REGISTRATION REPORT

Part B
Section 6: Ecotoxicological Studies

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 10 ECOTOXICOLOGICAL STUDIES

Introduction

This document summarises the ecotoxicological effects of the plant protection product GF-2372 containing the active substance sulfoxaflor, and where appropriate, the active substance and potentially relevant metabolites and evaluates the potential risk to various representatives of terrestrial, aquatic and soil organisms. A risk assessment according to Uniform Principles is provided which demonstrates that use of the product in accordance with the proposed label does not represent an unacceptable risk to the environment.

Sulfoxaflor is a new active substance which has been approuved since 18/08/2015 in the EU. Ireland (Pesticide Registration and Control Division, PRCD) is the rapporteur Member State (RMS). A dossier for the active substance was submitted by Dow AgroSciences, under Regulation (EC) 1107/2009, to the RMS in July 2011.
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. The adoption of MRL/Import tolerances was therefore aligned with the same timing as that of the active substance approval.

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	Commission Review Report	EFSA Scientific Report
Sulfoxaflor	Reg. (EU) 2015/1295 (27 July 2015)	SANTE/10665/2015 rev 2 (29 May 2015)	EFSA Journal 2014; 12(5):3692

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

According to Regulation (EU) 2015/1295, 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.

NOTE

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

The use pattern for sulfoxaflor evaluated in the EU assessment is illustrated in Table 10-2. The current submission includes cereals and cotton but not fruiting vegetables. The rates are increased (2 x 24 g a.s./ha) and an additional crop (oilseed rape) is also included. The current GAP is shown in Appendix 2 of this document and the critical GAP included in Table 10-2.

Table 10-2: GAP for sulfoxaflor that was evaluated at EU level as well as the critical GAP for uses of the product GF-2372 in the southern zone of the EU

Crop and/or situation	N or S	F/G or I	Application			Application rate per treatment
			Stage BBCH	Max. Number	Interval (d)	g a.s./ha max
Critical GAP for GF-2372 in the southern zone of the EU						
Rape seed	S	F	BBCH 10-87	2	21	24
Cotton seed	S	F	BBCH 20-87	2	7	24
Cereals [w, s]	S	F	BBCH 12-87	2	21	24

F, G, I = Field, glasshouse, indoor
N, S = Northern zone, Southern zone
w, s = winter, spring

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

Table 10-3: Agreed EU physical-chemical properties for sulfoxaflor used in this evaluation (EFSA Journal 2014; 12(5):3692)

Property	Sulfoxaflor
Molar mass	277.3 g/mol
Molecular formula	C_{10} H_{10} F_3 N_3 O S
Solubility in water	At 20°C, 99.7%: pH 5: 1380 mg/L pH 7: 568 mg/L pH 9: 551 mg/L
Vapour pressure	1.4 x 10^{-6} Pa (20°C, 99.7%)
log P_{OW}	At 20°C, 99.7%: pH 5: 0.806 pH 7: 0.802 pH 9: 0.799
Henry's Law Constant	At 20°C: Un-bufferred: 5.77 10^{-7} Pa.m^3/mol pH 5: 2.81 10^{-7} Pa.m^3/mol pH 7: 6.83 10^{-7} Pa.m^3/mol pH 9: 7.05 10^{-7} Pa.m^3/mol
Photolytic stability	Compound is not prone to direct (in sterile buffered solution) and to direct and indirect (in natural water) aqueous photolysis
Hydrolytic stability	Compound hydrolytically stable at pH=5, pH=7 and pH=9

Consideration of metabolites

Table 10-4: Sulfoxaflor and its metabolites considered in the EU assessment to require risk assessment (EFSA Journal 2014;12(5):3692)

Code number/name	Compartment(s)
Sulfoxaflor	Soil, groundwater, surface water, sediment, air
X11719474	Soil, groundwater, surface water, sediment
X11519540	Soil, groundwater, surface water
X11579457	Groundwater

IIIA 10.1 Effects on Birds

Effects on birds for GF-2372 were evaluated as part of the EU review of sulfoxaflor. Therefore all relevant data were assessed in the EU review. Risk assessments for GF-2372 with the proposed use pattern are provided here and are considered adequate.

The risk assessment for effects on birds is carried out according to the EFSA guidance (2009)[1]. The endpoints employed in the risk assessment for sulfoxaflor are provided in Table 10.1-1.

Table 10.1-1: EU Endpoints - Toxicity of sulfoxaflor, its metabolites and GF-2372 to birds

Compound	Test species	Endpoint	EU agreed endpoints*
Sulfoxaflor	Bobwhite quail	Acute oral LD_{50}	**676 mg/kg bw**
GF-2372	Bobwhite quail	Acute oral LD_{50}	1655 mg prep./kg bw[a]
X11719474	Bobwhite quail	Acute oral LD_{50}	>2250 mg/kg bw
X11721061	Bobwhite quail	Acute oral LD_{50}	1038 mg/kg bw
Sulfoxaflor	Bobwhite quail	Short-term LDD_{50}	>1152 mg/kg bw/day
Sulfoxaflor	Mallard duck	Short-term LDD_{50}	>1049 mg/kg bw/day
Sulfoxaflor	Bobwhite quail	Reproduction NOEL	84.4 mg/kg bw/day
Sulfoxaflor	Mallard duck	Reproduction NOEL	**25.9 mg/kg bw/day**

* EFSA Journal 2014; 12(5):3692
[a]: The endpoint is equivalent to 827 mg a.s./kg diet.
Endpoints used in the risk assessment are in **bold**.

A screening dietary assessment has been conducted on the basis of the proposed uses of GF-2372 as summarised in Table 10-2.

In addition, an assessment of the risk from exposure to potentially relevant metabolites and an assessment of the risk from consumption of contaminated drinking water risk assessment have been conducted.

Sulfoxaflor has a log P_{ow} value of 0.802 (at pH 7) indicating a low potential for bioaccumulation in earthworm and fish tissues. Risk assessments for birds feeding on fish and earthworms are not necessary for this active substance and have not been conducted.

IIIA 10.1.1 Acute toxicity exposure ratio (TERA)

Screening assessment

The initial acute avian screening risk assessment is based on the toxicity value given in Table 10.1-1 and considers the worst-case exposure scenarios for the proposed uses of GF-2372 (Table

[1] European Food Safety Authority (2009). Guidance Document on Risk Assessment for Birds & Mammals on request from EFSA. EFSA Journal 2009, 7(12): 1438

10-2). The estimated daily dietary doses (DDDs) and associated toxicity exposure ratios (TERs) for the relevant indicator species are presented in the table below (Table 10.1.1-1).

Table 10.1.1-1: Acute screening risk assessment (TER_A) for birds from GF-2372 uses

Crop	Indicator bird	App. Rate (kg/ha)	Shortcut value (acute)	MAF	DDD (mg/kg bw)	LD_{50} (mg/kg bw)	TER_A [10]
Cereals, Oilseed rape	Small omnivorous	0.024	158.8	1.2	4.57	676	148
Cotton	Small omnivorous	0.024	160.3	1.4	5.39	676	125

MAF = multiple application factor (MAF for 14 day interval used as a worst-case for uses on cereals and OSR)
DDD = daily dietary dose

Based on the screening assessment, the TER_A values are greater than the trigger of 10, indicating an acceptable acute risk to birds from sulfoxaflor following the proposed uses of GF-2372.

IIIA 10.1.2 Short and long-term toxicity exposure ratios (TERST and TERLT)

Short-term toxicity exposure ratio (TER_{ST})

There is no requirement for the calculation of TER_{ST} for birds under the EFSA birds and mammals guidance document (EFSA Journal 2009; 7(12): 1438) and, consequently, a risk assessment for short-term toxicity has not been conducted.

Long-term toxicity exposure ratio (TER_{LT})

Screening assessment

The initial long-term avian screening risk assessment is based on the toxicity value given in Table 10.1-1 and considers the worst-case exposure scenarios for the proposed uses of GF-2372 (Table 10.1-2). The estimated daily dietary doses (DDDs) and associated toxicity exposure ratios (TERs) for the relevant indicator species are presented in the table below (Table 10.1.2-1).

Table 10.1.2-1: Long-term screening risk assessment (TER_{LT}) for birds from GF-2372 uses

Crop	Indicator bird	App. rate (kg/ha)	Shortcut value (long-term)	f_{TWA}	MAF	DDD (mg/kg bw/day)	NOEC (mg/kg bw/day)	TER_{LT} [5]
Cereals, Oilseed rape	Small omnivorous	0.024	64.8	0.53	1.4	1.15	25.9	22.4
Cotton	Small omnivorous	0.024	65.4	0.53	1.6	1.33	25.9	19.5

MAF = multiple application factor (MAF for 14 day interval used as a worst-case for cereals and OSR)
DDD = daily dietary dose
F_{TWA} = time weighted average factor

Based on the screening assessment, the TER_{LT} values are greater than the trigger of 5, indicating an acceptable long-term risk to birds from sulfoxaflor following the proposed uses of GF-2372.

Metabolites

In accordance with the EFSA guidance document, the risk to birds from metabolites formed in plants and vertebrate compartments has to be considered.

Birds can be exposed *via* diet to environmental metabolites of sulfoxaflor, particularly from metabolites formed in plant matter tissues, insects, soil organisms or combinations thereof. There are two major metabolites formed in plant tissue: X11719474 and X11721061, and two major soil metabolites: X11719474 and X11519540.

Metabolite X11719474: The acute oral LD_{50} of X11719474 was determined to be > 2250 mg/kg bw. The acute oral toxicity of sulfoxaflor was 676 mg/kg bw. Thus, X11719474 exhibits substantially less toxicity than parent sulfoxaflor and the avian risk assessment for X11719474 may be based upon the results of the risk assessment for the parent sulfoxaflor.

Metabolite X11519540: This metabolite is a major metabolite in aerobic soil (12.2%), but a minor metabolite in plants (2.1 - 6.9%). The relevant extent of the potential formation of X11519540 in plants and soil is approximately equivalent to the extent of formation in birds and mammals. In the goat metabolism study X11519540 was observed at up to 1.8% of initial parent residues and in the hen metabolism study at up to 6.8% of initial parent residues. Therefore, the toxicity of X11519540 can be considered to be accounted for by toxicity studies in birds of the parent material sulfoxaflor and the avian risk assessment for X11519540 may be based upon the results of the risk assessment for the parent sulfoxaflor.

Metabolite X11721061: The acute oral LD_{50} of X11721061 was determined to be 1038 mg/kg bw. The acute oral toxicity of sulfoxaflor was 676 mg/kg bw. Thus, X11721061 exhibits substantially less toxicity than parent sulfoxaflor and the avian risk assessment for X11721061 may be based upon the results of the risk assessment for the parent sulfoxaflor.

Drinking water assessment

The EFSA Bird and Mammal Guidance Document (EFSA Journal 2009; 7(12):1438) proposes an assessment methodology for the risk to birds from active substances in drinking water using a small granivorous bird as an indicator species. Considering the intended uses the relevant scenario for birds is the puddle scenario which assumes a bird taking drinking water from water on the soil surface after a heavy rainfall event follows application of the product.

Due to the characteristics of the exposure scenario in connection with the standard assumptions for water uptake by animals, no specific calculations of exposure and TER are necessary since the ratio of effective application rate (in g/ha) to acute and long-term endpoint (in mg/kg bw/d) does not exceed 50 in the case of less sorptive substances (Koc < 500 L/kg) or 3000 in the case of more sorptive substances (Koc ≥ 500 L/kg).

Sulfoxaflor has a Koc of 14 - 35 L/kg. The proposed worst-case rate of use of GF-2372 is 2 x 0.024 kg a.s./ha in cotton. The ratios of effective application rate to relevant endpoints are presented in the following table.

Table 10.1.2-2: Screening step for drinking water assessment– ratio of application rate to relevant endpoint for birds

Substance	Koc (L/kg)	Effective application rate (g a.s./ha)*	Toxicity endpoint (mg a.s./kg bw)	Ratio	Trigger
Sulfoxaflor	14 - 35	38.4	Acute: 676	0.06	50
			Long-term: 25.9	1.50	

*AR_{eff} = AR x MAF_m, MAF_m = 1.6 based on default $DT_{50, soil}$ = 10 days (worst-case compared to $DT_{50, soil}$(field)= 7.43)

The ratios for acute and reproductive endpoints for sulfoxaflor do not exceed the threshold value of 50. Thus, no specific calculations of exposure for birds through drinking water are necessary. In conclusion, the risk through exposure *via* drinking water from the intended uses of GF-2372 is acceptable.

IIIA 10.1.3 Baits: Concentration of active substance in bait in mg/kg

GF-2372 is not formulated as a bait.

IIIA 10.1.4 Pellets, granules, prills or treated seed

GF-2372 is not formulated as pellets, granules, prills or treated seeds.

IIIA 10.1.4.1 Amount of active substance in or on each item

Not applicable.

IIIA 10.1.4.2 Proportion of active substance LD_{50} per 100 items and per gram of items

Not applicable.

IIIA 10.1.5 Size and shape of pellet, granule or prill

Not applicable.

IIIA 10.1.6 Acute toxicity of the formulation

An acute toxicity study with the formulation GF-2372 performed on the bobwhite quail was assessed in the EU review and is summarised below.

Report:	**IIIA 10.1.6/01, [redacted] (2010)**
Title:	GF-2372: An Acute Oral Toxicity Study with the Northern Bobwhite
Document No:	Dow Study ID: 101312
Guidelines:	OPPTS Number 850.2100 and FIFRA Subdivision E, Section 71-1
GLP	Yes (certified laboratory)

Review Comments: IIIA 10.1.9	Already reviewed in the EU DAR of Sulfoxaflor.
Agreed Endpoints: IIIA 10.1.9	Acute oral LD_{50} is 1655 mg GF-2372/kg bw (equivalent to 827 mg sulfoxaflor/kg bw).

IIIA 10.1.8 Acceptance of bait, granules or treated seeds (palatability testing)

The information concerned is not relevant since GF-2372 is intended for use as a spray.

IIIA 10.1.9 Effects of secondary poisoning

The EFSA birds and mammals guidance document (EFSA Journal 2009; 7(12): 1438) states that a log P_{ow} ≥3 is used to indicate that there might be a potential for bioaccumulation (see Section 5.6 Bioaccumulation and food chain behaviour). Sulfoxaflor has a log P_{ow} value of 0.802 (at pH 7) indicating a low potential for bioaccumulation in earthworm and fish tissues. Risk assessments for birds feeding on fish and earthworms are not necessary for this active substance and have not been conducted.

IIIA 10.2 Effects on Aquatic Organisms

The EU agreed endpoints for the effects of sulfoxaflor, its potentially relevant metabolites and GF-2372 to aquatic life are listed in Tables 10.2-1 and 10.2-2. No additional data have been submitted with this dossier.

