March 2015, the residue definition in soil for monitoring purpose is Sulfoxaflor and its metabolite X11719474 (N-(methyl(oxido){1-[6-(trifluoromethyl)pyridin-3-yl]ethyl}-λ4-sulfanylidene) urea).

Analytical methods are active substance data and were provided in the EU review of sulfoxaflor and were considered adequate (EFSA Scientific Report (2014); 12(5):3692). Details of the EU agreed methods are provided below in Table 5.4-01.

Table 5.4-01 EU Conclusions: Analytical methods for residues of sulfoxaflor in soil

Matrix	Study	EU agreed method1		
		Method	Analyte	LOQ (mg/kg)
Soil	Method	**Wendelburg and Olberding, 2011** Study Id 091185	Sulfoxaflor X11719474 X11519540 X11579457	0.001
Soil	ILV	**Gravelle, 2010** Id. 101100 EPSL: 29727 ILV	Sulfoxaflor X11719474 X11519540 X11579457	0.001

[1] EFSA Scientific Report (2014); 12(5):3692

For monitoring purpose, an analytical method (Wendelburg and Olberding, 2011a method 091185) using HPLC-MS/MS confirmed by validation for two mass transitions and its ILV (Gravelle, 2010 study 101100) have been provided and can be considered as fully validated for the determination of sulfoxaflor and its metabolite X11719474 in soil with LOQ = 0.001 mg/kg.

IIIA 5.5 Description of methods for the analysis of sediment

This is not an EC data requirement/ not required by Regulation 1107/2009.

IIIA 5.6 Description of methods for the analysis of water

According to EFSA Journal 2014;12(5):3692 revised March 2015, the residue definition in water for monitoring purpose is Sulfoxaflor and its metabolite X11719474 (N-(methyl(oxido){1-[6-(trifluoromethyl)pyridin-3-yl]ethyl}-λ4-sulfanylidene) urea).

Analytical methods are active substance data and were provided in the EU review of sulfoxaflor and were considered adequate (EFSA Scientific Report (2014); 12(5):3692. Details of the EU agreed methods are provided below in Table 5.6-01.

Table 5.6-01: EU Conclusions: Analytical methods for residues of sulfoxaflor in water

Matrix	Study	EU agreed method1		
		Method	Analyte	LOQ (µg/L)
Water (pound, well and tap)	Method	**Wendelburg and Olberding, 2011** Id. 091186	Sulfoxaflor X11719474 X11579457 X11519540	0.050 (with SPE) 0.250 (without SPE)
Water (tap, ground and surface)	ILV	**Li, 2010** Id. 101650 ILV	Sulfoxaflor X11719474 X11519540 X11579457	0.001

[1] EFSA Scientific Report (2014); 12(5):3692

For monitoring purpose, an analytical method (Wendelburg and Olberding, 2011b method 091186) using HPLC-MS/MS confirmed by validation for two mass transitions and its ILV (Li, 2010 study 101650) have been provided and fully validated for the determination of sulfoxaflor in water with LOQ = 0.05 µg/L.

IIIA 5.7 Description of methods for the analysis of air

According to EFSA Journal 2014;12(5):3692 revised March 2015, the residue definition in air for monitoring purpose is Sulfoxaflor only.

Analytical methods are active substance data and were provided in the EU review of sulfoxaflor and were considered adequate (EFSA Scientific Report (2014); 12(5):3692. Details of the EU agreed methods are given below in Table 5.7-01.

Table 5.7-01 EU Conclusions: Analytical methods for residues of sulfoxaflor in air

Matrix	Study	EU agreed method1		
		Method	Analyte	LOQ (µg/m3)
Air	Method	091133	Sulfoxaflor	0.30

[1] EFSA Scientific Report (2014); 12(5):3692.

For monitoring purpose, and based on the actual definition of residue (sulfoxaflor only), an analytical method (Merdian, 2010 method 091133) using HPLC-MS/MS confirmed by validation for two mass transitions has been provided and fully validated for the determination of sulfoxaflor in air with LOQ = 0.3 µg/m^3.

IIIA 5.8 Description of methods for the analysis of body fluids and tissues

Sulfoxaflor is not classified as toxic or very toxic and therefore a method for body fluids or tissues is not required.

IIIA 5.9 Other/special studies

Report:	**Rawle, N. W. 2012a**
Title:	Residues of XDE-208 in oil seed rape at intervals and harvest following a single application of GF-2032– Northern and Southern Europe – 2008 and 2009
Document No	CEMR-3927
GLP	yes
Owner	Dow AgroSciences
Laboratory facility	CEM analyticals Services Ltd, Glendale park, Berkshire SL5 8JB, UK

Report:	**Rawle, N. W. 2014**
Title:	Residues of sulfoxaflor in oil seed rape at intervals and harvest following multiple application of GF-2372 – Southern Europe – 2013
Document No	CEMR-5945
GLP	yes
Owner	Dow AgroSciences
Laboratory facility	CEM analyticals Services Ltd, Glendale park, Berkshire SL5 8JB, UK

Report:	**Rawle, N. W. 2012b**
Title:	Residues of sulfoxaflor in cotton at intervals and harvest following a single application of GF-2372 – Southern Europe – 2011
Document No	CEMR-5007
GLP	yes
Owner	Dow AgroSciences
Laboratory facility	CEM analyticals Services Ltd, Glendale park, Berkshire SL5 8JB, UK

Report:	**Rawle, N. W. 2012c**
Title:	Residues of sulfoxaflor in barley at intervals and harvest following multiple applications of GF-2372 – Northern and Southern Europe – 2011

Document No	CEMR-5006
GLP	yes
Owner	Dow AgroSciences
Laboratory facility	CEM analyticals Services Ltd, Glendale park, Berkshire SL5 8JB, UK

Report:	**Rawle, N. W 2012d**
Title:	Residues of sulfoxaflor in barleygrain and process fractions at harvest following multiple applications of GF-2372 – 2011
Document No	CEMR-5034
GLP	yes
Owner	Dow AgroSciences
Laboratory facility	CEM analyticals Services Ltd, Glendale park, Berkshire SL5 8JB, UK

Report:	**Rawle, N. W. 2012e**
Title:	Residues of sulfoxaflor in wheat at intervals and harvest following multiple applications of GF-2372 – Northern and Southern Europe – 2011
Document No	CEMR-5005
GLP	yes
Owner	Dow AgroSciences
Laboratory facility	CEM analyticals Services Ltd, Glendale park, Berkshire SL5 8JB, UK

The determination of sulfoxaflor (XDE-208) and its metabolites X11719474 and X11721061 (studies Rawle, N. W. 2012a to e and 2014) in high fat, high water content and dry commodities (oil seed rape whole plant, oil seed, cotton whole plant, cotton seed, barley whole plant, barley straw, barley grains, barley process fractions, wheat grain, wheat whole plant, wheat straw) was performed using an analytical method Rodrigues junior, 2010 (method 091031, Regulatory sciences and government affairs - Mogi Mirim). This analytical method used in the trials has been fully validated in the monograph of sulfoxaflor with its ILV Seal, 2010 (Study 101097) for the determination of sulfoxaflor and its metabolites X11719474 and X11721061 residues by LC-MS/MS in plants (high water, high fat, high dry and high acid content commodities) with LOQ = 0.01 mg/kg.

Residues of sulfoxaflor and metabolites are extracted from the sample matrices by homogenizing and shaking with an acetonitrile/water 80:20 solution. A solution containing 0.1 µg/mL of stable isotopes from the three compounds is added to a 0.5-mL aliquot of the extraction solution, which is then evaporated and hydrolyzed at 50°C with 0.01 N NaOH. The mixture is acidified with 0.25% formic

acid and is incubated at 50°C with a 10 mg/mL glucosidase from *Aspergillus Niger* solution (to convert X11721061 conjugates to the free form). The solution is purified using a reverse-phase polymeric solid-phase extraction (SPE) cartridge and then analyzed through a liquid chromatography with positive-ion electrospray ionization tandem mass spectrometry (LC-MS/MS).

Mass transitions used:
Sulfoxaflor m/z: 278 → 174 (278 → 154 for confirmation)
X11719474 m/z: 296 → 174 (296 → 105 or 296 → 104 for confirmation)
X11721061 m/z: 192 → 130 (192 → 78 for confirmation)
Column: Synergi Hydro-RP 80A (4.6x75 mm, 4.0 µm)

Findings

Specificity
Chromatograms have been obtained condensing the diastereoisomers in a unique peak, for better quantification of the residue.
For each transition analytes/matrix, chromatograms of blank control (untreated samples), standards of calibration (1.25 ng/mL) and fortified sample (LOQ) are given.
Residues in control samples were below 30% × LOQ. There was no interference in the blank chromatogram in the region of the analyte peaks (sulfoxaflor: 6.30 min, X11719474: 5.70 min, X11721061: 6.12 min).

Linearity
For each analyte, linearity was proven over a concentration range from 0.075 ng/mL to 125 ng/mL. The calibration curves have been tested with at eleven concentrations (duplicate) and the correlation coefficient were > 0.9990.

Recovery and Repeatability
The accuracy of the method was determined by comparing theoretical and measured concentrations of the recovery experiments. Precision of the method was determined from the replicate analysis at each fortification level by calculating the relative standard deviation (RSD).
Accuracy and precision results are summarized in the following Table.

Study	Matrix	Analyte	Fortification level (mg/kg)	N	Recoveries (%)	Mean recovery	RSD (%)
Rawle, N. W. 2012a	Oil seed rape whole plant	sulfoxaflor	0.01	6	97/101/100/98/91/105	99	4.7
			0.10	2	86/78	82	6.9
			1.0	2	100/95	98	3.6
	Oil seed		0.01	6	91/83/84/94/107/90	92	9.5
			0.10	2	92/85	89	5.6
			1.0	2	87/85	86	1.6
	Oil seed rape rest of plant		0.01	6	99/111/105/105/92/96	101	6.9
			0.10	2	85/90	88	4.0
			1.00	2	103/98	101	3.5
Rawle, N.	Oil seed rape whole plant	X11719474	0.01	6	104/104/115/86/92/91	99	11.0
			0.10	2	85/82	94	2.5
			1.0	2	99/95	97	2.9
	Oil seed		0.01	6	104/105/100/92/93/95	98	5.7

W. 2012a			0.10	2	86/82	84	3.4
			1.0	2	98/93	96	3.7
	Oil seed rape rest of plant		0.01	6	101/109/105/83/89/78	94	13.4
			0.10	2	79/76	78	2.7
			1.00	2	97/96	97	0.7
Rawle, N. W. 2012a	Oil seed rape whole plant	X11721061	0.01	6	77/76/77/97/93/103	87	13.7
			0.10	2	85/86	86	0.8
			1.0	2	98/89	94	6.8
	Oil seed		0.01	6	90/91/107/94/96/88	94	7.2
			0.10	2	85/81	83	3.4
			1.0	2	91/85	88	4.8
	Oil seed rape rest of plant		0.01	6	73/81/92/93/94/88	87	9.5
			0.10	2	72/69	71	3.0
			1.00	2	92/92	92	0.0
Rawle, N. W. 2014	Oil seed rape whole plant	sulfoxaflor	0.01	3	89/93/101	94	6.5
			0.10	2	75/95	85	16.6
	Oil seed		0.01	3	81/86/88	85	4.2
			0.10	2	89/86	88	2.4
	Oil seed rape rest of plant		0.01	3	88/91/83	87	4.6
			0.10	2	94/86	90	6.3
Rawle, N. W. 2014	Oil seed rape whole plant	X11719474	0.01	3	85/85/99	90	9.0
			0.10	2	74/84	79	9.0
	Oil seed		0.01	3	90/92/89	90	1.7
			0.10	2	80/87	84	5.9
	Oil seed rape rest of plant		0.01	3	88/89/88	88	0.7
			0.10	2	88/85	87	2.5
Rawle, N. W. 2014	Oil seed rape whole plant	X11721061	0.01	3	111/115/84	103	16.3
			0.10	2	72/101	87	23.7
	Oil seed		0.01	3	114/109/108	110	2.9
			0.10	2	99/87	93	9.1
	Oil seed rape rest of plant		0.01	3	82/106/93	94	12.8
			0.10	2	89/95	92	4.6
Rawle, N. W. 2012b	Cotton whole plant	sulfoxaflor	0.01	3	80/96/106	94	14.0
			0.10	2	81/78	80	2.7
	Cotton non delinted seed		0.01	3	87/73/83	81	8.9
			0.10	2	77/78	78	0.9
	Cotton Gin by-products		0.01	3	73/73/100	82	19.0
			0.10	2	70/72	71	2.0
Rawle, N. W. 2012b	Cotton whole plant	X11719474	0.01	3	75/85/73	78	8.3
			0.10	2	76/76	76	0.0
	Cotton non delinted seed		0.01	3	81/70/77	76	7.3
			0.10	2	77/79	78	1.8

	Cotton Gin by-products		0.01	3	94/83/70	82	14.6
			0.10	2	74/72	73	1.9
Rawle, N. W. 2012b	Cotton whole plant	X11721061	0.01	3	74/108/98	93	18.7
			0.10	2	74/78	76	3.7
	Cotton non delinted seed		0.01	3	95/101/73	90	16.4
			0.10	2	76/80	78	3.6
	Cotton Gin by-products		0.01	3	123/104/95	107	13.3
			0.10	2	82/82	82	0.0
Rawle, N. W. 2012c	barley whole plant	sulfoxaflor	0.01	3	100/98/72	90	17.4
			1.00	2	94/95	95	0.7
	Barley grain		0.01	3	94/94/82	90	7.7
			1.00	2	83/88	86	4.1
	Barley straw		0.01	3	94/95/106	98	6.8
			1.00	2	83/96	90	10.3
Rawle, N. W. 2012c	barley whole plant	X11719474	0.01	3	119/92/105	105	12.8
			1.00	2	76/81	79	4.5
	Barley grain		0.01	3	84/94/90	89	5.6
			1.00	2	89/97	93	6.1
	Barley straw		0.01	3	116/97/107	107	8.9
			1.00	2	90/79	85	9.2
Rawle, N. W. 2012c	barley whole plant	X11721061	0.01	3	81/105/110	99	15.7
			1.00	2	84/75	80	8.0
	Barley grain		0.01	3	97/88/107	97	9.8
			1.00	2	82/89	86	5.8
	Barley straw		0.01	3	110/82/99	97	14.5
			1.00	2	81/84	83	2.6
Rawle, N. W. 2012d	Barley grain	sulfoxaflor	0.01	3	73/78/93	81	12.8
			1.00	2	70/79	75	8.5
	Pearled barley		0.01	3	123/106/98	109	11.7
			1.00	2	79/74	77	4.6
	Pot barley		0.01	3	101/93/87	94	7.5
			1.00	2	93/93	93	0.0
	Bran barley		0.01	3	97/101/68	89	20.3
			1.00	2	90/93	92	2.3
	Barley flour		0.01	3	80/73/86	80	8.2
			1.00	2	82/89	86	5.8
	Cleaned barley		0.01	6	83/85/79/107/80/83	86	12.1
			1.00	4	92/84/86/108	93	11.8
	Brewing malt		0.01	3	79/106/85	90	15.8
			1.00	2	108/87	98	15.2
	Malt sprouts		0.01	3	90/83/120	98	20.1
			1.00	2	96/108	102	8.3
	Spent grains and flocs		0.01	3	67/79/72	73	8.3
			1.00	2	93/90	92	2.3
	Brewer's		0.01	3	94/97/93	95	2.2