Table 10.2-1: EU Endpoints - Toxicity of sulfoxaflor and its metabolites to aquatic species

Compound	Test species	Endpoint	EU agreed endpoints* (mg/L)
Fish			
Sulfoxaflor	*Cyprinodon variegatus*	96-h LC_{50}	**266 (mm)**
X11719474	*Oncorhynchus mykiss*	96-h LC_{50}	**>478 (mm)**
X11519540	*Oncorhynchus mykiss*	96-h LC_{50}	**>330 (mm)**
Sulfoxaflor	*Cyprinodon variegatus*	38-d NOEC	**1.21 (mm)**
Invertebrates			
Sulfoxaflor	*Daphnia magna*	48-h EC_{50}	**>399 (mm)**
X11719474	*Daphnia magna*	48-h EC_{50}	**>205 (mm)**
X11519540	*Daphnia magna*	48-h EC_{50}	**>350 (mm)**
Sulfoxaflor	*Daphnia magna*	21-d NOEC	**12.5** (nom)
Sulfoxaflor	*Americamysis bahia*	96-h LC_{50}	**0.643 (mm)**
X11719474	*Americamysis bahia*	96-h LC_{50}	**>114 (mm)**
X11519540	*Americamysis bahia*	96-h LC_{50}	**>120 (mm)**
Sulfoxaflor	*Americamysis bahia*	28-d NOEC	**0.114 (mm)**
X11719474	*Americamysis bahia*	28-d NOEC	**2.12 (mm)**
Sulfoxaflor	*Chironomus dilutus*	96-h LC_{50}	**0.622 (mm)**
Sulfoxaflor	*Chironomus dilutus*	10-d LC_{50}	**0.119 mg/kg sediment (mm)**
X11719474	*Chironomus dilutus*	96-h LC_{50}	**>281 (mm)**
X11519540	*Chironomus dilutus*	96-h LC_{50}	**>360 (mm)**
Sulfoxaflor	*Chironomus riparius*	28-d NOEC	**0.0384 (mm)**

Compound	Test species	Endpoint	EU agreed endpoints* (mg/L)
X11719474	*Chironomus riparius*	28-d NOEC	**10.4 (mm)**
X11519540	*Chironomus riparius*	28-d NOEC	**10 (mm)**
Algae			
Sulfoxaflor	*Navicula pelliculosa*	72-h E_bC_{50} 72-h E_yC_{50} 72-h E_rC_{50}	**85.7 (mm)** >101 (mm) >101 (mm)
X11719474	*Navicula pelliculosa*	72-h E_yC_{50} 72-h E_rC_{50}	**>124 (mm)** >124 (mm)
X11519540	*Navicula pelliculosa*	72-h E_yC_{50} 72-h E_rC_{50}	**>110 (mm)** >110 (mm)
Higher plant			
Sulfoxaflor	*Lemna gibba*	7 day EC_{50}	**>100 (nom)**

* EFSA Journal 2014; 12(5):3692.
Endpoints used in the risk assessment are in **bold**.

Table 10.2-2: EU Endpoints - Toxicity of GF-2372 to aquatic species

Compound	Test species	Endpoint	EU agreed endpoints* (mg/L)
GF-2372	*Oncorhynchus mykisss*	96-h LC_{50}	**19.5 (mm)**
GF-2372	*Daphnia magna*	48-h EC_{50}	**>100 (nom)**
GF-2372	*Americamysis bahia*	96-h LC_{50}	**1.1 (nom)**
GF-2372	*Chironomus dilutus*	96-h LC_{50}	**>24 (nom)**
GF-2372	*Navicula pelliculosa*	72-h E_yC_{50} 72-h E_rC_{50}	**28 (nom)** >100 (nom)

* EFSA Journal 2014; 12(5):3692
Endpoints used in the risk assessment are in **bold**.

Classification of the active substance:

Active substances	Reference	New classification (CLP) 2nd ATP to the regulation 1272/2008	
		Hazard category	Code H
Sulfoxaflor	zRMS proposal	Aquatic acute 1 Aquatic chronic 1	H400 Very toxic to aquatic life H410 Very toxic to aquatic life with long lasting effects.

Proposal of classification of the preparation

Preparation	Reference	New classification (CLP) 2nd ATP to the regulation 1272/2008	
		Hazard category	Code H
GF-2372 (TRANSFORM)	zRMS proposal	Aquatic chronic 1[1]	H410 Very toxic to aquatic life with long lasting effects.

[1]Determined by calculation based on the aquatic toxicity of the active substance and principal constituents of the preparation assuming a chronic M factor of 1.

The aquatic risk assessment has been conducted on the basis of the proposed uses of GF-2372 as summarised in Table 10-2.

A summary of the predicted exposure in the aquatic environment is presented in the following tables. For full details please refer to Section 5: Environmental Fate (IIIA 9.7 and 9.8).

IIIA 10.2.1 Toxicity exposure ratios

IIIA 10.2.1.1 TER_A for fish

TER_A values for fish have been determined for the active substance and the metabolites using the maximum initial FOCUS Step 1 PECsw values. An acute TER_A for the product has also been calculated using the maximum drift PECsw at 1 m. The acute risk assessment for fish is summarised in the following table.

Table 10.2.1.1-1: Fish acute TER values after applications of GF-2372

Substance	Critical endpoint (µg/L)	FOCUS SW Step	PEC_{SW} (µg/L)	TER_A [100]
GF-2372	19850	Spray drift in SWASH	0.3084*	64364
Sulfoxaflor	266000	1	15.73	16910
X11719474	>478000	1	16.72	>28589
X11519540	>330000	1	1.75	>188571

*Highest calculated drift PECsw value for ditch and stream scenarios

The above TER_A values are greater than the trigger value of 100 demonstrating an acceptable acute risk to fish for all proposed uses of GF-2372.

IIIA 10.2.1.2 TER_{LT} for fish

A TER_{LT} value for fish has been determined for the active substance using the maximum initial FOCUS Step 1 PECsw value. The long-term risk assessment for fish is summarised in the following table.

Table 10.2.1.2-1: Fish long-term TER value after applications of GF-2372

Substance	Critical endpoint (µg/L)	FOCUS SW Step	PEC_{SW} (µg/L)	TER_{LT} [10]
Sulfoxaflor	1210	1	15.73	76.9

The above TER_{LT} value is greater than the trigger value of 10 demonstrating an acceptable long-term risk to fish for all proposed uses of GF-2372.

IIIA 10.2.1.3 TER_A for *Daphnia*

TER_A values for *Daphnia* have been determined for the active substance and its metabolites using the maximum initial FOCUS Step 1 PECsw values. An acute TER_A for the product has also been calculated using the maximum drift PECsw at 1 m. The acute risk assessment for *Daphnia* is summarised in the following table.

Table 10.2.1.3-1: Aquatic invertebrate acute TER values after applications of GF-2372

Substance	Critical endpoint (µg/L)	FOCUS SW Step	PEC_{SW} (µg/L)	TER_A [100]
GF-2372	>100000	Spray drift in SWASH	0.3084*	>324254
Sulfoxaflor	>399000	1	15.73	>25366
X11719474	>205000	1	16.72	>12261
X11519540	>350000	1	1.75	>200000

*Highest calculated drift PECsw value for ditch and stream scenarios

The above TER_A values are greater than the trigger value of 100 demonstrating an acceptable acute risk to *Daphnia* for all proposed uses of GF-2372.

IIIA 10.2.1.4 TER_{LT} for *Daphnia*

A TER_{LT} value for *Daphnia* has been determined for the active substance using the maximum initial FOCUS Step 1 PECsw value. The long-term risk assessment for *Daphnia* is summarised in the following table.

Table 10.2.1.4-1: Aquatic invertebrate long-term TER value after applications of GF-2372

Substance	Critical endpoint (µg/L)	FOCUS SW Step	PEC_{SW} (µg/L)	TER_{LT} [10]
Sulfoxaflor	12500	1	15.73	795

The above TER_{LT} value is greater than the trigger value of 10 demonstrating an acceptable long term risk to *Daphnia* for all proposed uses of GF-2372.

IIIA 10.2.1.5 TER_A for aquatic insect

TER_A values for *Chironomus* have been determined for the active substance and the metabolites using the maximum initial FOCUS Step 1 PECsw values. An acute TER_A for the product has also been calculated using the maximum drift PECsw at 1 m. For the active substance a second TER_A has been calculated based on the maximum initial FOCUS Step 1 PECsed value and an acute toxicity endpoint from a study exposing *Chironomus* to spiked sediment. The acute risk assessment for *Chironomus* is summarised in the following table.

Table 10.2.1.5-1: Aquatic insect acute TER values after applications of GF-2372

Substance	**Critical endpoint (µg/L)**	**FOCUS SW Step**	**PEC_{SW} (µg/L)**	**TER_A [100]**
GF-2372	>24000	Spray drift in SWASH	0.3084*	>77821
Sulfoxaflor	622	1	15.73	**39.5**
X11719474	>281000	1	16.72	>16806
X11519540	>360000	1	1.75	>205714
Substance	**Critical endpoint (µg/kg sediment)**	**FOCUS SW Step**	**PEC_{sed} (µg/kg sediment)**	**TER_A [100]**
Sulfoxaflor	119	1	5.43	**21.9**

*Highest calculated drift PECsw value for ditch and stream scenarios
TERs shown in **bold** fall below the relevant trigger

The above TER_A values for the active substance are lower than the trigger value of 100 demonstrating that concern remains regarding the acute risk to *Chironomus* using the relevant FOCUS Step 1 PECsw and PECsed values for all proposed uses. However, the TER_A values for all the metabolites are greater than the trigger value demonstrating an acceptable risk to *Chironomus*. Therefore, TER_A values for the active substance using the maximum initial FOCUS Step 2 PECsw and PECsed values for the use on cotton (worst-case scenario) are presented in the following table.

Table 10.2.1.5-2: Aquatic insect acute TER values after applications of GF-2372 on cotton (worst-case scenario)

Substance	**Critical endpoint (µg/L)**	**FOCUS SW Step**	**PEC_{SW} (µg/L)**	**TER_A [100]**
Sulfoxaflor	622	2	0.37*	1681
Substance	**Critical endpoint (µg/kg sediment)**	**FOCUS SW Step**	**PEC_{sed} (µg/kg sediment)**	**TER_A [100]**
Sulfoxaflor	119	2	0.12*	992

*Highest calculated PEC values for applications of GF-2372 in cotton

The above TER_A values are greater than the trigger value of 100 demonstrating an acceptable acute risk to *Chironomus* for all proposed uses of GF-2372.

IIIA 10.2.1.6 TER_{LT} for aquatic insect

TER_{LT} values for *Chironomus* have been determined for the active substance and its metabolites using the maximum initial FOCUS Step 1 PECsw values. The long-term risk assessment for *Chironomus* is summarised in the following table.

Table 10.2.1.6-1: Aquatic insect long-term TER values after applications of GF-2372

Substance	Critical endpoint (µg/L)	FOCUS SW Step	PEC_{SW} (µg/L)	TER_{LT} [10]
Sulfoxaflor	38.4	1	15.73	**2.44**
X11719474	10400	1	16.72	622
X11519540	10000	1	1.75	5714

TER shown in **bold** falls below the relevant trigger

The above TER_{LT} value for the active substance is lower than the trigger value of 10 demonstrating that concern remains regarding the long-term risk to *Chironomus* for all proposed uses of GF-2372. However, the TER_{LT} values for the metabolites are greater than the trigger value demonstrating an acceptable risk to *Chironomus*. Therefore, a TER_{LT} value for the active substance using the maximum initial FOCUS Step 2 PECsw value for the use on cotton (worst-case scenario) is presented in the following table.

Table 10.2.1.6-2: Aquatic insect long-term TER value after applications of GF-2372 on cotton (worst-case scenario)

Substance	Critical endpoint (µg/L)	FOCUS SW Step	PEC_{SW} (µg/L)	TER_{LT} [10]
Sulfoxaflor	38.4	2	0.37*	104

*Highest calculated PEC value for applications of GF-2372 in cotton

The above TER_{LT} value is greater than the trigger value of 10 demonstrating an acceptable long-term risk to *Chironomus* for all proposed uses of GF-2372.

IIIA 10.2.1.7 TER_A for aquatic crustacean

TER_A values for *Americamysis bahia* have been determined for the active substance and its metabolites using the maximum initial FOCUS Step 1 PECsw values. An acute TER_A for the product has also been calculated using the FOCUS drift PECsw at 1 m. The acute risk assessment for *Americamysis bahia* is summarised in the following table.

Table 10.2.1.7-1: Aquatic crustacean acute TER values after applications of GF-2372

Substance	Critical endpoint (µg/L)	FOCUS SW Step	PEC_{SW} (µg/L)	TER_A [100]
GF-2372	1100	Spray drift in SWASH	0.3084*	3567
Sulfoxaflor	643	1	15.73	**40.9**
X11719474	>114000	1	16.72	>6818
X11519540	>120000	1	1.75	>68571

*Highest calculated drift PECsw value for ditch and stream scenarios
TER shown in **bold** falls below the relevant trigger

The above TER_A value for the active substance is lower than the trigger value of 100 demonstrating that concern remains regarding the acute risk to *Americamysis bahia*. However, the TER_A values for the metabolites are greater than the trigger value demonstrating an acceptable risk to *Americamysis bahia*. Therefore, the TER_A value for the active substance using the maximum initial FOCUS Step 2 PECsw value is presented in the following table.

Table 10.2.1.7-2: Aquatic crustacean acute TER value after applications of GF-2372 on cotton (worst-case scenario)

Substance	Critical endpoint (µg/L)	FOCUS SW Step	PEC_{SW} (µg/L)	TER_A [100]
Sulfoxaflor	643	2	0.37*	1738

*Highest calculated PECsw value for applications of GF-2372 in cotton

The above TER_A value is greater than the trigger value of 100 demonstrating an acceptable acute risk to *Americamysis bahia* for all proposed uses of GF-2372.

IIIA 10.2.1.8 TER_{LT} for aquatic crustacean

TER_{LT} values for *Americamysis bahia* have been determined for the active substance and the metabolite X11719474 using the maximum initial FOCUS Step 1 PECsw values. The long-term risk assessment for *Americamysis bahia* is summarised in the following table.

Table 10.2.1.8-1: Aquatic crustacean long-term TER values after applications of GF-2372

Substance	Critical endpoint (µg/L)	FOCUS SW Step	PEC_{SW} (µg/L)	TER_{LT} [10]
Sulfoxaflor	114	1	15.73	**7.25**
X11719474	2120	1	16.72	127

TER shown in **bold** falls below the relevant trigger

The above TER_{LT} value for the active substance is lower than the trigger value of 10 demonstrating that concern remains regarding the long-term risk to *Americamysis bahia* for all proposed uses of GF-2372. However, the TER_{LT} value for the metabolites X11719474 is greater than the trigger value demonstrating an acceptable risk to *Americamysis bahia*. Therefore, the

TER_{LT} value for the active substance using the maximum initial FOCUS Step 2 PECsw value for the use on cotton (worst-case scenario) is presented in the following table.

Table 10.2.1.8-2: Aquatic crustacean long-term TER value after applications of GF-2372 on cotton (worst-case scenario)

Substance	Critical endpoint (µg/L)	FOCUS SW Step	PEC_{SW} (µg/L)	TER_{LT} [10]
Sulfoxaflor	114	2	0.37*	308

*Highest calculated PECsw value for applications of GF-2372 in cotton

The above TER_{LT} value is greater than the trigger value of 10 demonstrating an acceptable long-term risk to *Americamysis bahia* for all proposed uses of GF-2372.

IIIA 10.2.1.9 TER_A for aquatic gastropod mollusc

Not required.

IIIA 10.2.1.10 TER_{LT} for aquatic gastropod mollusc

Not required.

IIIA 10.2.1.11 TER_{LT} for algae

TER_{LT} values for algae have been determined the active substance and its metabolites using the maximum initial FOCUS Step 1 PECsw values. A TER_{LT} value for the product has also been calculated using the FOCUS drift PECsw at 1 m. The risk assessment for algae is summarised in the following table.

Table 10.2.1.11-1: Algal TER values after applications of GF-2372

Substance	Critical endpoint (µg/L)	FOCUS SW Step	PEC_{SW} (µg/L)	TER_{LT} [10]
GF-2372	28000	Spray drift in SWASH	0.3084*	90791
Sulfoxaflor	85700	1	15.73	5448
X11719474	>124000	1	16.72	>7416
X11519540	>110000	1	1.75	>62857

*Highest calculated drift PECsw value for ditch and stream scenarios

The above TER_{LT} values are greater than the trigger value of 10 demonstrating an acceptable long-term risk to algae for all proposed uses of GF-2372.