	yeast		1.00	2	71/82	77	10.2
	beer		0.01	3	100/93/85	93	8.1
			1.00	2	101/71	86	24.7
Rawle, N. W. 2012d	Barley grain	X11719474	0.01	3	92/90/98	93	4.5
			1.00	2	86/86	86	0.0
	Pearled barley		0.01	3	73/77/77	76	3.1
			1.00	2	75/72	74	2.9
	Pot barley		0.01	3	74/81/76	77	4.7
			1.00	2	84/78	81	5.2
	Bran barley		0.01	3	83/81/78	81	3.1
			1.00	2	80/76	78	3.6
	Barley flour		0.01	3	68/93/78	80	15.8
			1.00	2	83/79	81	3.5
	Cleaned barley		0.01	6	66/77/70/91/76/97	80	15.2
			1.00	4	80/79/102/103	91	14.6
	Brewing malt		0.01	3	75/87/82	81	7.4
			1.00	2	84/86	85	1.7
	Malt sprouts		0.01	3	86/75/81	81	6.8
			1.00	2	81/85	83	3.4
	Spent grains and flocs		0.01	3	87/75/70	77	11.3
			1.00	2	81/80	81	0.9
	Brewer's yeast		0.01	3	72/69/71	71	2.2
			1.00	2	76/75	76	0.9
	beer		0.01	3	70/70/78	74	6.4
			1.00	2	76/71	73	4.8
Rawle, N. W. 2012d	Barley grain	X11721061	0.01	3	86/75/87	83	8.1
			1.00	2	82/82	82	0.0
	Pearled barley		0.01	3	94/75/90	86	11.6
			1.00	2	73/74	74	1.0
	Pot barley		0.01	3	95/79/76	83	12.3
			1.00	2	77/76	77	0.9
	Bran barley		0.01	3	99/80/96	92	11.1
			1.00	2	76/74	75	1.9
	Barley flour		0.01	3	106/76/71	84	22.4
			1.00	2	84/75	80	8.0
	Cleaned barley		0.01	6	89/75/84/82/78/102	85	11.3
			1.00	4	89/79/88/96	88	7.9
	Brewing malt		0.01	3	92/85/80	86	7.0
			1.00	2	85/81	83	3.4
	Malt sprouts		0.01	3	94/99/83	92	8.9
			1.00	2	94/80	87	11.4
	Spent grains and flocs		0.01	3	85/67/77	76	11.8
			1.00	2	84/82	83	1.7
	Brewer's yeast		0.01	3	74/67/82	74	10.1
			1.00	2	76/74	75	1.9
	beer		0.01	3	71/111/92	91	21.9
			1.00	2	77/75	76	1.9
	Wheat whole plant		0.01	3	81/91/89	87	6.1
			1.00	2	91/90	91	0.8
	Wheat grain		0.01	3	92/72/71	78	15.1

Rawle, N. W. 2012e	Wheat straw	sulfoxaflor	0.5	2	78/82	80	3.5
			0.01	3	72/79/93	81	13.1
			0.5	2	88/91	90	2.4
Rawle, N. W. 2012e	Wheat whole plant	X11719474	0.01	3	70/72/77	73	4.9
			1.00	2	83/78	81	4.4
	Wheat grain		0.01	3	90/79/83	84	6.6
			0.5	2	87/87	87	0.0
	Wheat straw		0.01	3	91/91/89	90	1.3
			0.5	2	91/84	88	5.7
Rawle, N. W. 2012e	Wheat whole plant	X11721061	0.01	3	82/83/75	80	5.4
			1.00	2	81/83	82	1.7
	Wheat grain		0.01	3	87/87/101	92	8.8
			0.5	2	89/81	85	6.7
	Wheat straw		0.01	3	109/97/83	96	13.5
			0.5	2	81/79	80	1.8

The mean recoveries obtained for each analyte at both fortification levels (0.01 mg/kg and hiher level) for each matrix are in the range 70-120%. The corresponding relative standard deviations complied with the acceptance criteria that the RSD in general should be ≤ 20%.

For the matrix with 3/2 samples per fortifications levels, and due to previous validation of the methods Rodrigues junior, 2010 (method 091031) with its ILV Seal, 2010 (Study 101097) in the DAR, minimum recovery data were provided and considered acceptable only for the matrices which are the same than the ones for which the main method was validated for (high dry and high fat content commodities and straw). Therefore, the number of fortified samples for the recovery is not enough for the matrices barley flour, brewing malt, malt sprouts, brewer's yeast and beer (studies Rawle 2012d) for each analyte: sulfoxaflor, X11719474 and X11721061. A full validation of the method used in the trial Rawle 2012d in the laboratory facility (CEM analyticals Services Ltd, Glendale park, Berkshire SL5 8JB, UK) is required for the determination of sulfoxaflor, X11719474 and X11721061 in: barley flour, brewing malt, malt sprouts, brewer's yeast and beer. If provided data are not considered acceptable, are not fully or are not provided, trial using the method will be considered inacceptable.

Study Comments:	The studies Rawle, N. W. 2012a to e and 2014 are validated for the determination of sulfoxaflor and its metabolites X11719474, X11721061 in oil seed rape whole plant, oil seed, cotton whole plant, cotton seed, barley whole plant, barley straw, barley grains, barley process fractions, wheat grain, wheat whole plant, wheat straw with a LOQ of 0.01 mg/kg. A full validation of the method used in the trial Rawle 2012d in the laboratory facility (CEM analyticals Services Ltd, Glendale park, Berkshire SL5 8JB, UK) is required for the determination of sulfoxaflor, X11719474 and X11721061 in: barley flour, brewing malt, malt sprouts, brewer's yeast and beer. If provided data are not considered acceptable, are not fully or are not provided, trial using the method will be considered inacceptable.
Agreed endpoint:	

Report:	Semrau, J. 2013
Title:	Determination of residues of XDE-208 after one application of GF-2626 on bare soil in rotational crops (radish, leaf lettuce, spring onion and barley) at 2 sites in Northern Europe and 2 sites in Southern Europe 2011 / 2012
Document No	DAS report 110385
GLP	yes
Owner	Dow AgroSciences
Laboratory facility	Eurofins Agroscience Services GmbH

The purpose of this phase of the study was the analysis of samples of soil (including deposition trays), filter paper, radish (leaves and roots), leaf lettuce, spring onion, barley grain and barley straw samples generated from a crop rotation study. This study used 3 differents analytical methods.

1- The determination of sulfoxaflor (XDE-208) and its metabolites X11719474 and X11519540 and X11579457 in soil samples was performed using an analytical method Seymour 2008 (method STM1906A.01). This analytical method used in the trials has never been evaluated. The target limit LOQ is 0.001µg/g for all analytes.

Residues of sulfoxaflor and its metabolites are extracted from the soil with acetonitrile/1.0N HCl (90/10) solution. After evaporation to dryness, the sample is diluted in 1 mL of water/acetonitrile/acetic acid (95/05/0.1) solution and purified using SPE. The residues are analyzed by HPC-MS/MS (ESI +).

Instrumentation: Spark Holland Symbiosis Pharma Online SPE LC System
MDS SCIEX API 4000 LC/MS/MS System
MDS SCIEX Analyst 1.4.1 data system

Column: Phenomenex Synergi hydro (75x4.6 mm id)

Column Temperature: Ambient

Injection Volume: 5 to 10 µL depending on sensitivity and linearity of instrument

Mobile Phase: A –Acetonitrile with 0.01% formic acid
B –Water with 0.01% formic acid

Flow Rate: 1.0 mL/min. The eluent may be split before entering the source. Whether to split and amount of the split is to be determined depending on sensitivity and linearity of instrument

Gradient: Note: Gradient may be modified to obtain better separation.

Time, min	A, %	B, %
0:00	0	100
3:01	0	100
3:05	10	90
8:15	100	0
10:00	100	0
10:15	0	100
14:00	0	100

Compound:	Ion, *m/z*		Time, ms	DP/CE/CXP
	Q1	Q3		
XDE-208 quant	278.0	174.0	150	50/11/16
XDE-208 conf	278.0	154.0	150	50/37/16
XDE-208-urea quant	296.0	174.0	150	35/15/16
XDE-208-urea conf	296.0	105.0	150	35/23/16
X11519540 sulfone quant	254.1	175.1	150	60/26/16
X11519540 sulfone conf	254.0	51.1	150	60/123/14
X11579457 sulfoximine quant	253.1	174.1	150	41/13/16
X11579457 sulfoximine conf	253.1	80.0	150	41/17/16
XDE-208-M+3 stable isotope (ISTD)	281.1	177.0	150	26/23/16
XDE-208-M+3 stable isotope (ISTD) Alternative Ions	281.1	106.0	150	26/15/16
XDE-208-urea-M+3 stable isotope (ISTD)	299.0	177.2	150	36/17/16

Findings

Specificity
Chromatograms have been obtained condensing the diastereoisomers in a unique peak, for better quantification of the residue.
For each transition analytes/matrix, chromatograms of blank control (untreated samples), standards of calibration (2.5 ng/mL) and fortified sample (LOQ, 10LOQ and 100LOQ) are given.
Residues in control samples were below 30% × LOQ. There was no interference in the blank chromatogram in the region of the analyte peaks (sulfoxaflor: 6.40 min, X11719474: 5.90 min, X11519540: 6.90 min and X11579457: 5.90 min).

Linearity
For each analyte, linearity was proven over a concentration range from 0.075 ng/mL (equivalent to 0.3 ng/g) to 50 ng/mL (equivalent to 200 ng/g). For each analyte transitions, the calibration curves have been tested at ten concentrations and the correlation coefficient were > 0.9970.

Recovery and Repeatability
The recovery of Sulfoxaflor (XDE-208), X11719474, X11519540 and X11579457 from control soil fortified at 0.001 mg/kg, 0.01 mg/kg and 0.1 mg/kg was measured. Five determinations were carried out at each fortification level. The mean recovery at each level and the overall mean recovery were determined and were in the range 70% to 120%. The corresponding relative standard deviations complied with the acceptance criteria that the RSD in general should be ≤ 20%.

Sulfoxaflor:

Analytes	Fortification Level (mg/kg)	Number of Samples (n)	Recovery Range (%)	Mean (%)	SD (%)	RSD (%)
Sulfoxaflor - Quant	0.001	5	94 - 103	98	3.8	3.9
Sulfoxaflor - Quant	0.01	5	91 - 109	101	7.9	7.9
Sulfoxaflor - Quant	0.1	5	99 - 101	100	0.7	0.7
Sulfoxaflor - Quant	0.001 - 0.1	15	91 - 109	100	4.8	4.9
Sulfoxaflor - Conf	0.001	5	100-114	107	5.2	4.8
Sulfoxaflor - Conf	0.01	5	90-108	101	8.3	8.3
Sulfoxaflor - Conf	0.1	5	94-104	100	3.8	3.8
Sulfoxaflor - Conf	0.001 - 0.1	15	90-114	102	6.5	6.3

X11719474:

Analytes	Fortification Level (mg/kg)	Number of Samples (n)	Recovery Range (%)	Mean (%)	SD (%)	RSD (%)
X11719474 - Quant	0.001	5	91-109	99	8.0	8.1
X11719474 - Quant	0.01	5	82-98	92	6.1	6.7
X11719474 - Quant	0.1	5	89-100	94	4.3	4.5
X11719474 - Quant	0.001 - 0.1	15	82-109	95	6.5	6.9
X11719474 - Conf	0.001	5	91-114	104	9.5	9.1
X11719474 - Conf	0.01	5	89-108	101	7.4	7.3
X11719474 - Conf	0.1	5	97-103	100	2.8	2.8
X11719474 - Conf	0.001 - 0.1	15	89-114	102	6.8	6.7

X11519540:

Analytes	Fortification Level (mg/kg)	Number of Samples (n)	Recovery Range (%)	Mean (%)	SD (%)	RSD (%)
X11519540 - Quant	0.001	5	100-115	107	6.2	5.8
X11519540 - Quant	0.01	5	97-114	104	6.3	6.1
X11519540 - Quant	0.1	5	91-110	100	8.6	8.6
X11519540 - Quant	0.001 - 0.1	15	91-115	104	7.1	6.8
X11519540 - Conf	0.001	5	80-104	91	8.9	9.8
X11519540 - Conf	0.01	5	90-108	100	8.6	8.5
X11519540 - Conf	0.1	5	93-111	99	8.1	8.2
X11519540 - Conf	0.001 - 0.1	15	80-111	97	9.0	9.3

X11579457:

Analytes	Fortification Level (mg/kg)	Number of Samples (n)	Recovery Range (%)	Mean (%)	SD (%)	RSD (%)
X11579457 - Quant	0.001	5	71-95	86	9.2	10.8
X11579457 - Quant	0.01	5	82-95	88	5.4	6.2
X11579457 - Quant	0.1	5	80-95	89	5.8	6.5
X11579457 - Quant	0.001 - 0.1	15	71-95	88	6.7	7.6
X11579457 - Conf	0.001	5	68-108	94	16.4	17.4
X11579457 - Conf	0.01	5	86-105	98	8.0	8.2
X11579457 - Conf	0.1	5	90-105	96	5.8	6.0
X11579457 - Conf	0.001 - 0.1	15	68-108	96	10.4	10.8

2- The determination of sulfoxaflor (XDE-208) and its metabolites X11719474 and X11519540 and X11579457 in filters papers was performed using an analytical method Semrau, J. 2013a. This analytical method used in the trials has never been evaluated. The validation was carried out with a LOQ = 10 µg/specimen.

Filter papers were extracted by shaking with acetonitrile/water (80/20, v/v) before dilution with water/acetonitrile (95/5,v/v) containing 0.1% formic acid and analysis by LC-MS/MS (ESI+).