IIIA 10.2.1.12 Risk for aquatic plants

A TER_{LT} value for aquatic plants has been determined for the active substance using the maximum initial FOCUS Step 1 PECsw value. The risk assessment for aquatic plants is summarised in the following table.

Table 10.2.1.12-1: Aquatic plant TER value after applications of GF-2372

Substance	Critical endpoint (µg/L)	FOCUS SW Step	PEC_{SW} (µg/L)	TER_{LT} [10]
Sulfoxaflor	>100000	1	15.73	>6357

The above TER_{LT} value is greater than the trigger value of 10 demonstrating an acceptable long-term risk to aquatic plants for all proposed uses of GF-2372.

IIIA 10.2.2 Acute toxicity of the formulation

IIIA 10.2.2.1 Fish

The following fish acute toxicity study performed on GF-2372 was assessed in the EU review and is available in the DAR (2013) Annex B.9.

Report:	**IIIA 10.2.2.1/01 [redacted] (2010)**
Title:	GF-2372: Acute Toxicity to the Rainbow Trout, *Oncorhynchus mykiss*, Determined Under Static-Renewal Test Conditions.
Document No:	Dow Study ID: 101313
Guidelines:	OECD 203
GLP	Yes

Study Comments: IIIA 10.2.2.1/01	Already reviewed in the EU DAR of Sulfoxaflor.
Agreed Endpoints: IIIA 10.2.2.1/01	Based on nominal concentrations, the 96-hour LC50 is 19.5 mg GF-2372/L (equivalent to 9.75 mg sulfoxaflor/L).

IIIA 10.2.2.2 Aquatic invertebrates (*Daphnia*)

The following *Daphnia* acute toxicity study performed on GF-2372 was assessed in the EU review and is available in the DAR (2013) Annex B.9.

Report:	**IIIA 10.2.2.2/01, Bergfield, A. (2010)**
Title:	GF-2372: Acute Toxicity to the Water Flea, *Daphnia magna*, Determined Under Static-Renewal Test Conditions.
Document No:	Dow Study ID: 101314
Guidelines:	OECD 202

Deviations:	None
GLP	Yes

Study Comments: IIIA 10.2.2.2/01	Already reviewed in the EU DAR of Sulfoxaflor.
Agreed Endpoints: IIIA 10.2.2.2/01	Based on nominal concentrations, a 48-hour EC_{50} is >100 mg GF-2372/L (equivalent to >50 mg sulfoxaflor/L).

IIIA 10.2.2.3 Algae

The following algae toxicity study performed on GF-2372 was assessed in the EU review and is available in the DAR (2013) Annex B.9.

Report:	**IIIA 10.2.2.3/01, Rebstock, M. (2010)**
Title:	GF-2372: Growth Inhibition Test with the Freshwater Diatom, *Navicula pelliculosa*.
Document No:	Dow Study ID: 101315
Guidelines:	OECD Guideline 201
GLP	Yes

Study Comments: IIIA 10.2.2.3/01	Already reviewed in the EU DAR of Sulfoxaflor.
Agreed Endpoints: IIIA 10.2.2.3/01	Based on nominal concentrations, the 72-hour E_rC_{50} is >100 mg GF-2372/L (equivalent to >50 mg sulfoxaflor/L) and E_yC_{50} is 28 mg GF-2372/L (equivalent to 14 mg sulfoxaflor/L) and NOEC is 3.7 mg GF-2626/L (equivalent to 1.8 mg sulfoxaflor/L).

IIIA 10.2.2.4 Marine or estuarine organisms

The following toxicity study with the Mysid Shrimp performed on GF-2372 was assessed in the EU review and is available in the DAR (2013) Annex B.9.

Report:	**IIIA 10.2.2.4/01, Gerke, A. (2011)**
Title:	GF-2372: Acute Toxicity to the Mysid Shrimp, *Americamysis bahia*, Determined Under Static-Renewal Test Conditions.

Document No:	Dow Study ID: 102000.
Guidelines:	OPPTS 850.1035
GLP	Yes

Study Comments: IIIA 10.2.2.4/01	Already reviewed in the EU DAR of Sulfoxaflor
Agreed Endpoints: IIIA 10.2.2.4/01	Based on nominal concentrations, the 96-hour LC_{50} is 1.1 mg GF-2372/L (equivalent to 0.55 mg sulfoxaflor/L).

IIIA 10.2.2.5 Marine sediment invertebrates

Not required.

IIIA 10.2.3 Microcosm or mesocosm study

A microcosm or mesocosm study is not required for GF-2372 as the risk assessments above indicate an acceptable risk.

IIIA 10.2.4 Residue data in fish

Studies providing residue data in fish are not required for GF-2372 as the active substance has low potential to partition to or remain in fish tissues.

IIIA 10.2.5 Chronic toxicity to fish

IIIA 10.2.5.1 28 day study

Not required.

IIIA 10.2.5.2 Fish early life stage test

Not required.

IIIA 10.2.5.3 Fish life cycle test

Not required.

IIIA 10.2.6 Chronic toxicity to aquatic invertebrates

IIIA 10.2.6.1 21 day test (*Daphnia magna*)

Not required.

IIIA 10.2.6.2 Aquatic insect

The following toxicity study with the Midge, *Chironomus dilutus* performed on GF-2372 was assessed in the EU review and is available in the DAR (2013) Annex B.9.

Report:	**IIIA 10.2.6.2/01, Gerke, A. (2010)**
Title:	GF-2372: Acute 96 Hour Toxicity to the Midge, *Chironomus dilutus*, Determined Under Static Test Conditions.
Document No:	Dow Study ID: 101316.
Guidelines:	OECD Guideline 202, ASTM E729
GLP	Yes

Study Comments: IIIA 10.2.6.2/01	Already reviewed in the EU DAR of Sulfoxaflor
Agreed Endpoints: IIIA 10.2.6.2/01	Based on nominal concentrations, the 96-hour LC_{50} is >24 mg GF-2372/L (equivalent to > 12 mg sulfoxaflor/L).

IIIA 10.2.6.3 Aquatic gastropod mollusc

Not required.

IIIA 10.2.7 Accumulation in aquatic non-target organisms

Bioaccumulation of the active substance under natural conditions is not expected to occur (refer to Section 10.2.4) and a study is not necessary to determine bioaccumulation in aquatic non-target organisms.

IIIA 10.3 Effects on Terrestrial Vertebrates Other Than Birds

GF-2372 was one of the representative formulations in the EU review of sulfoxaflor. However new assessment parameters are now considered in the risk assessment to wild mammals and has been performed according to the proposed use pattern.

The risk assessment for effects on mammals is carried out according to the European Food Safety Authority Guidance Document on Risk Assessment for Birds and Mammals on request from EFSA (EFSA Journal 2009; 7(12): 1438).

The endpoints employed in the risk assessment for mammals are indicated in Table 10.3-1.

Table 10.3-1: EU Endpoints - Toxicity sulfoxaflor, its metabolites and GF-2372 to mammals

Compound	Test species	Endpoint	EU agreed endpoints*
Sulfoxaflor	Rat	Acute oral LD_{50}	1000 mg/kg bw
Sulfoxaflor	Mice	Acute oral LD_{50}	**750 mg/kg bw**
GF-2372	Rat	Acute oral LD_{50}	>2000 mg prep./kg bw[a]
X11719474	Rat	Acute oral LD_{50}	>5000 mg/kg bw
X11519540	Rat	Acute oral LD_{50}	566 mg/kg bw
X11579457	Rat	Acute oral LD_{50}	>2000 mg/kg bw
X11721061	Rat	Acute oral LD_{50}	2000 mg/kg bw
Sulfoxaflor	Rat	2-generation reproduction NOAEL	**6.63 mg/kg bw/day**
X11719474	Rat	Reproduction screening NOAEL	396 mg/kg bw/day
X11719474	Rat	Developmental toxicity NOAEL	368 mg/kg bw/day

*EFSA Journal 2014; 12(5):3692
[a]: The endpoint is equivalent to >1000 mg a.s./kg bw.
Endpoints used in the risk assessment are in **bold**

Mammals are typically exposed to dry residues on their food items following the dilution and spraying of the formulated product. On this basis, the risk to mammals from the proposed uses of GF-2372 will be assessed using data on sulfoxaflor. Furthermore, an acute formulation toxicity study is available which does not demonstrate the formulation to be any more toxic than expected based on the content of the active substance.

A screening dietary assessment has been conducted on the basis of the proposed uses of GF-2372 as summarised in Table 10-2. Where necessary, first tier risk assessments have also been included.

In addition, an assessment of the risk from exposure to potentially relevant metabolites and an assessment of the risk from consumption of contaminated drinking water risk assessment have been conducted.

Sulfoxaflor has a log P_{ow} value of 0.802 (at pH 7) indicating a low potential for bioaccumulation in earthworm and fish tissues. Risk assessments for mammals feeding on fish and earthworms are not necessary for this active substance and have not been conducted.

IIIA 10.3.1 Toxicity exposure ratios

IIIA 10.3.1.1 Acute toxicity exposure ratio (TER_A)

Screening assessment

The initial acute mammalian screening risk assessment is based on the toxicity value given in Table 10.3-1 and considers the worst-case exposure scenarios for the proposed uses of GF-2372 (Table 10-2). The estimated daily dietary doses (DDDs) and associated toxicity exposure ratios (TERs) are presented in the table below (Table 10.3.1.1-1).

Table 10.3.1.1-1: Acute screening risk assessment (TER_A) for mammals from GF-2372 uses

Crop	Substance	Indicator mammal	App. rate (kg/ha)	Shortcut value (acute)	MAF	DDD (mg/kg bw)	LD_{50} (mg/kg bw)	TER_A [10]
Cereals, oilseed rape	Sulfoxaflor	Small herbivorous	0.024	118.4	1.2	3.41	750	220
Cotton	Sulfoxaflor	Small herbivorous	0.024	136.4	1.4	4.58	750	164

MAF = multiple application factor (MAF for 14 day interval used as a worst-case for cereals and OSR)
DDD = daily dietary dose

Based on the screening assessment, the TER_A values are greater than the trigger of 10, indicating an acceptable acute risk to mammals from sulfoxaflor following applications of GF-2372 at the proposed label rate.

IIIA 10.3.1.2 Short-term toxicity exposure ratio (TER_{ST})

There is no requirement for the calculation of TER_{ST} for mammals under the EFSA birds and mammals guidance document (EFSA Journal 2009; 7(12): 1438) and, consequently, a risk assessment for short-term toxicity has not been conducted.

IIIA 10.3.1.3 Long-term toxicity exposure ratio (TER_{LT})

Screening assessment

The initial long-term mammalian screening risk assessment is based on the toxicity value given in Table 10.3-1 and considers the worst-case exposure scenarios for the proposed uses of GF-

2372 (Table 10-2). The estimated daily dietary doses (DDDs) and associated toxicity exposure ratios (TERs) are presented in the table below (Table 10.3.1.3-1).

Table 10.3.1.3-1: Long-term screening risk assessment (TER_{LT}) for mammals from GF-2372 uses

Crop	Indicator mammal	App. rate (kg/ha)	Shortcut value (long-term)	f_{TWA}[a]	MAF	DDD (mg/kg bw/day)	NOEL (mg/kg bw/day)	TER_{LT} [5]
Cereals, oilseed rape	Small herbivorous	0.024	48.3	1	1.4	1.62	6.63	**4.09**
Cotton	Small herbivorous		72.3	1	1.6	2.78		**2.39**

[a] f_{TWA} = During the EU review (DAR, 2012) it was concluded that due to the short-term effects on pups observed in the mammalian reproduction study from which the endpoint has been derived, the default value of 0.53 cannot be used as a time weighted average factor and that in this case the most appropriate value is 1.
MAF = multiple application factor (MAF for 14 day interval used as a worst-case for cereals and OSR)
DDD = daily dietary dose
TERs shown in bold fall below the relevant trigger

Based on the screening assessment, the TER_{LT} values are lower than the trigger of 5, indicating that concern remains regarding the long-term risk to mammals from sulfoxaflor following application of GF-2372 at the proposed rates in cereals, oilseed rape and cotton.

Therefore, a long-term dietary first tier assessment has been conducted.

First-tier assessment

In the first tier risk assessment generic focal species are selected relevant to the proposed crop and growth stages. The first tier daily dietary doses (DDDs) and associated toxicity exposure ratios (TERs) are presented in the table below.

Table 10.3.1.3-2: Long-term first tier risk assessment (TER_{LT}) for mammals from GF-2372 uses

Scenario	Generic focal species	App. rate (kg/ha)	Shortcut value (long-term)	f_{TWA}[a]	MAF	DDD (mg/kg bw/day)	NOEL (mg/kg bw/day)	TER_{LT} [5]
Crop: Cereals								
BBCH 10-19	Shrew	0.024	4.2	1	1.4	0.14	6.63	47.0
BBCH > 20	Shrew		1.9			0.06		104
BBCH > 40	Vole		21.7			0.73		9.09
BBCH early (shoots)	Lagomorph		22.3			0.75		8.85
BBCH 10-29	Mouse		7.8			0.26		25.3
BBCH 30-39	Mouse		3.9			0.13		50.6
BBCH > 40	Mouse		2.3			0.08		85.8
Crop: Oilseed rape								
BBCH 10-19	Shrew	0.024	4.2	1	1.4	0.14	6.63	47.0
BBCH > 20	Shrew		1.9			0.06		104
BBCH > 40	Vole		18.1			0.61		10.9
BBCH early (shoots)	Lagomorph		14.3			0.48		13.8
BBCH 10-29	Mouse		7.8			0.26		25.3
BBCH 30-39	Mouse		2.3			0.08		85.8
BBCH > 40	Mouse		1.9			0.06		104
Crop: Cotton								
BBCH > 20	Shrew	0.024	1.9	1	1.6	0.07	6.63	90.9
BBCH 40-49	Vole		72.3			2.78		**2.39**
BBCH > 50	Vole		18.1			0.70		9.54
BBCH 10-49	Mouse		7.8			0.30		22.1
BBCH > 50	Mouse		1.9			0.07		90.9

[a] f_{TWA} = During the EU review (DAR, 2012) it was concluded that due to the short-term effects on pups observed in the mammalian reproduction study from which the endpoint has been derived, the [a] f_{TWA} was set to 1.
MAF = multiple application factor
DDD = daily dietary dose
TER(s) shown in **bold** fall below the relevant trigger

Based on the first tier assessment, all TER_{LT} values are greater than the trigger of 5 demonstrating an acceptable long-term risk to mammals for all proposed uses of GF-2372 with the exception of one scenario (application of GF-2372 in cotton, BBCH 40-49) for which the TER_{LT} is lower the trigger of 5, indicating that concern remains regarding the long-term risk to voles.

It is noted that the cotton application of GF-2372 is proposed for use in Spain and Greece. Given that the "vole" is not considered as a protected focal species in Spain and Greece, it would be reasonable to consider that based on the first tier risk assessment the long-term risks to mammals is therefore acceptable.

However, a long-term dietary refined assessment for voles has been conducted regardless of this point, if the vole should be considered as a protected focal species.

zRMS comment:
zRMS considers that, for the present evaluation, the 'vole' is not a representative species for the following reasons:
- High fecundity and population recuperation of the vole.
- Primary source of food outside crops fields for the vole.
- Necessity of population control measures since the vole is considered a crop pest when high population levels are reached.

Consequently, voles are actively controlled by intense culturing, catching or by use of biocides/pesticides. In consideration of this, it is obvious that it is not possible to apply the same protection goal to the vole as to the other indicator species. Instead, it is more appropriate to use a lagomorph in combination to a small omnivorous speciesas representative generic focal species of herbivores.

For Cotton, a refined risk assessment for small herbivorous mammals is necessary. Notifier refinement, in particular that onebased on deposition factor, is considered sufficent to show an acceptable risk to small herbivorous mammals and further considerations for lagomorph are not considered required..