Instrumentation:	Spark Holland Symbiosis Pharma system Applied Biosystems API 4000 LC/MS/MS System MDS/Sciex Analyst 1.4.2 data system
Column:	Zorbax SB-C8 3.5 µm, 4.6 x 75 mm
Injection Volume:	50 µL
Injection Mode:	Partial loopfill
Speed: Flush volume:	Normal 2 x needle volume
Injection optimized for:	Flexibility
Needle height: Septum depth:	5 mm 8 mm
Air segment:	On
Needle wash program:	700 µL water 700 µL acetonitrile/water (80:20) containing 0.1% formic acid 700 µL methanol
Run Time:	6.1 minutes
Mobile Phase:	A – acetonitrile containing 0.01% formic acid B – water containing 0.01% formic acid
Flow Rate:	1000 µL/min

Gradient:

Time, min:sec	Solvent A, %	Solvent B, %
00:01	0	100
01:01	0	100
01:05	10	90
03:00	100	0
03:30	100	0
03:50	0	100
06:00	0	100

Analytes:	Precursor Ion Q1	Product Ion Q3	Dwell Time (msec)	Declustering Potential	Collision Energy	Cell Exit Potential
XDE-208 – quant.	278.3	174.2	150	58 V	10 V	12.5 V
XDE-208 – conf.	278.3	154.2	200	63 V	37 V	9.5 V
X11719474 – quant.	296.3	174.1	150	58 V	15 V	12.5 V
X11719474 – conf.	296.3	105.1	150	58 V	23 V	6.5 V
X11519540 – quant.	254.0	174.10	150	55 V	40 V	10 V
X11519540 – conf.	254.0	154.10	150	50 V	55 V	10 V
X11579457 – quant.	253.00	174.30	150	28 V	10 V	11 V
X11579457 – conf.	253.0	80.0	150	28 V	17 V	4.25 V

Findings

Specificity
Chromatograms have been obtained condensing the diastereoisomers in a unique peak, for better quantification of the residue.
For each transition analytes/matrix, chromatograms of blank control (untreated samples), standards of calibration (10 ng/mL) and fortified sample (LOQ, 10LOQ) are given.
Residues in control samples were below 30% × LOQ. There was no interference in the blank chromatogram in the region of the analyte peaks (sulfoxaflor: 6.40 min, X11719474: 5.90 min, X11519540: 6.90 min and X11579457: 5.90 min).

Linearity
For each analyte, linearity was proven over a concentration range from 1.0 ng/mL to 100 ng/mL. For each analyte transitions, the calibration curves have been tested at nine concentrations and the correlation coefficient were > 0.9970.

Recovery and Repeatability
The recovery of Sulfoxaflor (XDE-208), X11719474, X11519540 and X11579457 from control filters fortified at 10µg and 100µg was measured. Five determinations were carried out at each fortification level. The mean recovery at each level and the overall mean recovery were determined and were in the range 70% to 120%. The corresponding relative standard deviations complied with the acceptance criteria that the RSD in general should be ≤ 20%.

Sulfoxaflor:

Analytes	Fortification Level (µg/specimen)	Number of Samples (n)	Recovery Range (%)	Mean (%)	SD (%)	RSD (%)
XDE-208 - Quant	10	5	96-107	102	4.4	4.4
XDE-208 - Quant	100	5	92-107	99	5.4	5.4
XDE-208 - Quant	10-100	10	92-107	100	4.9	4.8
XDE-208 - Conf	10	5	100-107	104	2.9	2.8
XDE-208 - Conf	100	5	87-110	98	9.4	9.6
XDE-208 - Conf	10-100	10	87-110	101	7.3	7.2

X11719474:

Analytes	Fortification Level (µg/specimen)	Number of Samples (n)	Recovery Range (%)	Mean (%)	SD (%)	RSD (%)
XDE-208 - Quant	10	5	105-107	106	0.8	0.8
XDE-208 - Quant	100	5	100-113	106	4.9	4.7
XDE-208 - Quant	10-100	10	100-113	106	3.3	3.2
XDE-208 - Conf	10	5	93-115	105	9.8	9.3
XDE-208 - Conf	100	5	93-115	107	8.8	8.2
XDE-208 - Conf	10-100	10	93-115	106	8.8	8.3

X11519540:

Analytes	Fortification Level (µg/specimen)	Number of Samples (n)	Recovery Range (%)	Mean (%)	SD (%)	RSD (%)
X11519540 - Quant	10	5	103-112	106	3.4	3.2
X11519540 - Quant	100	5	94-114	106	8.4	7.9
X11519540 - Quant	10-100	10	94-114	106	6.0	5.5
X11519540 - Conf	10	5	108-115	113	2.9	2.5
X11519540 - Conf	100	5	92-115	107	9.3	8.7
X11519540 - Conf	10-100	10	92-115	110	7.2	6.6

X11579457:

Analytes	Fortification Level (µg/specimen)	Number of Samples (n)	Recovery Range (%)	Mean (%)	SD (%)	RSD (%)
X11579457 - Quant	10	5	108-113	111	2.2	1.9
X11579457 - Quant	100	5	106-113	109	2.7	2.5
X11579457 - Quant	10-100	10	106-113	110	2.6	2.4
X11579457 - Conf	10	5	108-112	110	2.0	1.9
X11579457 - Conf	100	5	102-117	109	5.5	5.1
X11579457 - Conf	10-100	10	102-117	109	4.0	3.6

3- The determination of sulfoxaflor (XDE-208) and its metabolites X11719474 and X11519540 and X11579457 in crops samples (radish (leaves and roots), leaf lettuce, spring onion, barley grain and barley straw) was performed using an analytical method Semrau, J. 2013b. This analytical method used in the trials has never been evaluated. The full validation was carried out with a LOQ = 0.01 mg/kg.

Crops were extracted by shaking with acetonitrile/water (80/20, v/v). The two stable isotopes were added to an aliquot of the extraction solution before evaporation and hydrolyzation at 40°C with 0.01 N sodium hydroxide. The samples were then acidified and incubated at 40°C with glucosidase before undergoing purification by online SPE and analysis by LC-MS/MS (ESI+).

Instrumentation:	Spark Holland Symbiosis Pharma system Applied Biosystems QTRAP 5500 LC/MS/MS System MDS/Sciex Analyst 1.5.1 data system
Column:	Zorbax SB-C8 3.5 µm, 4.6 x 75 mm
Injection Volume:	10 µL

Run Time:	14.0 minutes
Mobile Phase:	A – acetonitrile containing 0.01% formic acid B – water containing 0.01% formic acid
Flow Rate:	1000 µL/min (approx 400 µL/min split to waste)

Gradient:

Time, min:sec	Solvent A, %	Solvent B, %
00:00	0	100
03:01	0	100
03:05	10	90
08:15	100	0
10:00	100	0
10:15	0	100
14:00	0	100

Typical Mass Spectrometry Operating Conditions

Interface:	Electrospray
Polarity:	Positive
Scan Type:	MRM
Resolution:	Q1 – unit, Q3 – unit
Curtain Gas (CUR):	20
Collision Gas (CAD):	Medium
Temperature (TEM):	500°C
Ion Source Gas 1 (GS1):	40
Ion Source Gas 2 (GS2):	40
Period 1	
Pre-acquisition Delay:	0.0 min
Acquisition Time	9.0 min
IonSpray Voltage (IS):	5250 volts
Entrance Potential (EP):	10 volts
Dwell Time:	50 ms

Analytes:	Precursor Ion Q1	Product Ion Q3	Declustering Potential	Collision Energy	Cell Exit Potential
XDE-208 - quantitation	278.09	174.00	51 V	15 V	25 V
XDE-208 - confirmation	278.09	154.00	51 V	41 V	25 V
X11719474 - quantitation	296.00	174.00	51 V	27 V	25 V
X11719474 - confirmation	296.00	104.90	51 V	17 V	25 V
X11579457 - quantitation	253.10	174.10	52 V	12 V	22 V
X11579457 - confirmation	253.10	154.10	52 V	35 V	20 V
X11519540 - quantitation	254.10	175.10	86 V	26 V	22 V
X11519540 - confirmation	254.10	154.10	86 V	55 V	20 V

Findings

Specificity

Chromatograms have been obtained condensing the diastereoisomers in a unique peak, for better quantification of the residue.

For each transition analytes/matrix, chromatograms of blank control (untreated samples), standards of calibration (2.5 ng/mL) and fortified sample (LOQ and 100LOQ) are given.

Residues in control samples were below 30% × LOQ. There was no interference in the blank chromatogram in the region of the analyte peaks (sulfoxaflor: 6.40 min, X11719474: 5.90 min, X11519540: 6.90 min and X11579457: 5.90 min).

Linearity

For each analyte, linearity was proven over a concentration range from 0.075 ng/mL to 62.5 ng/mL. For each analyte transitions, the calibration curves have been tested at ten concentrations and the correlation coefficient were > 0.9970.

Recovery and Repeatability

The recovery of Sulfoxaflor (XDE-208), X11719474, X11519540 and X11579457 from crops samples fortified at 0.001 mg/kg and 1.0 mg/kg was measured. Five determinations were carried out at each fortification level. In most case, the mean recovery at each level and the overall mean recovery were determined and were in the range 70% to 120%. The corresponding relative standard deviations complied with the acceptance criteria that the RSD in general should be ≤ 20%.

But for the analyte X11519540, the mean recovery at 1mg/kg in lettuce and in onion was 121% and the RSD at 1 mg/kg in barley straw was 21.5%. For the analyte X11579457, the mean recovery at 1mg/kg in onions was 121%. The value are not acceptable and a justification is required.

Accuracy and precision results are summarized in the following Table.

Sulfoxaflor

Radish leaves:

Analytes	Fortification Level (mg/kg)	Number of Samples (n)	Recovery Range (%)	Mean (%)	SD (%)	RSD (%)
Sulfoxaflor - Quant	0.01	5	86-98	90	5.1	5.7
Sulfoxaflor - Quant	1	5	86-94	89	3.1	3.5
Sulfoxaflor - Quant	0.01 - 1	10	86-98	90	4.1	4.5
Sulfoxaflor – Conf	0.01	5	78-110	98	12.0	12.3
Sulfoxaflor – Conf	1	5	90-98	94	3.2	3.4
Sulfoxaflor – Conf	0.01 - 1	10	78-110	96	8.5	8.9

Radish roots:

Analytes	Fortification Level (mg/kg)	Number of Samples (n)	Recovery Range (%)	Mean (%)	SD (%)	RSD (%)
Sulfoxaflor - Quant	0.01	5	85-94	89	3.6	4.1
Sulfoxaflor - Quant	1	5	75-86	82	4.6	5.7
Sulfoxaflor - Quant	0.01 - 1	10	75-94	86	5.5	6.5
Sulfoxaflor - Conf	0.01	5	80-99	92	7.5	8.2
Sulfoxaflor - Conf	1	5	80-89	86	3.7	4.3
Sulfoxaflor - Conf	0.01 - 1	10	80-99	89	6.3	7.1

Lettuce:

Analytes	Fortification Level (mg/kg)	Number of Samples (n)	Recovery Range (%)	Mean (%)	SD (%)	RSD (%)
Sulfoxaflor - Quant	0.01	5	81-90	86	3.5	4.1
Sulfoxaflor - Quant	1	5	82-91	87	3.5	4.0
Sulfoxaflor - Quant	0.01 - 1	10	81-91	86	3.3	3.9
Sulfoxaflor - Conf	0.01	5	81-110	94	14.1	15.0
Sulfoxaflor - Conf	1	5	83-90	88	3.9	4.5
Sulfoxaflor - Conf	0.01 - 1	10	81-110	91	10.3	11.3

Onions:

Analytes	Fortification Level (mg/kg)	Number of Samples (n)	Recovery Range (%)	Mean (%)	SD (%)	RSD (%)
Sulfoxaflor - Quant	0.01	5	83-93	87	3.6	4.2
Sulfoxaflor - Quant	1	5	76-93	85	6.8	8.0
Sulfoxaflor - Quant	0.01 - 1	10	76-93	86	5.3	6.1
Sulfoxaflor - Conf	0.01	5	95-99	97	2.0	2.1
Sulfoxaflor - Conf	1	5	80-97	89	6.8	7.6
Sulfoxaflor - Conf	0.01 - 1	10	80-99	93	6.4	6.9

Barley grains:

Analytes	Fortification Level (mg/kg)	Number of Samples (n)	Recovery Range (%)	Mean (%)	SD (%)	RSD (%)
Sulfoxaflor - Quant	0.01	5	84-98	90	6.2	6.8
Sulfoxaflor - Quant	1	5	74-83	78	3.7	4.7
Sulfoxaflor - Quant	0.01 - 1	10	74-98	84	8.0	9.5
Sulfoxaflor - Conf	0.01	5	95-109	103	6.3	6.1
Sulfoxaflor - Conf	1	5	73-83	79	3.9	5.0
Sulfoxaflor - Conf	0.01 - 1	10	73-109	91	13.7	15.0

Barley straw:

Analytes	Fortification Level (mg/kg)	Number of Samples (n)	Recovery Range (%)	Mean (%)	SD (%)	RSD (%)
Sulfoxaflor - Quant	0.01	5	83-96	89	5.9	6.6
Sulfoxaflor - Quant	1	5	69-78	75	3.5	4.7
Sulfoxaflor - Quant	0.01 - 1	10	69-96	82	8.9	10.8
Sulfoxaflor - Conf	0.01	5	81-102	94	8.1	8.6
Sulfoxaflor - Conf	1	5	71-83	78	5.0	6.4
Sulfoxaflor - Conf	0.01 - 1	10	71-102	86	10.8	12.5

X11719474
Radish leaves:

Analytes	Fortification Level (mg/kg)	Number of Samples (n)	Recovery Range (%)	Mean (%)	SD (%)	RSD (%)
X11719474 - Quant	0.01	5	97-132	110	15.0	13.6
X11719474 - Quant	1	5	81-105	91	9.6	10.5
X11719474 - Quant	0.01 - 1	10	81-132	100	15.4	15.4
X11719474 - Conf	0.01	5	97-160	118	25.5	21.6
X11719474 - Conf	1	5	93-105	101	5.5	5.4
X11719474 - Conf	0.01 - 1	10	93-160	109	19.4	17.7

Radish roots:

Analytes	Fortification Level (mg/kg)	Number of Samples (n)	Recovery Range (%)	Mean (%)	SD (%)	RSD (%)
X11719474 - Quant	0.01	5	82-102	88	8.2	9.3
X11719474 - Quant	1	5	71-90	82	7.1	8.6
X11719474 - Quant	0.01 - 1	10	71-102	85	7.9	9.3
X11719474 - Conf	0.01	5	71-89	80	7.3	9.1
X11719474 - Conf	1	5	62-80	70	8.6	12.2
X11719474 - Conf	0.01 - 1	10	62-89	75	9.1	12.1

Lettuce:

Analytes	Fortification Level (mg/kg)	Number of Samples (n)	Recovery Range (%)	Mean (%)	SD (%)	RSD (%)
X11719474 - Quant	0.01	5	91-109	101	6.7	6.7
X11719474 - Quant	1	5	92-105	99	5.4	5.4
X11719474 - Quant	0.01 - 1	10	91-109	100	5.8	5.8
X11719474 - Conf	0.01	5	100-124	114	11.1	9.8
X11719474 - Conf	1	5	90-104	98	6.2	6.3
X11719474 - Conf	0.01 - 1	10	90-124	106	12.1	11.5

Onions:

Analytes	Fortification Level (mg/kg)	Number of Samples (n)	Recovery Range (%)	Mean (%)	SD (%)	RSD (%)
X11719474 - Quant	0.01	5	91-113	107	9.2	8.5
X11719474 - Quant	1	5	100-112	106	5.9	5.6
X11719474 - Quant	0.01 - 1	10	91-112	106	7.3	6.9
X11719474 - Conf	0.01	5	107-125	115	6.7	5.8
X11719474 - Conf	1	5	94-102	97	3.5	3.6
X11719474 - Conf	0.01 - 1	10	94-125	106	10.5	10.0

Barley grains:

Analytes	Fortification Level (mg/kg)	Number of Samples (n)	Recovery Range (%)	Mean (%)	SD (%)	RSD (%)
X11719474 - Quant	0.01	5	73-108	88	12.8	14.6
X11719474 - Quant	1	5	72-85	77	6.4	8.4
X11719474 - Quant	0.01 - 1	10	72-108	82	11.3	13.7
X11719474 - Conf	0.01	5	84-106	94	8.9	9.4
X11719474 - Conf	1	5	72-83	78	4.2	5.4
X11719474 - Conf	0.01 - 1	10	72-106	86	10.8	12.6

Barley straw:

Analytes	Fortification Level (mg/kg)	Number of Samples (n)	Recovery Range (%)	Mean (%)	SD (%)	RSD (%)
X11719474 - Quant	0.01	5	85-107	97	8.5	8.7
X11719474 - Quant	1	5	68-98	84	11.6	13.9
X11719474 - Quant	0.01 - 1	10	68-107	91	11.9	13.1
X11719474 - Conf	0.01	5	83-100	93	8.0	8.6
X11719474 - Conf	1	5	64-91	81	10.6	13.1
X11719474 - Conf	0.01 - 1	10	64-100	87	10.7	12.4

X11519540
Radish leaves:

Analytes	Fortification Level (mg/kg)	Number of Samples (n)	Recovery Range (%)	Mean (%)	SD (%)	RSD (%)
X11519540 - Quant	0.01	5	73-107	91	13.9	15.3
X11519540 - Quant	1	5	72-82	77	4.4	5.7
X11519540 - Quant	0.01 - 1	10	72-107	84	12.1	14.4
X11519540 - Conf	0.01	5	63-98	84	14.5	17.3
X11519540 - Conf	1	5	70-79	74	3.3	4.5
X11519540 - Conf	0.01 - 1	10	63-98	79	11.2	14.3

Radish roots:

Analytes	Fortification Level (mg/kg)	Number of Samples (n)	Recovery Range (%)	Mean (%)	SD (%)	RSD (%)
X11519540 - Quant	0.01	5	99-136	117	13.8	11.8
X11519540 - Quant	1	5	84-112	97	11.1	11.5
X11519540 - Quant	0.01 - 1	10	84-136	107	15.8	14.5
X11519540 - Conf	0.01	5	90-140	115	18.6	16.2
X11519540 - Conf	1	5	73-100	90	10.8	12.0
X11519540 - Conf	0.01 - 1	10	73-140	102	19.4	19.0

Lettuce:

Analytes	Fortification Level (mg/kg)	Number of Samples (n)	Recovery Range (%)	Mean (%)	SD (%)	RSD (%)
X11519540 - Quant	0.01	5	94-107	101	5.1	5.0
X11519540 - Quant	1	5	115-126	121*	4.8	4.0
X11519540 - Quant	0.01 - 1	10	94-126	111	11.5	10.4
X11519540 - Conf	0.01	5	78-119	100	17.1	17.0
X11519540 - Conf	1	5	98-122	108	9.0	8.3
X11519540 - Conf	0.01 - 1	10	78-122	104	13.4	12.9

*Mean recovery >110% acceptance at 1.0 mg/kg. Data acceptable as good overall mean and %RSD.

Onions:

Analytes	Fortification Level (mg/kg)	Number of Samples (n)	Recovery Range (%)	Mean (%)	SD (%)	RSD (%)
X11519540 - Quant	0.01	5	105-134	118	14.8	12.6
X11519540 - Quant	1	5	109-131	121*	9.7	8.0
X11519540 - Quant	0.01 - 1	10	105-134	119	11.9	10.0
X11519540 - Conf	0.01	5	98-123	110	12.2	11.1
X11519540 - Conf	1	5	103-127	118	9.1	7.7
X11519540 - Conf	0.01 - 1	10	98-127	114	11.1	9.8

*Mean recovery >110% acceptance at 1.0 mg/kg. Data acceptable as good overall mean and %RSD.

Barley grains:

Analytes	Fortification Level (mg/kg)	Number of Samples (n)	Recovery Range (%)	Mean (%)	SD (%)	RSD (%)
X11519540 - Quant	0.01	5	82-93	87	4.3	4.9
X11519540 - Quant	1	5	66-90	84	10.0	11.9
X11519540 - Quant	0.01 - 1	10	66-93	85	7.5	8.7
X11519540 - Conf	0.01	5	74-91	80	7.3	9.2
X11519540 - Conf	1	5	62-85	74	9.9	12.6
X11519540 - Conf	0.01 - 1	10	62-91	77	8.5	11.1

Barley straw:

Analytes	Fortification Level (mg/kg)	Number of Samples (n)	Recovery Range (%)	Mean (%)	SD (%)	RSD (%)
X11519540 - Quant	0.01	5	109-133	118	9.3	7.8
X11519540 - Quant	1	5	81-131	98	21.2	21.5*
X11519540 - Quant	0.01 - 1	10	81-133	108	18.6	17.2
X11519540 - Conf	0.01	5	102-117	109	5.4	5.0
X11519540 - Conf	1	5	72-107	89	15.0	16.8*
X11519540 - Conf	0.01 - 1	10	72-117	99	14.8	15.0

* >15% acceptance at 1.0 mg/kg. Data acceptable as good overall mean and %RSD.

X11579457
Radish leaves:

Analytes	Fortification Level (mg/kg)	Number of Samples (n)	Recovery Range (%)	Mean (%)	SD (%)	RSD (%)
X11579457 - Quant	0.01	5	64-89	80	10.1	12.6
X11579457 - Quant	1	5	75-91	82	6.8	8.3
X11579457 - Quant	0.01 - 1	10	64-91	81	8.2	10.1
X11579457 - Conf	0.01	5	70-105	84	14.4	17.2
X11579457 - Conf	1	5	72-87	80	5.6	7.0
X11579457 - Conf	0.01 - 1	10	70-105	82	10.5	12.9

Radish roots:

Analytes	Fortification Level (mg/kg)	Number of Samples (n)	Recovery Range (%)	Mean (%)	SD (%)	RSD (%)
X11579457 - Quant	0.01	5	83-99	92	6.4	7.0
X11579457 - Quant	1	5	79-88	81	3.8	4.7
X11579457 - Quant	0.01 - 1	10	79-99	87	7.5	8.7
X11579457 - Conf	0.01	5	75-116	93	15.8	17.0
X11579457 - Conf	1	5	78-90	82	4.7	5.8
X11579457 - Conf	0.01 - 1	10	75-116	88	12.4	14.2

Lettuce:

Analytes	Fortification Level (mg/kg)	Number of Samples (n)	Recovery Range (%)	Mean (%)	SD (%)	RSD (%)
X11579457 - Quant	0.01	5	79-112	93	13.0	14.0
X11579457 - Quant	1	5	85-102	96	6.8	7.1
X11579457 - Quant	0.01 - 1	10	79-112	95	9.9	10.5
X11579457 - Conf	0.01	5	94-107	100	5.1	5.1
X11579457 - Conf	1	5	84-107	97	8.3	8.6
X11579457 - Conf	0.01 - 1	10	84-107	98	6.7	6.8

Onions:

Analytes	Fortification Level (mg/kg)	Number of Samples (n)	Recovery Range (%)	Mean (%)	SD (%)	RSD (%)
X11579457 - Quant	0.01	5	99-128	110	11.8	10.7
X11579457 - Quant	1	5	110-128	121*	7.9	6.6
X11579457 - Quant	0.01 - 1	10	99-128	116	11.2	9.7
X11579457 - Conf	0.01	5	85-99	93	5.6	6.0
X11579457 - Conf	1	5	96-107	99	4.8	4.8
X11579457 - Conf	0.01 - 1	10	85-107	96	5.7	5.9

*Mean recovery >110% acceptance at 1.0 mg/kg. Data acceptable as good overall mean and %RSD.