Notifier proposal:

Higher tier long-term mammalian risk assessment

A higher tier long-term assessment is required for the following focal species and scenarios:

- Small herbivorous mammal ("vole"), cotton; BBCH 40-49

The Bird and Mammal guidance (2009) proposes the common vole (*Microtus arvalis*) as the representative herbivorous focal species in cotton. However, this species is not considered to be

a representative habitant of this crop, but rather inhabits adjacent landscapes as summarised below:

Habitat of common voles

The preferred primary habitat of common voles is steppe, which comprises grassland, pasture and meadow with mixed grassland, herbs and weeds that provide appropriate cover to avoid predation (Le Louarn & Quere, 2003[2]). For common voles, many cropped areas are considered to be secondary habitats, and significant invasion into them occurs when there is a population outbreak (Stein, 1958 [3]). In contrast to primary habitats, these secondary habitats cannot maintain common vole populations sustainably for long periods owing to the seasonal nature of farming, where populations are regularly disrupted by harvest and tilling (Ognev, 1947[4]; Jacob, 2003[5]).

The optimum habitat of common voles comprises large open, dry, uniform grassy areas (Stein, 1958; Schröpfer & Hildenhagen, 1984 [6]).

Stein (1958), who provided one of the first comprehensive reviews of common vole biology, distinguished prime habitats such as set-asides, grassy heath land, vegetated margins of ditches and farm tracks from secondary habitats, i.e. arable land. Based on results of more recent studies (e.g. Delattre *et al*. 1992 [7]; Butet & Leroux 2001 [8]) perennial crop cultivations, e.g. alfalfa and clover should be included as prime habitats. The prime habitats that generally are of smaller scale compared to surrounding secondary habitats are essential for the survival of local populations and serve as donor habitats for secondary habitats in years of mass occurrences in the prime habitats. Secondary habitats are characterized by periods of immigration of voles during mass occurrences (from prime habitats) and multi-annual periods of (almost) complete non-existence.

In a comprehensive field study in France (Delattre *et al*., 1992) have categorised the population kinetics of common voles in dependence of agricultural land use. They stress the importance of permanent grassland in farmland for the population dynamics of common voles. If grassland cover diminished so did populations of common voles and on the inverse an increase in grassland was followed by an enhancement of vole populations. Besides the proportion of permanent grassland in farmland, the existence of a highly connected grassy network along ditches, roads, tracks etc. abundantly and permanently covered with vegetation is a key factor for the occurrence of common voles.

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[2] Le Louarn, H. and Quere, J.P., Les Rongeurs de France. INRA Editions, Paris, France, 1–256 (2003).

[3] Stein, G. H. W. 1958. Die Feldmaus (*Microtus arvalis* Pallas). Neue Brehm Bücherei Bd. 225 A. Ziemsen Verlag, Wittenberg Lutherstadt.

[4] Ognev, S.J., The Mammals of the USSR and Adjacent Countries. Nauka, Moscow, USSR, 685 pp. (1947)

[5] Jacob, J., Short-term effects of farming practices on populations of common voles. Agric Ecosyst Environ 95(1):321–325 (2003).

[6] Schröpfer, R. & Hildenhagen, U. 1984. Die Säugetiere Westfalens. Feldmaus - *Microtus arvalis* (Pallas, 1779). Abhandlungen aus dem Westfälischen Museum für Naturkunde, 46(4): 204-215.

[7] Delattre, P.; Giraudoux, P.; Baudry, J.; Musard, P.; Toussaint, M.; Truchetet, D.; Stahl, P.; Poule, M. L.; Artois, M.; Damange, P. & Quere, J.-P. 1992. Land use patterns and types of common vole (*Microtus arvalis*) population kinetics. Agriculture, Ecosystems and Environment 39: 153-169.

[8] Butet, A. & Leroux, A. B. A. 2001. Effects of agriculture development on vole dynamics and conservation of Montagu `s harrier in western French wetlands. Biological Conservation 100: 289-295.

In the eastern French department of Jura a two-year field study covering 18000 ha on the population dynamics of common voles has been conducted in different landscape types (Delattre *et al.* 1996[9]). Highest vole abundances were found on permanent grassland. Here mass occurrences of common voles were favoured.

In a nine-year field study in eastern France on rodent communities on abandoned agricultural land, 11 624 rodents of 8 species were caught in a landscape consisting of forests and grassland with a proportion of less than 1% ploughed land. *Microtus arvalis* was the most common species. The conversion of agricultural land into permanent grassland resulted in a marked increase in populations of common voles (Giraudoux *et al*. 1994[10]).

In a multi-annual field-study in Germany a total of 1 421 common voles were caught of which 7.1% were in sugar beets and cabbage, 13.9% in cereals, and 79% in an adjacent grassy ditch (Boye , 2000[11]).

Population Dynamics

The population density of common voles undergoes major fluctuations both within season and between years. The frequency of mass occurrences varies between 3 and 5 years (Lauenstein 1979, Heise & Stubbe 1987[12], Mackin-Rogalska & Nabaglo 1990[13]). These mass occurrences are commonly followed by a population breakdown, which can result in local extinction. Several years of inconspicuous population development might then be again followed by a mass occurrence incident. The key factor in population kinetics is the proportion of permanent grassland in a given landscape. If grassland cover diminishes in favour of arable land so do populations of common voles and on the inverse an increase of grassland is followed by an expansion of vole populations. Vole populations on arable land suffer from regular extinctions due to agricultural operations and an increased risk of predation.

In reality, based on the preferred habitat and population dynamics of the vole as described above, cotton is not considered to be an attractive field for foraging. It is clear that voles require permanent and undisturbed vegetation cover but for the proposed crops agricultural practice, i.e. the extensive use of herbicides is commonly used to minimise the growth of weeds / grasses that could compete for resources with the crops; therefore reducing any potential feed items that a small herbivorous mammals would seek in the treated field

Refinements of the TER_{LT} calculation

9) Delattre, P., Giraudoux, P., Baudry, J., Quéré, J. P. & Fichet, E. 1996. Effect of landscape structure on common vole (*Microtus arvalis*) distribution and abundance at several space scales. Landscape Ecology 11(5): 279-288.

10) Giraudoux, P., P. Delattre, J.-P. Quere, and P. Damange. 1994. Structure and kinetics of rodent populations, in a region under agricultural land abandonment. Acta Ecologica 15: 385-400.

11) Boye, P. 2000. Populationsökologische Untersuchungen an Nagetieren in der Agrarlandschaft bei Bonn. PhD-Study. University of Rostock, Rostock.

12 Heise, S. & Stubbe, M. (1987). Populationsökologische Untersuchungen zu Massenwechsel der Feldmaus *Microtus arvalis* (Pallas, 1779). Säugetierkundliche Informationen 11(2): 403-414.

13 Mackin-Rogalska, R. & Nabaglo, L. (1990). Geographical variation in cyclic periodicity and synchrony in the common vole, *Microtus arvalis*. Oikos 59: 343-348.

1. Interception factor

This refinement is based on interception which was not considered in the first tier risk assessment. Worst case deposition factors in line with the Generic Guidance for Tier 1 FOCUS Ground Water Assessments (2012) are used in the following refined risk assessment.

In the first tier risk assessment for small herbivorous mammals for the scenario "cotton, BBCH 40-49" the deposition factor incorporated in the short-cut value for long-term exposure is 1 (see Appendix A, EFSA 2009) assuming no interception at this growth stage of cotton. However, as the crop foliage will not be an attractive food source at this growth stage and it is only the weeds within the field which will be consumed, it is appropriate to consider interception. In line with the Generic Guidance for Tier 1 FOCUS Ground Water Assessments (2012), interception by cotton is assumed at BBCH stages 40-89 to be 75%. Therefore, a refined long-term TER is presented below (Table 10.3.1.3-4) using a deposition factor (DF) of 0.25.

2. Fraction of food type in diet (PD)

Based on an extensive survey of the habitat preferences of the vole as described above, off-field exposure is the most likely route of exposure to GF-2372 when this is applied in cotton. However, in-field foraging cannot be entirely excluded. In this event, the following refinement is considered in calculating the higher tier TER_{LT} values in-field for voles foraging in GF-2372 treated cotton.

The vole feeds on a broad variety of plants and exhibits a pronounced selective food intake. A study by Rinke(1990[14]) on feeding preference of voles in grassland areas demonstrated the diet of the vole to consist of 35% monocotyledonous (grass) and 65% dicotyledonous plants. The dicotyledonous *Taraxacum officinale* (dandelions) (23.95%) and *Trifolium pratense* (red clover) (18.6%) are by far the most important food items, accounting for 42.55% of the diet. All other plant species contribute between 0.01 to 5.91% of the diet (Rinke, 1990; Rinke, 1991[15]). Therefore, the diet that would be relevant for this scenario is assumed to consist of 35% monocotyledonous plants and 65% dicotyledonous plants (PD: 0.35 grass; 0.65 non-grass herbs).

Calculated high tier long-term TER for voles

For the proposed use of GF-2732 in cotton the refined long-term DDD and corresponding TER value for the vole is provided in Table 10.3.1.3-3.

[14] Rinke, T. (1990). Zur Nahrungsökologie von Microtus arvalis (Pallas, 1779) auf Dauergrünland. I: Allgemeine Nahrungspräferenzen. Z. Säugetierkunde 55, 106-114.

[15] Rinke, T. (1991). Percentage of volume versus number of species: availability and intake of grasses and forbs in *Microtus arvalis*. Folia Zoologica 40 (2), 143-151.

Table 10.3.1.3-3: Refined TER for small herbivorous mammal "vole"

Food items	FIR/bw	RUD (mg a.s./kg)	PD	PT	f_{twa}	MAF	DF	DDD (mg a.s./kg bw)	Endpoint (mg a.s./kg bw)	TER_{LT} [5]
Vole in cotton (App. Rate: 2 x 0.024 kg as/ha)										
Grasses and cereal shoots	1.33	54.2	0.35	1	1	1.6	0.25	0.242	6.63	12.2
Non grass herbs	1.68	28.7	0.65					0.300		
							Sum:	0.543		

FIR/bw: food intake rate per body weight (from Appendix A of the EFSA Guidance, 2009)
RUD: residues per unit dose (from Appendix A of the EFSA Guidance, 2009)
DF: deposition factor (from FOCUS, 2012)
MAF: multiple application factor
f_{TWA}: time weighted average factor
PT: proportion of diet obtained in the treated area
DDD: daily dietary dose

The above refined assessment demonstrates an acceptable long-term risk to small herbivorous mammals "voles" from the proposed use of GF-2372 in cotton even under the worst case unrealistic assumption that a vole is obtaining 100% of its diet from a cotton field at BBCH 40-49.

Metabolites

In accordance with the EFSA guidance document, the risk to mammals from metabolites formed in plants and vertebrate compartments has to be considered.

Mammals can be exposed *via* diet to environmental metabolites of sulfoxaflor, particularly from metabolites formed in plant matter tissues, insects, soil organisms or combinations thereof. There are two major metabolites formed in plant tissue: X11719474 and X11721061, and two major soil metabolites: X11719474 and X11519540.

Metabolite X11719474: The acute oral LD_{50} of X11719474 in rats was determined to be > 5000 mg/kg bw. The acute oral toxicity of sulfoxaflor in rats was 1000 mg/kg bw and in mice was 750 mg a.s./kg bw. Regarding long-term effects, a number of mammalian studies have been conducted on X11719474. Most relevant to the evaluation for wild mammals are the rat reproduction screening test and the rat development toxicity study. In the rat reproduction screening test, the NOAEL for reproduction and developmental toxicity was 162 mg/kg bw/day, based on a weak treatment effect at PND1 and 4 at the highest dose tested - lowered pup survival that is outside concurrent and (revised) historical control data. In the rat developmental toxicity study, the NOAEAL was 368 mg/kg bw/d, the highest level tested. There were no effects on neonatal survival or developmental alterations. Thus, X11719474 exhibits substantially less toxicity than parent sulfoxaflor and the mammalian risk assessment for X11719474 may be based upon the results of the risk assessment for the parent sulfoxaflor.

Metabolite X11519540: The acute oral LD_{50} of X11519540 in rats was determined to be 566 mg/kg bw. The acute oral toxicity of sulfoxaflor in rats was 1000 mg/kg bw and in mice was 750 mg a.s./kg bw. As the acute oral endpoints for X11519540 and the parent are within a factor of 2 (the trigger value for which endpoints are considered to be relevant in line with the Guidance Document on the Assessment of the Equivalence of Technical Materials of Substances Regulated under Regulation (EC) No. 1107/2009[16]) these two compounds are considered to be of comparable toxicity. Thus, the mammalian risk assessment for X11519540 may be based upon the results of the risk assessment for the parent sulfoxaflor.

The relative extent of potential formation of X11519540 in plants is approximately equivalent to the extent of formation in mammals (goat metabolism study). In soil, because of the low bioaccumulation potential of X11519540 (log Kow = 0.7), the relative extent of formation of X11519540 in mammalian studies on the parent are likely to be representative of long-term exposures potentially occurring in soil organisms. Therefore, the long-term toxicity of X11519540 can be considered to be accounted for by the toxicity studies in mammals of the parent material sulfoxaflor and the long-term mammalian risk assessment for X11519540 may be based upon the results of the risk assessment for the parent sulfoxaflor.

Metabolite X11721061: The extent of potential formation of metabolite X11721061 in plants, when considering the summed contribution of plant conjugates of X11721061 with that of free X11721061, substantially exceeds that observed in mammals and birds. Therefore, like X11719474, an acute oral toxicity study in rats was conducted to compare the relative potency of the metabolite to that of the parent. The acute oral LD_{50} of X11721061 in rats was determined to be 2000 mg/kg bw. The acute oral toxicity of sulfoxaflor in rats was 1000 mg/kg bw and in mice was 750 mg a.s./kg bw. Thus, X11721061 exhibits substantially less toxicity than parent sulfoxaflor and the mammalian acute risk assessment for X11721061 may be based upon the results of the risk assessment for the parent sulfoxaflor.

Drinking water assessment

The EFSA Bird and Mammal Guidance Document (EFSA Journal 2009; 7(12):1438) proposes an assessment methodology for the risk to mammals from active substances in drinking water using a small granivorous mammal as an indicator species. The relevant scenario for mammals is the puddle scenario which assumes a mammal taking drinking water from water on the soil surface after a heavy rainfall event follows application of the product.

Due to the characteristics of the exposure scenario in connection with the standard assumptions for water uptake by animals, no specific calculations of exposure and TER are necessary since the ratio of effective application rate (in g/ha) to acute and long-term endpoint (in mg/kg bw/d) does not exceed 50 in the case of less sorptive substances (Koc < 500 L/kg) or 3000 in the case of more sorptive substances (Koc ≥ 500 L/kg).

[16] SANCO/10597/2003, 2012

Sulfoxaflor has a Koc of 14 - 35 L/kg. The proposed worst-case rate of use of GF-2372 is a 2 x 0.024 kg a.s./ha (7 d interval) in cotton. The ratios of effective application rate to relevant endpoints are presented in the following table.

Table 10.3.1.3-5: Screening step for drinking water assessment – ratio of application rate to relevant endpoint for mammals

Substance	Koc (L/kg)	Effective application rate (g a.s./ha)*	Toxicity endpoint (mg a.s./kg bw)	Ratio	Trigger
Sulfoxaflor	14 - 35	38.4	Acute: 750	0.05	50
			Long-term: 6.63	5.79	

*AR_{eff} = AR x MAF_m, MAF_m = 1.6 based on default $DT_{50, soil}$ = 10 days (worst-case compared to $DT_{50, soil}$(field)= 7.43)

The ratios for acute and reproductive endpoints for sulfoxaflor do not exceed the threshold value of 50. Thus, no specific calculations of exposure for mammals through drinking water are necessary. In conclusion, the risk through exposure *via* drinking water from the intended uses of GF-2372 is acceptable.