Barley grains:

Analytes	Fortification Level (mg/kg)	Number of Samples (n)	Recovery Range (%)	Mean (%)	SD (%)	RSD (%)
X11579457 - Quant	0.01	5	91-109	101	8.6	8.5
X11579457 - Quant	1	5	81-100	91	6.9	7.6
X11579457 - Quant	0.01 - 1	10	81-109	96	9.2	9.6
X11579457 - Conf	0.01	5	83-112	98	12.3	12.6
X11579457 - Conf	1	5	81-105	91	9.4	10.4
X11579457 - Conf	0.01 - 1	10	81-112	95	10.9	11.5

Barley straw:

Analytes	Fortification Level (mg/kg)	Number of Samples (n)	Recovery Range (%)	Mean (%)	SD (%)	RSD (%)
X11579457 - Quant	0.01	5	87-127	104	15.9	15.3
X11579457 - Quant	1	5	83-117	101	12.4	12.3
X11579457 - Quant	0.01 - 1	10	83-127	103	13.6	13.2
X11579457 - Conf	0.01	5	72-117	96	21.4	22.4
X11579457 - Conf	1	5	80-107	96	9.8	10.2
X11579457 - Conf	0.01 - 1	10	72-117	96	15.7	16.4

Study Comments:	The study Semrau, J. 2013 is validated for the determination of sulfoxaflor, and its metabolites X11719474 and X11519540 and X11579457 in soil, in filter paper, and in crop (radish (leaves and roots), leaf lettuce, spring onion, barley grain and barley straw) with a LOQ = 0.001mg/kg in soil, with a LOQ = 10µg/specimen for filter papers and with a LOQ = 0.01 mg/kg for crop except for the analyte X11519540 in lettuce, onion and barley straw and for the analyte X11579457 in onion. In fact, for the analyte X11519540, the mean recovery at 1mg/kg in lettuce and in onion was 121% and the RSD at 1 mg/kg in barley straw was 21.5%. For the analyte X11579457, the mean recovery at 1mg/kg in onions was 121%. The value are not acceptable and a justification is required.
Agreed endpoint:	

Appendix 1 List of data submitted in support of the application

Data owner: DAS = Dow AgroSciences

Data protection statement

Dow AgroSciences is the first applicant for approval of this active substance. Data protection for the studies and tests indicated in the following reference list is claimed for a period of 10 years from the first authorisation of the formulation in each Member State in accordance with Article 59 of Regulation (EC) No 1107/2009.

These tests and studies are submitted to a Member State for the first time and as such, all are considered necessary for the authorisation. Relevant studies (as listed in SanCo Guidance Document 7109/VI/1995) have been conducted in compliance with the principles of GLP or GEP.

NOTE: Studies in bold were not evaluated at EU active approval

Annex Point	Author	Year	Title Source (where different from company) Company Report No. GLP or GEP status Published or unpublished	Data protection claimed (Y/N)	Relied on	Owner
5.2.1	Waid, C.	2010	Analytical Method and	Y	Y	DAS

Annex Point	Author	Year	Title Source (where different from company) Company Report No. GLP or GEP status Published or unpublished	Data protection claimed (Y/N)	Relied on	Owner
			Validation for the Determination of XDE-208 in GF-2372 and GF-2032 End Use Products and in XDE-208 Technical Grade Active Ingredient			

Appendix 2 Table of intended uses, GAP and justification for the risk envelope

Crop and/or situation (a)	Member State or Country	Product Name	F or G (b)	Pests or Group of pests controlled (c)	Formulation		Application				Application rate per treatment			PHI days (k)	Remarks (l)
					Type (d-f)	Conc. of a.s. (i) g/L	Method Kind (f-h)	Growth stage (j)	Number min max	Interval between applications (min)	kg as/hl min max	Water (l/ha) min max	kg as./ha min max		
Cotton	South (EL)	GF-2372	F	Aphids	WG	500 g/kg	Ground applied foliar spray, broadcast	BBCH 20-87 May-Sep	1-2	7	0.004-0.0016	300 - 1000	0.024	14	Two applications would be minimum 7 days interval.
Oilseed Rape	South (FR)	GF-2372	F	Aphids	WG	500 g/kg	Ground applied foliar spray, broadcast	BBCH 10 - 29 Sep-Dec BBCH 30 – 87 Apr-Jun	1-2	21	0.004-0.016	100-600	0.024	28	Two applications would be minimum 21 days interval. Only 1 application is allowed in the Sep-Dec interval followed by 1 application in the April-June period. If no autumn application, 2 spring

Crop and/or situation (a)	Member State or Country	Product Name	F or G (b)	Pests or Group of pests controlled (c)	Formulation		Application				Application rate per treatment			PHI days (k)	Remarks (l)
					Type (d-f)	Conc. of a.s. (i) g/L	Method Kind (f-h)	Growth stage (j)	Number min max	Interval between applications (min)	kg as/hl min max	Water (l/ha) min max	kg as./ha min max		
															applications are possible.
Cereal (Wheat, Barley, Oats, Rye, Spelt, Triticale) [W, S]	South (FR, IT)	GF-2372	F	Aphids	WG	500 g/kg	Ground applied foliar spray, broadcast	BBCH 12-29 Sep-Dec BBCH 30 – 87 Mar-Jul	1-2	21	0.004-0.016	100-600	0.024	21	Two applications would be minimum 21 days interval. Only 1 application is allowed in the Sep-Dec interval followed by 1 application in the March-July period. If no autumn application, 2 spring applications are possible.

(a) For crops, the EU and Codex classifications (both) should be used; where relevant, the use situation should be described (*e.g.* fumigation of a structure)

(b) Outdoor or field use (F), glasshouse application (G) or indoor application (I)

(c) *e.g.* biting and suckling insects, soil born insects, foliar fungi, weeds

(d) *e.g.* wettable powder (WP), emulsifiable concentrate (EC), granule (GR)

(e) GCPF Codes - GIFAP Technical Monograph No 2, 1989

(f) All abbreviations used must be explained

(g) Method, *e.g.* high volume spraying, low volume spraying, spreading, dusting, drench

(h) Kind, *e.g.* overall, broadcast, aerial spraying, row, individual plant, between the plant - type of equipment used must be indicated

(i) g/kg or g/l

(j) Growth stage at last treatment (BBCH Monograph, Growth Stages of Plants, 1997, Blackwell, ISBN 3-8263-3152-4), including where relevant, information on season at time of application

(k) Indicate the minimum and maximum number of application possible under practical conditions of use

(l) PHI - minimum pre-harvest interval

(m) Remarks may include: Extent of use/economic importance/restrictions