IIIA 10.3.2 Other studies

IIIA 10.3.2.1 Acute oral toxicity of the preparation

The following acute oral rat toxicity study performed on GF-2372 was assessed in the EU review and is available in the DAR (2013) Annex B.6.

Report:	**IIIA 10.3.2.1/01, [redacted] (2009)**
Title:	Acute Oral Up and Down Procedure in Rats.
Document No:	Dow Study ID: 090348
Guidelines:	OPPTS 870.1200, OECD 402
GLP	Yes (certified laboratory)

Study Comments: IIIA 10.3.2.1/01	Already reviewed in the EU DAR for Sulfoxaflor.
Agreed Endpoints: IIIA 10.3.2.1/01	LD_{50} > 2000 mg GF-2372 /kg of body weight.

IIIA 10.3.2.2 Acceptance of bait, granules or treated seed (palatability testing)

GF-2372 is not formulated as a bait, granule or as treated seeds and, consequently, studies to determine palatability are not applicable.

IIIA 10.3.2.3 Effects of secondary poisoning

The EFSA birds and mammals guidance document (EFSA Journal 2009; 7(12): 1438) states that a log K_{ow} ≥3 is used to indicate that there might be a potential for bioaccumulation (see Section 5.6 Bioaccumulation and food chain behaviour). Sulfoxaflor has a log K_{ow} value of 0.802 (at pH 7), indicating a low potential for bioaccumulation in earthworm and fish tissues. Risk assessments for mammals feeding on fish and earthworms are not necessary for this active substance and have not been conducted.

IIIA 10.3.3 Supervised cage or field trials

Supervised cage/field trials with the formulation were not performed, since an acceptable risk to mammals indicates that further studies are not required.

IIIA 10.4 Effects on Bees

GF-2372 was one of the representative formulations in the EU review of sulfoxaflor. However new risk assessment parameters are now considered in the assessment of risk to bees and hence an appropriate risk assessment with the proposed use pattern is provided and is considered adequate. The risk assessment has been conducted in line with the Guidance Document on Terrestrial Ecotoxicology (SANCO/10329/2002 rev. 2 final).

The critical endpoints employed in the risk assessment for bees are indicated in Tables 10.4-1 to 10.4-3.

Table 10.4-1: EU Endpoints - Toxicity of sulfoxaflor and its metabolites to honeybees

Compound	Test species	Endpoint	EU agreed endpoints* (µg/bee)
Sulfoxaflor	*Apis mellifera*	Acute oral 48h LD_{50}	0.146
Sulfoxaflor	*Apis mellifera*	Acute contact 72h LD_{50}	0.379
X11719474	*Apis mellifera*	Acute oral 96h LD_{50}	> 100
X11519540	*Apis mellifera*	Acute oral 48h LD_{50}	> 91.2
X11579457	*Apis mellifera*	Acute oral 48h LD_{50}	45.7
X11721061	*Apis mellifera*	Acute oral 48h LD_{50}	> 103.5
GF-2032	*Bombus terrestris*	Acute oral LD_{50}	0.027 (a.s.)
GF-2032	*Bombus terrestris*	Acute oral LD_{50}	7.554 (a.s.)

* EFSA Journal 2014; 12(5):3692

Table 10.4-2: EU Endpoints - Toxicity of GF-2372 to honeybees

Compound	Test species	Endpoint	EU agreed endpoints* (µg a.s./bee)
GF-2372	*Apis mellifera*	Acute oral 48h LD_{50}	0.075
		Acute contact 48h LD_{50}	0.224

* EFSA Journal 2014; 12(5):3692

Table 10.4-3 EU Endpoints - semi-field tests

Test substance (location)	Study treatments	Findings	Reference *
GF-2626 (Germany)	Pre-flowering without bees: 1) 48 g a.s./ha Evening application after bee flight: 1) 24 g a.s./ha 2) 48 g a.s./ha Daytime application during bee flight: 1) 24 g a.s./ha	Negative effects on adult mortality: in evening application 24 g a.s./ha on day 0, in evening application 48 g a.s./ha on day 0-1, in daytime application on day 0-1. Negative effects on foraging activity: in evening application 48 g a.s./ha on day 0-2, in daytime application on day 0-1. Negative effects on bee brood cannot be excluded.	Schmitzer (2011a)
GF-2626 (Germany)	Pre-flowering without bees: 1) 48 g a.s./ha Evening application after bee flight: 1) 24 g a.s./ha Daytime application during bee flight: 1) 24 g a.s./ha	Negative effects on adult mortality: in evening application on day 0, in daytime application on day 0-1. Negative effects on foraging activity: in daytime application on day 0-1. Negative effects on bee brood cannot be excluded.	Schmitzer (2011b)

* EFSA Journal 2014; 12(5):3692

Both the active substance and formulation data have been used to calculate hazard quotients (HQs), as well as the metabolite data. A summary of the proposed GAP for GF-2372 is provided in Table 10-2. The maximum proposed rate of use (equivalent to 24 g a.s./ha) has been considered in the following risk assessment.

IIIA 10.4.1 Hazard quotients for bees

IIIA 10.4.1.1 Oral exposure Q_{HO}

The acute oral risk assessment for bees is summarised in the table below.

Table 10.4.1.1-1: Acute oral risk to bees from exposure to sulfoxaflor, metabolites and GF-2372

Test species	Test substance	Application rate (g a.s./ha)	LD_{50} (µg a.s./bee)	Q_{HO} [50]
Honeybee	GF-2372	24	0.075	**320**
Honeybee	Sulfoxaflor		0.146	**164**
Honeybee	X11719474*		> 100	< 0.24
Honeybee	X11519540*		> 91.2	< 0.26
Honeybee	X11579457*		45.7	0.53
Honeybee	X11721061*		> 103.5	< 0.23

HQs shown in **bold** are above the relevant trigger
*Risk assessment conducted assuming 100% formation of metabolites as a worst-case approach

The above calculated oral hazard quotients for sulfoxaflor and GF-2372 are above the trigger of 50 indicating the need for a refined risk assessment.

The hazard quotients for all metabolites are less than the trigger of 50, indicating that all metabolites of sulfoxaflor pose an acceptable acute oral risk to bees.

IIIA 10.4.1.2 Contact exposure Q_{HC}

The acute contact risk assessment for bees is summarised in the table below.

Table 10.4.1.2-1: Acute contact risk to bees from exposure to sulfoxaflor and GF-2372

Test species	Test substance	Application rate (g a.s./ha)	LD_{50} (µg a.s./bee)	Q_{HC} [50]
Honeybee	GF-2372	24	0.224	**107**
Honeybee	Sulfoxaflor		0.379	**63.6**

HQs shown in **bold** are above the relevant trigger

The above calculated contact hazard quotients for sulfoxaflor and GF-2372 are above the trigger of 50 indicating the need for a refined risk assessment.

Refined risk assessment (oral and contact exposure)

The first tier risk assessments demonstrate a potential acute risk to honeybees *via* oral and contact exposure following the proposed uses of GF-2372. Therefore, higher tier studies should be taken into consideration. A foliar residue contact laboratory study with GF-2372 (IIIA 10.4.3/01) and semi-field studies with GF-2626 (IIIA 10.4.7/01 to 10.4.7/03) are available. The available studies were all GLP compliant and conducted in line with standard guidelines. It is considered appropriate to extrapolate from data on GF-2626 to GF-2372 as these products were shown to be of comparable toxicity to honeybees in the acute contact and oral laboratory studies.

Foliar residues contact laboratory study

The EFSA Conclusion (2014) states that "*The results of foliage residue contact laboratory test indicated that mortality is not expected when bees are exposed to dry residues (aged residues) on over sprayed foliage.*" In this study, the toxicity of GF-2372 residues on foliage to honeybees was assessed in a 24 hour study. Bees were exposed to alfalfa foliage sprayed with GF-2372 at a nominal rate of 100 and 200 g a.s./ha. The residues were allowed to weather in the field for 3, 6 and 24 hours before being placed in cages and the bees exposed in the laboratory. Contact time for the bees was 24 hours. No significant adverse effects on the bees were observed after exposure to foliar residues up to 200 g a.s./ha, after ageing for 3, 6 or 24 hours. As this rate is over x4 the proposed maximum application rate (48 g a.s./ha), this study clearly demonstrates an acceptable risk to bees from contact exposure following the proposed uses of GF-2372.

Semi-field data

However, the EFSA Conclusion (2014) also states that "*increased mortality was observed in the tunnel tests when sulfoxaflor was applied on flowering Phacelia during bee flight, and also when the application was in the previous evening (after bee flight). The increase in mortality was only apparent on the day of the application or on the following day. Potential adverse effects on bee brood could not be excluded from the available data and assessment."*

Further information is given on this in the DAR (2013), which states that; "*In two of the studies detailed assessments on brood following OECD 75 guideline and on colony condition and strength were made up to approximately 4 weeks after exposure. No adverse impacts on colony health or performance were noted between the control colonies and those exposed to applications of sulfoxaflor at any of the treatments tested, except for the parameter of brood termination rate with rather questionable results."*

The results for brood termination rate were concluded to be questionable due to the relatively high loss of eggs in the control, high variability in the brood termination rate among individual replicates and poor statistical power of these measures.

Therefore, the results in terms of mortality and brood termination rate from each of the three semi-field studies have been considered in further detail below.

I) Schmitzer (2011a); IIIA 10.4.7/01

This study assessed the effects of GF-2626 on honeybee colonies, including brood development, when bees were enclosed within tunnels containing *Phacelia tanacetifolia* for 7 to 10 days. Observations then continued for up to 27 days after application. The following scenarios were assessed:

- 48 g a.s./ha - pre-flowering
- 24 and 48 g a.s./ha - evening application after bee flight
- 24 g a.s./ha - during bee flight

Only the first two scenarios which will be focused on here, as GF-2372 is not proposed for use when bees are actively foraging. With regards mortality of worker bees the following results were found (refer to Table IIIA 10.4.7/01-2 for full details):

48 g a.s./ha before flowering:
No statistically significant differences in mortality compared to control up to day 7 a.a., statistically significant differences on day 9 a.a. (mean mortality of 0.0 and 6.0 in the control and treatment group, respectively) and also in mean days 8 to 27 a.a. (mean mortality of 2.2 and 3.53 bees in the control and treatment group, respectively) and mean days 0 to 27 a.a. (mean mortality of 7.1 and 10.9 bees in the control and treatment group, respectively).

24 g a.s./ha evening application after bee flight:
Statistically significant differences in mortality compared to control on day 0 (mean mortality of 17.3 and 79.3 in the control and treatment group, respectively) and on day 9 a.a. (mean mortality of 0.0 and 3.3 in the control and treatment group, respectively).

48 g a.s./ha evening application after bee flight:
Statistically significant differences in mortality compared to control on day 0 (mean mortality of 17.3 and 113.7 in the control and treatment group, respectively), on day 1 a.a. (mean mortality of 9.7 and 39.0 in the control and treatment group, respectively), on day 9 a.a. (mean mortality of 0.0 and 3.3 in the control and treatment group, respectively), on day 16 a.a. (mean mortality of 0.7 and 7.0 in the control and treatment group, respectively) and also in mean days 8 to 27 a.a. (mean mortality of 2.2 and 4.27 in the control and treatment group, respectively).

Although, there were some statistically significant effects observed, these levels of mortality were generally very low, falling within the range of the mean mortality observed pre-treatment in all test groups (8.3 to 31.7 bees) and within the mean mortality observed in the control group from day 0 to 27 a.a. (0.0 to 33.3 bees). Only mortality in the 24 and 48 g a.s./ha (after bee flight) treatment groups at day 0 were out-with these ranges (mean mortality of 79.3 and 113.7 bees). However, this mortality is still low, especially when the size of the colonies are considered; mean number of bees per colony in the six treatment groups one day before application was 2610 to 3600 per colony. Overall, these levels of mortality can be concluded not to be ecologically relevant.

With regards to effects on the brood termination rate, following the assessment of single cells from the egg stage to successfully hatched worker bees, the mean termination rate in the control was 56.39%. It was considered in the DAR (2013) that the surrounding conditions where colonies were exposed during such a trial lead to this relatively high number of loss of eggs. The reason for this was thought to be the artificial housing, colony size and limited space of the colonies as well as weather conditions.

The brood termination rate was similar in the test groups; 48 g a.s./ha pre-flowering (58.06%) and 24 and 48 g a.s./ha in the evening (70.56 and 47.22%, respectively). There were no statistically significant differences in brood termination rate in any test item group compared to the control.

II) Schmitzer (2011b); IIIA 10.4.7/02

This study assessed the effects of GF-2626 on honeybee colonies, including brood development, when bees were enclosed within tunnels containing *Phacelia tanacetifolia* for 7 to 10 days.

Observations then continued for up to 27 days after application. The following scenarios were assessed:

- 48 g a.s./ha - pre-flowering
- 24 g a.s./ha - evening application after bee flight
- 24 g a.s./ha - during bee flight

Only the first two scenarios which will be focused on here, as GF-2372 is not proposed for use when bees are actively foraging. With regards mortality of worker bees the following results were found (refer to Table IIIA 10.4.7/02-2 for full details):

48 g a.s./ha before flowering:
Statistically significant differences in mortality compared to the control on day 9 a.a. (mean mortality of 1.7 and 8.7 in the control and treatment group, respectively) and also in mean days 0 to 7 a.a. (mean mortality of 20.4 and 29.17 in the control and treatment group, respectively)

24 g a.s./ha evening application after bee flight:
Statistically significant differences in mortality compared to the control on day 0 (mean mortality of 26.7 and 81.7 in the control and treatment group, respectively) and on day 12 a.a. (mean mortality of 0.0 and 3.3 in the control and treatment group, respectively).

Although there were some statistically significant effects observed, these levels of mortality were generally very low and comparable to the range of mean mortality observed pre-treatment in all test groups (6.0 to 24.7 bees) and within the mean mortality observed in the control group from day 0 to 27 a.a. (0.0 to 43.7 bees). Only mortality in the 24 g a.s./ha (after bee flight) treatment group at day 0 was out-with these ranges (mean mortality of 81.7 bees). However, this mortality is still low, especially when the size of the colonies are considered; mean number of bees per colony in the six treatment groups one day before application was 2460 to 3300 per colony. Overall, these levels of mortality can be concluded not to be ecologically relevant.

With regards effects on the brood termination rate, following the assessment of single cells from the egg stage to successfully hatched worker bees, the mean termination rate in the control was 65.28%. It was considered in the DAR (2013) that the surrounding conditions where colonies were exposed during such a trial lead to this relatively high number of loss of eggs. The reason for this was thought to be the artificial housing, colony size and limited space of the colonies as well as weather conditions.

The brood termination rate was similar or lower in the test groups; 48 g a.s./ha pre-flowering (65.56%) and 24 g a.s./ha in the evening (44.17%). There were no statistically significant differences in brood termination rate in any test item group compared to the control.

III) Schmitzer (2011c); IIIA 10.4.7/03

As this study only assessed daytime application during bee flight is has not been considered here. Furthermore, the reduced amount of brood stages in bee colonies, because of the progressed season, limits the utility of the study for evaluation of effects of the test substance on bee brood.

zRMS comment:

Based on semi-field studies, significant mortality on bees are observed at maximum rate of 48 g a.s./ha after bee flight and before flowering. The increase in mortality was only apparent on the day of the application or on the following day. Potential adverse effects on bee brood could also not be excluded from the available data and assessments.

Furthermore, a higher oral toxicity is observed with the similar formulation GF-2032 on bumble bee (0.027 µg a.s./bee) than on honey bee (0.146 µg a.s./bee). This indicates a possible higher sensibility of other pollinisators as bumble bees to sulfoxaflor.

The crop species in the GAP for GF-2372 include Cotton and Oilseed rape. They are considered attractive for bees during flowering for both pollen and nectar.

Therefore, a position paper based on a study has been provided by the notifier during the reviewing of GF-2372 by Czech Republic for central zone (summaries presented below). zRMS France choose to take into account those informations in the refined risk for bees. According to central zone assessment:
"The position paper is mainly based on the semi-field study by Liepold (2011; IIIA 10.4.7/04; not evaluated in EU review) which investigated the residues of sulfoxaflor, and the main plant metabolite X11719474, in pollen, nectar and plants following application to *Phacelia*. GF-2626 was applied at 24 and 48 g a.s./ha (T1 and T2) before the onset of flowering (BBCH 58) in three replicate tunnels. In separate tunnels GF-2626 was applied at 24 and 48 g a.s./ha (T3 and T4) during flowering (BBCH 64) and honey bee foraging. In order to evaluate the magnitude of residues of the test item GF-2626 and metabolite X11719474, nectar stomachs from forager bees, pollen samples from pollen traps and plants of *Phacelia* were taken for analysis. Samples were taken on day 0 after the application and on days +5 and +6.

The results showed that, when applications of GF-2626 at 24 and 48 g a.s./ha were made 5 days before flowering, residues of sulfoxaflor and X11719474 were not detectable or were below the LOQ in pollen and nectar samples taken during full flowering. Additionally, following applications of GF-2626 during flowering, low levels of sulfoxaflor and X11719474 were present in nectar (maximum of 0.0889 mg/kg of sulfoxaflor), and these levels rapidly declined to be below the level of quantification in nectar at 6 days after application. In pollen, levels were slightly higher (maximum of 0.809 mg/kg) but also declined rapidly to 0.0325 mg/kg, when applied at 48 g a.s./ha. From this study it can be concluded that residues of sulfoxaflor are not persistent in plant material, and that honey bees will not be exposed to residues of sulfoxaflor in pollen and nectar following pre-flowering applications."

It is concluded that the risk to honeybees is acceptable when the product is applied before flowering. Pre-flowering application made 5 days before flowering is considered sufficiently protective by zRMS. The following mitigation measure must be applied: Do not use where bees are actively foraging/ Do not apply 5 days before and during flowering.

Therefore, considering flowering plants other than crops, a mitigation measure is considered needed: "Do not apply when flowering weeds are present"

Finally, no information has been provided concerning the honeydew production and the possible way of transfert and exposure of Sulfoxaflor to bees. Then the following mitigation measure must be applied for all intended uses: “To protect bees and pollinating insects do not apply to crop plants when in flower or during the honeydew production period”. This conclusion is considered to be conservative for bumble bees.

It is noted, that according to Regulation (EU) 2015/1295, the Notifier 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. This information should be submitted by 18 August 2017

IIIA 10.4.2 Acute toxicity of the formulation to bees

IIIA 10.4.2.1 Oral

The following acute oral toxicity study with the honeybee performed on GF-2372 was assessed in the EU review and is available in the DAR (2013) Annex B.9.

Report:	**IIIA 10.4.2.1/01, Vinall, S. (2010)**
Title:	Laboratory bioassay to determine the acute oral toxicity of GF-2372 to the honeybee, *Apis mellifera*.
Document No:	Dow Study ID: 10-16
Guidelines:	OECD 213
GLP	Yes

Study Comments: IIIA 10.4.2.1/01	Already reviewed in the EU DAR for Sulfoxaflor (2013).
Agreed Endpoints: IIIA 10.4.2.1/01	48-h-LD_{50} Oral =0.153 µg GF/2372/bee (equivalent to 0.075 µg Sulfoxaflor/bee)

IIIA 10.4.2.2 Contact

The following acute contact toxicity study with the honeybee performed on GF-2372 was assessed in the EU review and is available in the DAR (2013) Annex B.9.

Report:	**IIIA 10.4.2.2/01, Vinall, S. (2009)**
Title:	Laboratory bioassay to determine the acute contact toxicity of GF-2372 to the honeybee, *Apis mellifera*.
Document No:	Dow Study ID: 09-30
Guidelines:	OECD 214
GLP	Yes

Study Comments: IIIA 10.4.2.2/01	Already reviewed in the EU DAR for Sulfoxaflor (2013).
Agreed Endpoints: IIIA 10.4.2.2/01	48-h-LD_{50} Contact =0.224 µg Sulfoxaflor/bee

The following acute oral and contact toxicity study to bumblebee performed on GF-2032 was assessed in the EU review and is available in the DAR (2013) Annex B.9. GF-2032 is a SC formulation containing 22% wt/wt sulfoxaflor and GF-2372 is a WP formulation of similar composition containing 50% wt/wt sulfoxaflor.

IIIA 10.4.3 Effects on bees of residues on crops

The following toxicity of residues on foliage to the Honeybee performed on GF-2372 was assessed in the EU review and is available in the DAR (2013) Annex B.9.

Report:	**IIIA 10.4.3/01, Bergfield, A. (2009)**
Title:	GF-2372: Toxicity of Residues on Foliage to the Honeybee, *Apis mellifera*
Document No:	Dow Study ID: 090151
Guidelines:	U.S. EPA FIFRA Subdivision L, Section 141-2 U.S. EPA OPPTS Guideline 850.3030
GLP	Yes

Study Comments: IIIA 10.4.3/01	Already reviewed in the EU DAR for Sulfoxaflor (2013).
Agreed Endpoints: IIIA 10.4.3/01	No significant adverse effects to bees when exposed to foliar residues of GF-2372 treated 3, 6 or 24 hours previously at 100 and 200 g Sulfoxaflor/ha, were determined.

IIIA 10.4.4 Cage tests

No data submitted.

IIIA 10.4.5 Field tests

No data submitted.

IIIA 10.4.6 Investigation into special effects

IIIA 10.4.6.1 Larval toxicity

No data submitted.

IIIA 10.4.6.2 Long residual effects

No data submitted.

IIIA 10.4.6.3 Disorienting effects on bees

No data submitted.

IIIA 10.4.7 Tunnel tests

The following semi-field tests with honeybee performed on GF-2626 were assessed in the EU review and are available in the DAR (2013) Annex B.9.

Report:	**IIIA 10.4.7/01, Schmitzer, S (2011a)**
Title:	Study on the Effect of GF-2626 on Honey Bee Brood (*Apis mellifera* L.) under Semi-Field Conditions - Tunnel Test.
Document No:	Dow Study ID: 80755
Guidelines:	OEPP/EPPO guideline No. 170 (3) (OEPP/EPPO, 2001) OECD No. 75 ENV/JM/MONO(2007)22.
GLP	Yes

Study Comments: IIIA 10.4.7./01	Already reviewed in the EU DAR for Sulfoxaflor (2013).
Agreed Endpoints: IIIA 10.4. 7./01	The potential effects of GF-2626 on honey bee colonies including brood development was assessed by exposing honey bees under the realistic but severe conditions of a semi-field (tunnel) test. For honey bees and colonies exposed to pre-flower treatment with 48 g

	sulfoxaflor/ha, to dried residues applied at 24 and 48 g sulfoxaflor/ha after bee flight and to direct exposure to 24 g sulfoxaflor/ha, no effects on mortality, flight intensity and behaviour were observed. Although significant effect on worker bee mortality on day 0 after application were observed in the 24 and 48 g a.s./ha after bee flight group and in the 24 g a.s./ha during bee flight group. In the 48 g a.s./ha after bee flight group and 24 g a.s./ha during bee flight group, the negative effects on mortality were observed also on the following day (day 1 a.a.). In these two test groups, significant effects on foraging activity were noticed on day 0 after application, observed also on days 1 and 2 a.a. in the 48 g a.s./ha after bee flight group and on day 1 a.a. in the 24 g a.s./ha during bee flight group. No effects on colony development, colony strength or bee brood were observed after exposure of the bees to pre-flower treatment with 48 g sulfoxaflor/ha, to dried residues applied at 48 g sulfoxaflor/ha after bee flight and to direct exposure to 24 g sulfoxaflor/ha. Following the application of 24 g sulfoxaflor/ha after the bee flight, brood termination rate of the bee colonies was higher compared to the control. Since this was not obvious in the higher rate with 48 g sulfoxaflor/ha and after direct application to the bees to 24 g sulfoxaflor/ha, this must be seen as not a test item related effect. No significant negative effects on pupae mortality, colony condition, colony strength and brood compensation index were noticed in any test item group compared to control. Clear adverse effects were observed in the reference item treated colonies (Insegar (300 g fenoxycarb/ha). No adverse effect on the overall survival of the colonies could be observed after application of GF-2626 at all rates and treatment scenarios.

Report:	**IIIA 10.4.7/02, Schmitzer, S (2011b)**
Title:	Study on the Effect of GF-2626 on Honey Bees and their Brood (*Apis mellifera* L.) under Semi-Field Conditions - Tunnel Test.
Document No:	Dow Study ID: 101599
Guidelines:	OEPP/EPPO guideline No. 170 (3) (OEPP/EPPO, 2001) OECD No. 75 ENV/JM/MONO(2007)22.
GLP	Yes

Study Comments: IIIA 10.4.7./01	Already reviewed in the EU DAR for Sulfoxaflor (2013).
Agreed Endpoints:	The potential effects of GF-2626 on honey bee colonies including brood development was assessed by exposing honey bees under the realistic but

IIIA 10.4. 7./01	severe conditions of a semi-field (tunnel) test. For honey bees and colonies exposed to pre-flower treatment with 48 g sulfoxaflor/ha, to dried residues applied at 24 and 48 g sulfoxaflor/ha after bee flight and to direct exposure to 24 g sulfoxaflor/ha, no effects on mortality, flight intensity and behaviour were observed. Although significant effect on worker bee mortality on day 0 after application were observed in the 24 and 48 g a.s./ha after bee flight group and in the 24 g a.s./ha during bee flight group. In the 48 g a.s./ha after bee flight group and 24 g a.s./ha during bee flight group, the negative effects on mortality were observed also on the following day (day 1 a.a.). In these two test groups, significant effects on foraging activity were noticed on day 0 after application, observed also on days 1 and 2 a.a. in the 48 g a.s./ha after bee flight group and on day 1 a.a. in the 24 g a.s./ha during bee flight group. No effects on colony development, colony strength or bee brood were observed after exposure of the bees to pre-flower treatment with 48 g sulfoxaflor/ha, to dried residues applied at 48 g sulfoxaflor/ha after bee flight and to direct exposure to 24 g sulfoxaflor/ha. Following the application of 24 g sulfoxaflor/ha after the bee flight, brood termination rate of the bee colonies was higher compared to the control. Since this was not obvious in the higher rate with 48 g sulfoxaflor/ha and after direct application to the bees to 24 g sulfoxaflor/ha, this must be seen as not a test item related effect. No significant negative effects on pupae mortality, colony condition, colony strength and brood compensation index were noticed in any test item group compared to control. Clear adverse effects were observed in the reference item treated colonies (Insegar (300 g fenoxycarb/ha). No adverse effect on the overall survival of the colonies could be observed after application of GF-2626 at all rates and treatment scenarios.

Report:	**IIIA 10.4.7/03, Schmitzer, S (2011c)**
Title:	Toxicity Testing of GF-2626 on Honey Bees (*Apis mellifera* L.) under Semi-Field Conditions - Tunnel Test.
Document No:	Dow Study ID: 101602
Guidelines:	OEPP/EPPO guideline No. 170 (3) (OEPP/EPPO, 2001)
GLP	Yes

Study Comments: IIIA 10.4.7./03	Already reviewed in the EU DAR for Sulfoxaflor (2013).
Agreed Endpoints:	The development of the colony strength among the colonies in all treatment groups followed more or less the same pattern. Following the start of the study the colony strength was decreasing in all treatment

IIIA 10.4. 7./03	groups. Given the time of the season it is clear that there is no large growth in bee brood. Since these patterns are very similar it can be concluded that there was no test item related influence on the overall strength of the colonies. Strongest decrease was seen in both reference item treated groups. For honey bees and colonies exposed to GF-2626 applied at 4, 8 and 24 g sulfoxaflor/ha during bee flight no effects on mortality, flight intensity, behaviour or brood and overall colony condition were observed.

Following reports has been provided by the Notifier during the assessment by the Czech Republic of the Central Zone registration:

Report:	**IIIA 10.4.7/04, Liepold K. (2011)**
Title:	A Semi-field Study to Investigate Residues in Honeybee Products (*Apis mellifera carnica* L.; (Hymenoptera, Apidae) in *Phacelia tanacetifolia* in Germany in 2010.
Document No:	Study Code S10-01824. Dow AgroSciences unpublished report no. 2009317. DAS Study ID: 110414.
Guidelines:	IVA (BEUTEL et al., 1992), EU (1997)
GLP	Yes

Test material

Test item:	GF-2626
Purity:	128 g/L XDE-208 (analysed)
Description:	Off-white to tan liquid
Lot No./Batch No. :	E-3144-36

Test system

Organism (Species):	Honey bee, *Apis mellifera carnica* L. (Hymenoptera, Apidae)
Study Type:	Semi-field study
GLP Status:	GLP
Guidelines followed:	IVA (BEUTEL et al., 1992), EU (1997)
Guideline deviations reported by Study Director:	None.
Study design:	Application before flowering in treatment groups T1 and T2 and application during flowering and during daily bee-flight in treatment groups T3 and T4. Nectar stomachs from forager bees, pollen samples from pollen traps and plants of *Phacelia tanacetifolia* were taken for analysis on day of application during bee flight, 5 and 6 days after application during bee flight. The condition of the colonies and bee brood was assessed once before set-up of the colonies in the tunnels. 1 replicate (tunnel) per treatment group, each consisting

	of 1 honey bee colony.
Test concentrations:	24 g a.i./ha (T1 and T3), 48 g a.i./ha (T2 and T4)

Methodology
This study included five treatment groups. The test item GF-2626 (active substance: XDE-208) was applied at rates of 24 g a.i./ha (treatment groups T1 and T3) and 48 g a.i./ha (treatment groups T2 and T4) in separated tunnels. A fifth group (tunnel) left untreated served as control. Applications in treatment group T1 and T2 were conducted before flowering; applications in treatment group T3 and T4 were made during flowering and during daily bee-flight. All applications were made with a rate of 400 L water/ha. The effect of the test item was examined on commercial bee colonies in tunnels (approx. 200 m2) placed on plots with *Phacelia tanacetifolia*. Condition of the colonies and the development of the bee brood were assessed once before the start of exposure of the honeybees in the tunnels. In order to evaluate the magnitude of residues of the test item GF-2626 nectar stomachs from forager bees, pollen samples from pollen traps and plants of *Phacelia tanacetifolia* were taken for analysis.

Results
The colony strength before set-up in the tunnels ranged from 17511 to 23888 honeybees in the different treatment groups and the control. Regarding the brood development, it can be stated that all colonies of all treatment groups (T1, T2, T3, T4 and control) had brood of all stages (eggs, larvae, sealed brood). Food (nectar and pollen) was also present in all colonies with a higher percentage of nectar (13.28 % to 37.50%) compared to pollen (7.34 % to 13.28 %).
No residues of XDE-208 and its metabolite X11719474 at or above the respective limit of detection (LOD) levels (0.003 mg/kg for plants, nectar and pollen) were found in any of the untreated control samples. In nectar samples from forager bees no residues of X11719474 were detected in all treatment groups for sampling 1 and 2. In sampling 3 (DAA6) residues were found in treatment group T2 and T4. However these residues were below the limit of quantification (LOQ 0.01 mg/kg). For treatment groups T1 and T2 no residues of XDE-208 were detected for all sampling dates. In treatment group T3 a mean (of 3 samples) of 0.0441 mg/kg was determined in sampling 1 (DAA0). In sampling 2 and 3 residues were below LOQ (0.01 mg/kg). Residues of XDE-208 in treatment group T4 were 0.0647 mg/kg (mean of 3 samples) in sampling 1 (DAA0), declined to 0.0109 in sampling 2 (DAA5) and were below LOQ for sampling 3 (DAA6).

In pollen samples from pollen traps no residues of XDE-208 and its metabolite X11719474 were determined in treatment group T1 for all samplings. In treatment group T2 residues of XDE-208 and X11719474 were below LOQ (0.01 mg/kg) or below LOD (0.003 mg/kg) for all sampling dates. No residues of the metabolite X11719474 were detected for all samplings in treatment group T3. The residues of XDE-208 in pollen in treatment group T3 ranged from 0.290 mg/kg to 0.0160 mg/kg. In treatment group T4 residues of XDE-208 declined from 0.809 mg/kg in sampling 1 (DAA0) to 0.0325 mg/kg in sampling 3 (DAA6) and residues of the metabolite X11719474 were below LOQ (0.01 mg/kg) or LOD (0.003 mg/kg).

In whole *Phacelia tanacetifolia* plants residues of XDE-208 and X11719474 in treatment group T1 were below LOQ (0.01 mg/kg) or LOD (0.003 mg/kg). In treatment group T2 residues of XDE-208 found in sampling 1 (DAA0) were 0.0342 mg/kg, whereas no residues were detected in the following samplings (DAA5 and DAA6). Residues of the metabolite X11719474 were below LOQ (0.01 mg/kg) for sampling 1 and 2; 0.0113 mg/kg were found in sampling 3 (DAA6). In treatment group T3 the residues of XDE-208 ranged from 0.516 to 0.0480 mg/kg. The metabolite X11719474 was not detectable in treatment group T3 for sampling 1 (DAA0) and was below the LOQ (0.01 mg/kg) for the subsequent samplings. In treatment group T4 residues of XDE-208 in plants were determined between 1.48 and 0.0507 mg/kg. The metabolite X11719474 was below LOQ (0.01 mg/kg) for sampling 1 (DAA0) and 2 (DAA5) and 0.0147 mg/kg for sampling 3 (DAA6).

A summary of the sulfoxaflor and X11719474 residues found in nectar, pollen and plants is presented in Tables 3, 4 and 5 below.

Table 3: Results of nectar analysis

Timing	Treatment	Application rate (g a.s./ha)	Sulfoxaflor residues (mg/kg)	X11719474 residues (mg/kg)
0 DAA	C	-	nd	nd
			nd	nd
			nd	nd
	T1	24	nd	nd
			nd	nd
			nd	nd
	T2	48	nd	nd
			nd	nd
			nd	nd
	T3	24	0.0438	nd
			0.0462	nd
			0.0424	nd
	T4	48	0.0889	nd
			0.0548	nd
			0.0503	nd
5 DAA	C	-	nd	nd
			nd	nd
			nd	nd
	T1	24	nd	nd
			nd	nd
			nd	nd
	T2	48	nd	nd
			nd	nd
			nd	nd
	T3	24	<LOQ (0.005)	nd
			<LOQ (0.005)	nd
			<LOQ (0.004)	nd
	T4	48	0.0106	nd
			0.0110	nd
			0.0111	nd
6 DAA	C	-	nd	nd
			nd	nd
			nd	nd
	T1	24	nd	nd
			nd	nd
			nd	nd
	T2	48	nd	<LOQ (0.004)
			nd	<LOQ (0.004)
			nd	<LOQ (0.004)
	T3	24	<LOQ (0.004)	nd
			<LOQ (0.004)	nd
			<LOQ (0.005)	nd

	T4	48	<LOQ (0.0097)	<LOQ (0.003)
			<LOQ (0.006)	<LOQ (0.004)
			<LOQ (0.008)	<LOQ (0.004)

DAA: days after application during bee flight
C: untreated; T1/T2/T3/T4: test item group 1/2/3/4
n.d.: not detected (residue value was less than 30% of the LOQ, 0.003 mg/kg)
Values between 0.003 mg/kg (30% of the LOQ) and 0.01 mg/kg (LOQ) are reported as < LOQ

Table 4: Results of pollen analysis

Timing	Treatment	Application rate (g a.s./ha)	Sulfoxaflor residues (mg/kg)	X11719474 residues (mg/kg)
0 DAA	C	-	nd	nd
	T1	24	nd	nd
	T2	48	<LOQ (0.005)	nd
	T3	24	0.290	nd
	T4	48	0.809	<LOQ (0.004)
5 DAA	C	-	nd	nd
	T1	24	nd	nd
	T2	48	nd	nd
	T3	24	<LOQ (0.003)	nd
	T4	48	0.0191	nd
6 DAA	C	-	nd	nd
	T1	24	nd	nd
	T2	48	nd	<LOQ (0.004)
	T3	24	0.0160	nd
	T4	48	0.0325	nd

DAA: days after application during bee flight
C: untreated; T1/T2/T3/T4: test item group 1/2/3/4
n.d.: not detected (residue value was less than 30% of the LOQ, 0.003 mg/kg)
Values between 0.003 mg/kg (30% of the LOQ) and 0.01 mg/kg (LOQ) are reported as < LOQ

Table 5: Results of whole plant analysis

Timing	Treatment	Application rate (g a.s./ha)	Sulfoxaflor residues (mg/kg)	X11719474 residues (mg/kg)
0 DAA	C	-	Nd	nd
	T1	24	<LOQ (0.009/0.009)	<LOQ (0.004/0.003)
	T2	48	0.0342	<LOQ (0.006)
	T3	24	0.516	nd
	T4	48	1.48	<LOQ (0.009)
5 DAA	C	-	nd/nd	nd/nd
	T1	24	<LOQ (0.004/0.004)	<LOQ (0.005/0.005)
	T2	48	nd/nd	<LOQ (0.0099/0.00999)
	T3	24	0.0274	<LOQ (0.004)
	T4	48	0.0520	<LOQ (0.009)

Timing	Treatment	Application rate (g a.s./ha)	Sulfoxaflor residues (mg/kg)	X11719474 residues (mg/kg)
6 DAA	C	-	Nd	nd
	T1	24	Nd	<LOQ (0.009)
	T2	48	Nd	0.0113
	T3	24	0.0480	<LOQ (0.007)
	T4	48	0.0507	nd

DAA: days after application during bee flight
C: untreated; T1/T2/T3/T4: test item group 1/2/3/4
n.d.: not detected (residue value was less than 30% of the LOQ, 0.003 mg/kg)
Values between 0.003 mg/kg (30% of the LOQ) and 0.01 mg/kg (LOQ) are reported as < LOQ

Conclusions
Residues of XDE-208 and its metabolite X11719474 were determined in plant tissue after an application before and during flowering. In pollen samples quantifiable residues of XDE-208 were determined in treatment groups T3 and T4 with an application during flowering and daily bee-flight. Quantifiable residues of XDE-208 were determined in nectar samples at DAA0 in treatment group T3 (24 g a.i./ha) and at DAA0 and DAA5 in treatment group T4 (48 g a.i./ha). Residues of the parent are at the highest level in samples after application and decline in later samplings. Residues of the metabolite were measured at day 6 above LOQ.

Study Comments: IIIA 10.4.7/04	The results show that, when applications of GF-2626 at 24 and 48 g a.s./ha were made 5 days before flowering, residues of sulfoxaflor and X11719474 were not detectable or were below the LOQ in pollen and nectar samples taken during full flowering. Additionally, following applications of GF-2626 during flowering, low levels of sulfoxaflor and X11719474 were present in nectar (maximum of 0.0889 mg/kg of sulfoxaflor), and these levels rapidly declined to be below the level of quantification in nectar at 6 days after application. In pollen, levels were slightly higher (maximum of 0.809 mg/kg) but also declined rapidly to 0.0325 mg/kg, when applied at 48 g a.s./ha.
Agreed Endpoints: IIIA 10.4.7/04	-

Report:	**IIIA 10.4.7/05, anonymous (2016)**
Title:	Pre-Flowering Applications of Sulfoxaflor: Exposure and Effects on Honey bees
Document No:	-
Guidelines:	n.a.

GLP	n.a.

Summary

To investigate the risk of pre-flowering applications of sulfoxaflor to foraging honey bees, field trials were conducted to determine exposure in pollen and nectar, and to evaluate effects on mortality, foraging activity and brood development of bees. Residues were not detected (or were below the limit of quantification) in the pollen and nectar of flowering crops following an application of sulfoxaflor made 4 days before the onset of flowering. Based on the negligible exposure, the corresponding risk is also expected to be low.

This assumption of low risk has been confirmed in tunnel trials conducted in *Phacelia* that show pre-flowering applications of sulfoxaflor at 48 g a.s./ha had no effect on honey bee mortality, foraging activity and development of brood. The low risk to bees from pre-flowering applications can be explained by the short persistence of sulfoxaflor in plant material and soil combined with the low toxicity of metabolites formed.

1. Introduction

Sulfoxaflor has a short persistence in crop plants, having an average DT_{50} of 7.5 days and a median DT_{50} of 5.5 days based on an extensive data base that includes 29 different crops and 316 decline events on fruits, vegetables, leaves, forage, seeds, grain and root/tuber commodities. Persistence of sulfoxaflor in soil is also short with a maximum soil field DT_{50} of 7.4 days.

Additionally, the metabolites of sulfoxaflor are known to have low toxicity to honey bees, as shown in the table below.

Table 1: Toxicity of sulfoxaflor and metabolites to honey bees (OECD 213 guideline studies conducted to GLP)

Test substance	Acute oral toxicity (LD_{50} µg a.s./bee)
Sulfoxaflor	0.146 (48h)
X11719474 (plant and major soil metabolite)	>100 (96h)
X11519540 (minor soil metabolite)	>91.2 (48h)
X11579457 (minor soil metabolite)	45.7 (48h)
X11721061 (plant metabolite)	>103.5 (48h)

It therefore follows that pre-flowering applications of sulfoxaflor are likely to show low risk to foraging honey bees. To investigate this assumption, pre-flowering applications of sulfoxaflor have been made to *Phacelia;* pollen and nectar have subsequently been collected from the crop when in flower and analysis of residues conducted. The effects of pre-flowering sulfoxaflor applications on the mortality and foraging activity of honey bees have also been investigated. This paper summarises the studies and provides a position on the acceptable risk to honey bees of pre-flowering sulfoxaflor applications.

2. Exposure of sulfoxaflor to bees in pollen and nectar following pre-flowering applications

A semi-field study has been conducted to investigate the residues of sulfoxaflor, and the main plant metabolite X11719474, in pollen, nectar and plants following application to *Phacelia* (Liepold, 2011[17]). A 120 g/L SC sulfoxaflor formulation (GF-2626) was applied at 24 and 48 g a.s./ha (T1 and T2) before the onset of flowering (BBCH 58) in three replicate tunnels. In separate tunnels GF-2626 was applied at 24 and 48 g a.s./ha (T3 and T4) during flowering (BBCH 64) and honey bee foraging. In order to evaluate the magnitude of residues of the test item GF-2626 and metabolite X11719474, nectar stomachs from forager bees, pollen samples from pollen traps and plants of *Phacelia* were taken for analysis. Samples were taken on day 0 after the application and on days +5 and +6. A summary of the application and sampling regime is presented in the table below and a full study summary is provided in the Appendix.

Table 2: Timing of GF-2626 application and sampling for residue analysis

Activity	DAA*	Date
Application before flowering (T1 and T2) BBCH 58	-10	15 Jul 2010
Brood assessment	-7	18 Jul 2010
Set up of the colonies in the tunnels	-6	19 Jul 2010
Application during flowering and bee-flight (T3 and T4) BBCH 64	0	25 Jul 2010
1st sampling of forager bees, pollen from pollen traps and whole plants	0	25 Jul 2010
2nd sampling of forager bees, pollen from pollen traps and whole plants	+5	30 Jul 2010
3rd sampling of forager bees, pollen from pollen traps and whole plants	+6	31 Jul 2010

*DAA: Days after application during bee flight

Colonies are generally moved into the tunnel when the crop has started to flower, it can therefore be assumed that, in this particular study, the pre-flowering application was made 4 days before the start of flowering. Additionally, the 1st sampling of pollen and nectar for residue analysis was made 10 days after the pre-flowering application.

A summary of the sulfoxaflor and X11719474 residues found in nectar, pollen and plants is presented in Tables 3, 4 and 5 below.

Table 3: Results of nectar analysis

Timing	Treatment	Application rate (g a.s./ha)	Sulfoxaflor residues (mg/kg)	X11719474 residues (mg/kg)
0 DAA	C	-	nd	nd
			nd	nd
			nd	nd
	T1	24	nd	nd
			nd	nd
			nd	nd
	T2	48	nd	nd
			nd	nd
			nd	nd

[17] Liepold, K. (2011). GF-2626: A semi-field study to investigate residues in honeybee products (*Apis mellifera carnica* L.; Hymenoptera, Apidae) in *Phacelia tanacetifolia* in Germany in 2010. Dow AgroSciences internal report no. 2009317.

	T3	24	0.0438	nd
			0.0462	nd
			0.0424	nd
	T4	48	0.0889	nd
			0.0548	nd
			0.0503	nd
5 DAA	C	-	nd	nd
			nd	nd
			nd	nd
	T1	24	nd	nd
			nd	nd
			nd	nd
	T2	48	nd	nd
			nd	nd
			nd	nd
	T3	24	<LOQ (0.005)	nd
			<LOQ (0.005)	nd
			<LOQ (0.004)	nd
	T4	48	0.0106	nd
			0.0110	nd
			0.0111	nd
6 DAA	C	-	nd	nd
			nd	nd
			nd	nd
	T1	24	nd	nd
			nd	nd
			nd	nd
	T2	48	nd	<LOQ (0.004)
			nd	<LOQ (0.004)
			nd	<LOQ (0.004)
	T3	24	<LOQ (0.004)	nd
			<LOQ (0.004)	nd
			<LOQ (0.005)	nd
	T4	48	<LOQ (0.0097)	<LOQ (0.003)
			<LOQ (0.006)	<LOQ (0.004)
			<LOQ (0.008)	<LOQ (0.004)

DAA: days after application during bee flight
C: untreated; T1/T2/T3/T4: test item group 1/2/3/4
n.d.: not detected (residue value was less than 30% of the LOQ, 0.003 mg/kg)
Values between 0.003 mg/kg (30% of the LOQ) and 0.01 mg/kg (LOQ) are reported as < LOQ

Table 4: Results of pollen analysis

Timing	Treatment	Application rate (g a.s./ha)	Sulfoxaflor residues (mg/kg)	X11719474 residues (mg/kg)
0 DAA	C	-	nd	nd
	T1	24	nd	nd
	T2	48	<LOQ (0.005)	nd
	T3	24	0.290	nd
	T4	48	0.809	<LOQ (0.004)
5 DAA	C	-	nd	nd

Timing	Treatment	Application rate (g a.s./ha)	Sulfoxaflor residues (mg/kg)	X11719474 residues (mg/kg)
	T1	24	nd	nd
	T2	48	nd	nd
	T3	24	<LOQ (0.003)	nd
	T4	48	0.0191	nd
6 DAA	C	-	nd	nd
	T1	24	nd	nd
	T2	48	nd	<LOQ (0.004)
	T3	24	0.0160	nd
	T4	48	0.0325	nd

DAA: days after application during bee flight
C: untreated; T1/T2/T3/T4: test item group 1/2/3/4
n.d.: not detected (residue value was less than 30% of the LOQ, 0.003 mg/kg)
Values between 0.003 mg/kg (30% of the LOQ) and 0.01 mg/kg (LOQ) are reported as < LOQ

Table 5: Results of whole plant analysis

Timing	Treatment	Application rate (g a.s./ha)	Sulfoxaflor residues (mg/kg)	X11719474 residues (mg/kg)
0 DAA	C	-	Nd	nd
	T1	24	<LOQ (0.009/0.009)	<LOQ (0.004/0.003)
	T2	48	0.0342	<LOQ (0.006)
	T3	24	0.516	nd
	T4	48	1.48	<LOQ (0.009)
5 DAA	C	-	nd/nd	nd/nd
	T1	24	<LOQ (0.004/0.004)	<LOQ (0.005/0.005)
	T2	48	nd/nd	<LOQ (0.0099/0.00999)
	T3	24	0.0274	<LOQ (0.004)
	T4	48	0.0520	<LOQ (0.009)
6 DAA	C	-	Nd	nd
	T1	24	Nd	<LOQ (0.009)
	T2	48	Nd	0.0113
	T3	24	0.0480	<LOQ (0.007)
	T4	48	0.0507	nd

DAA: days after application during bee flight
C: untreated; T1/T2/T3/T4: test item group 1/2/3/4
n.d.: not detected (residue value was less than 30% of the LOQ, 0.003 mg/kg)
Values between 0.003 mg/kg (30% of the LOQ) and 0.01 mg/kg (LOQ) are reported as < LOQ

The results show that, when applications of GF-2626 at 24 and 48 g a.s./ha were made 4 days before flowering, residues of sulfoxaflor and X11719474 were not detectable or were below the LOQ in pollen and nectar samples taken during full flowering. Additionally, following applications of GF-2626 during flowering, low levels of sulfoxaflor and X11719474 were present in nectar (maximum of 0.0889 mg/kg of sulfoxaflor), and these levels rapidly declined to be below the level of quantification in nectar at 6 days after application. In pollen, levels were slightly higher (maximum of 0.809 mg/kg) but also declined rapidly to 0.0325 mg/kg, when applied at 48 g a.s./ha. From this study it can be concluded that residues of sulfoxaflor are not persistent in plant material, and that honey bees will not be exposed to residues of sulfoxaflor in pollen and nectar following pre-flowering applications.

3. Effects of pre-flowering applications on bees

Two semi-field tunnel trials have been conducted to investigate the effects of applying sulfoxaflor before flowering on honey bees foraging on *Phacelia* in tunnels (Schmitzer, 2011a[18] and 2011b[19]). In both studies, a 120 g/L SC sulfoxaflor formulation (GF-2626) was applied to the crop before flowering at 48 g a.s./ha in three replicate tunnels. Five days after the application, bees were introduced to the tunnels as the crop started flowering and the exposure period lasted 10 days. Mortality, foraging activity, condition of the colonies and development of the brood was assessed until the end of the trial. In one trial 2 reference tunnels were used with fenoxycarb applied at 300 g a.s./ha and dimethoate applied at 600 g a.s./ha in separate tunnels, and in the second trial fenoxycarb was applied at 300 g a.s./ha. The results from both trials are summarised in Table 5 and 6 below.

[18] Schmitzer, S. (2011a). Study on the Effect of GF-2626 on Honey Bees and their Brood (*Apis mellifera* L.) under Semi-Field Conditions - Tunnel Test. Dow AgroSciences internal report no. 2009052.

[19] Schmitzer, S. (2011b). Study on the Effect of GF-2626 on Honey Bee Brood (*Apis mellifera* L.) under Semi-Field Conditions - Tunnel Test. Dow AgroSciences internal report no. 2008981.

Table 5: Effects of sulfoxaflor on honey bees and their brood under semi-field conditions (trial 1)

Parameter	Treatment [1)]			
	Control	Pre-flowering GF-2626 (48 g a.s./ha)	Reference Item Insegar (0.3 kg a.s./ha)	Reference Item Perfekthion (0.6 kg a.s./ha)
Mean mortality of worker bees / colony / day [%] during				
pre-application phase [2)]	10.6	18.6 (n.s.)	12.8 (n.s.)	12.8 (n.s.)
exposure phase in the tunnels [2)]	20.4	29.2 (n.s.)	22.5 (n.s.)	164.1 (*)
phase outside the tunnels [3)]	2.5	2.6 (n.s.)	3.0 (n.s.)	5.9 (*)
overall after application	7.6	10.2 (n.s.)	8.5 (n.s.)	51.1 (*)
Total mortality of larvae and pupae [n] during				
pre-application phase [2)]	4	0 (n.s.)	5 (n.s.)	1 (n.s.)
exposure phase in the tunnels [2)]	7	5 (n.s.)	20 (n.s.)	1 (n.s.)
phase outside the tunnels [3)]	0	1 (n.s.)	97 (*)	0 (n.s.)
overall after application	7	6 (n.s.)	117 (*)	1 (n.s.)
Mean foraging activity / m² / colony / day [n] during				
pre-application phase	10.7	10.0 (n.s.)	7.3 (n.s.)	10.0 (n.s.)
exposure phase in the tunnels	14.3	12.9 (n.s.)	12.4 (n.s.)	0.5 (*)
Mean brood termination rate [%]	65.3	65.6 (n.s.)	98.6 (n.s.)	100.0 (n.s.)

1) Each with three tunnels (replicate)
2) mean number of dead honeybees per day and colony found in dead bee traps and on gauze strips in the tunnels
3) mean number of dead honeybees per day and colony found in dead bee traps, only
Statistic: Dunnett`s t-test (mortality, foraging activity, termination rate), α=0.05, one-sided greater or one-sided smaller (foraging activity, brood indices)
n.s. = not statistically significant compared to the control;* = statistically significant compared to the control

Table 6: Effects of sulfoxaflor on honey bees and their brood under semi-field conditions (trial 2)

Parameter	Treatment [1)]		
	Control	Pre-flowering GF-2626 (48 g a.s./ha)	Reference Item Insegar (0.3 kg a.s./ha)
Mean mortality of worker bees / colony / day [%] during			
pre-application phase [2)]	15.2	16.7 (n.s.)	15.4 (n.s.)
exposure phase in the tunnels [2)]	19.3	29.5 (n.s.)	19.3 (n.s.)
phase outside the tunnels [3)]	2.2	3.5 (n.s.)	2.7 (n.s.)
overall after application	7.1	11.0 (n.s.)	7.4 (n.s.)
Total mortality of larvae and pupae [n] during			
pre-application phase [2)]	0	0 (n.d.)	0 (n.d.)
exposure phase in the tunnels [2)]	2	0 (n.s.)	2 (n.s.)
phase outside the tunnels [3)]	0	5 (n.s.)	529 (*)
overall after application	2	5 (n.s.)	531 (*)
Mean foraging activity / m² / colony / day [n] during			
pre-application phase	13.0	12.9 (n.s.)	12.7 (n.s.)
exposure phase in the tunnels	25.0	22.1 (n.s.)	24.6 (n.s.)
Mean brood termination rate [%]	56.4	58.1 (n.s.)	98.1 (*)

1) each with three tunnels (replicate)
2) mean number of dead honeybees per day and colony found in dead bee traps and on gauze strips in the tunnels
3) mean number of dead honeybees per day and colony found in dead bee traps, only
Statistic: Dunnett`s t-test (mortality, foraging activity) or Student t-test (termination rate), α=0.05, one-sided greater (mortality and termination rate) or one-sided smaller (foraging activity, brood indices)
n.s. = not statistically significant compared to the control;* = statistically significant compared to the control;
n.d. = not determined

The results from both semi-field tunnel trials show there were no effects on mortality of worker bees, larvae and pupae from pre-flowering applications of sulfoxaflor at 48 g a.s./ha. The control mean brood termination rate in both trials was high making a conclusion on brood development difficult, but the toxic standards clearly had a significant effect and sulfoxaflor was similar to the control, thus implying that if sulfoxaflor affected the brood it would have been identified in the study.

4. Conclusions

Sulfoxaflor is not persistent in plant material or soil, having a mean DT_{50} in plants of 7.5 days and a maximum field DT_{50} in soil of 7.4 days. The short persistence of sulfoxaflor is evident in the field work conducted to investigate the risk of pre-flowering applications to honey bees. Residues were not detected (or were below the limit of quantification) in the pollen and nectar of flowering crops following an application of sulfoxaflor made 4 days before the onset of flowering. The negligible exposure therefore means that subsequent risk to foraging bees will also be low. This has been confirmed in tunnel trials conducted in *Phacelia* that showed pre-flowering applications of sulfoxaflor at 48 g a.s./ha had no effect on honey bee mortality, foraging activity and development of brood.

Study Comments: IIIA 10.4.7/05	It is concluded that the risk to honeybees is acceptable when the product is applied before flowering. Pre-flowering application made 5 days before flowering is considered sufficiently protective by ZRMS.
Agreed Endpoints: IIIA 10.4.7/05	-

IIIA 10.5 Effects on Arthropods Other Than Bees

GF-2372 was one of the representative formulations in the EU review of sulfoxaflor. However new risk assessment parameters are now considered in the assessment of risk to non-target arthropods and hence an appropriate risk assessment with the proposed use pattern is provided and is considered adequate.

The critical endpoints employed in the risk assessment for non-target arthropods are indicated in the table below.

Table 10.5-1: EU Endpoints - Toxicity of GF-2372 to arthropods other than bees

Compound	Test species	Test substrate	EU agreed endpoints*	
Laboratory study				
GF-2372	*Aphidius rhopalosiphi*	Glass plate	Mortality: LR_{50} = 0.0062 g a.s./ha	
GF-2372	*Typhlodromus pyri*	Glass plate	Mortality: LR_{50} > 384 g a.s./ha	
Extended laboratory study				
GF-2372	*Aphidius rhopalosiphi*	Barley seedlings	Mortality: LR_{50} = 1.95 g a.s./ha Reproduction: ER_{50} = 1.0 g a.s./ha	
GF-2032	*Aleochara bilineata*	Sandy soil	Mortality: LR_{50} > 24 g a.s./ha Reproduction: ER_{50} > 24 g a.s./ha	
GF-2626	*Chrysoperla carnea*	*Phaseolus vulgaris* leaf discs	Mortality: LR_{50} > 48 g a.s./ha Reproduction: ER_{50} > 48 g a.s./ha	
Aged residue study				
GF-2372	*Aphidius rhopalosiphi*	Barley seedlings	0 DAT 96 48 14 7 DAT 96 48 14 14 DAT 96 48 14 21 DAT 96 48 28 DAT 96 7 DAT 96 48 14 14 DAT 96 48 14 21 DAT 96 48 28 DAT	Corrected mortality: 100 100 100 93 83 47 77 47 30 65 35 21 Corrected reproduction: - - 15.8 - 7.7 3.7 - -15.5

			96 mL GF-2372/ha	10.8
Field or semi-field tests				
GF-2372	**Cereal field test - S.W. France** GF-2372 applied once at a rate of 24 or 48 g sulfoxaflor/ha, or twice at 24 g sulfoxaflor/ha with a spray interval of 21 days, induced moderate and transient but statistically significant adverse effects on populations of certain orders (mainly Homopetera, Hymenoptera and few Diptera and Collembola). Recovery was seen for all these taxa within one or two months after the first application. There was no clear differentiation in effects related to test rate or application frequency. For few hymenopteran taxa the recovery period was slightly longer in the 2 x 24 g sulfoxaflor/ha rate. One mite taxon (Stigmaeidae) showed a delayed but persistent adverse effect in the 2 x 24 g sulfoxaflor/ha treatment, but differences compared to the control were statistically significant only on one sampling moment (*ca.* 3 months after the second application). These findings were confirmed by community analyses, although the observed responses of the arthropod communities were not statistically significant for any of the GF-2372 treatments tested. Based on De Jong *et al.* (2010), the effect of one application of GF-2372 at 24 or 48 g Sulfoxaflor/ha, or two applications at 24 g sulfoxaflor/ha in a commercial cereal field in Southern Europe (France), would be classified as 3 (clear response of taxa, but full recovery within two months after the first application for all but one taxon, full recovery of the community within two months after the first application). Hence, no sustained adverse effects on arthropod communities prevailing in a commercial cereal field in Southern Europe (France) are likely to occur, when GF-2372 (active ingredient sulfoxaflor) is applied at rates of up to 48 g sulfoxaflor/ha.			
GF-2372	**Cereal field test - the Netherlands** GF-2372 applied once at a rate of 24 or 48 g sulfoxaflor/ha, or twice at 24 g sulfoxaflor/ha with a spray interval of 22 days, induced moderate but statistically significant adverse effects on populations of certain orders (mainly Homopetera, Diptera, Hymenoptera and Collembola), but recovery was seen for almost all these taxa within one or two months after the first application. There was usually no clear differentiation in effects related to test rate or application frequency. For few hymenopteran taxa the recovery period was slightly longer in the 2 x 24 g sulfoxaflor/ha rate. Stronger effects were observed on aphids and a few associated specialist predators (Coccinellidae) and parasitoids (e.g. Aphelinidae). Aphid populations recovered within one month after application, before natural decline (migration). Related predators and parasitoids also disappeared from the field. It is expected that adverse effects observed for the specialist predators and parasitoids were at least partly due to indirect effects of reduced host availability. Multivariate analyses confirmed that recovery of the entire community occurred within approximately two months after the first application in all three GF-2372 treatments. Based on De Jong *et al.* (2010), the effect of one application of GF-2372 at 24 or 48 g Sulfoxaflor/ha, or two applications at 24 g sulfoxaflor/ha in a commercial cereal field in Northern Europe (The Netherlands), would be classified as 3 (clear response of taxa, but full recovery within two months after the first application). Hence, no sustained adverse effects on arthropod communities prevailing in a commercial cereal field in Northern Europe (The Netherlands) are likely to occur, when			

	GF-2372 (active ingredient Sulfoxaflor) is applied at rates of up to 48 g sulfoxaflor/ha.
GF-2626	**NTA off-field test - S.W, France** The impact of simulated drift events on arthropod populations and communities typical of grassy field margins in Southern Europe was evaluated for GF-2626 at exposures equivalent to 0.3, 0.6, 1.2, 2.4, 4.8 and 9.6 g sulfoxaflor/ha. At the community level no consistent rate related response was noted. For some test item rates faint and transient responses could be observed, but the magnitude was not related to the dose rate. At the population level no consistent dose related adverse effects from GF-2626 treatments were found, except for the collembolan taxon Bourletiellidae and for aphids. In all rates populations of the family Bourletiellidae were recovered within one or two months after application. Hence, no sustained adverse effects on arthropod communities prevailing in grasslands in South-West France are likely to occur, when GF-2626 (active ingredient sulfoxaflor) is applied at rates of up to 9.6 g sulfoxaflor/ha.

* EFSA Journal 2014; 12(5):3692

Risk Assessment for Arthropods other than Bees

The risk assessment for non-target arthropods for GF-2372 is based on two applications at a maximum rate of 48 g product/ha (equivalent to 24 g a.s./ha) for non-target arthropod populations present in the in-field area. Another area of risk is to non-target arthropod populations present in the off-field area where these species are exposed to spray drift at the time of application.

First tier risk assessment

A risk assessment for these scenarios may be conducted using the Hazard Quotient approach in ESCORT 2 (Guidance Document on Terrestrial Ecotoxicology: SANCO/10329/2002).

From the results in Table 10.5-1, the LR_{50} values for GF-2372 to the indicator species *T. pyri* and *A. rhopalosiphi*, under laboratory conditions, were estimated to be >384 and 0.0062 g a.s./ha, respectively. These values will be taken to represent the realistic worst case endpoints for non-target arthropods exposed to GF-2372. The risk assessment is presented in the table below.

Table 10.5-3: Risk to non-target arthropods from applications of GF-2372 – laboratory data

Scenario	Species	Exposure (g a.s./ha) *	Correction factor	VDF	LR_{50} (g a.s./ha)	HQ
In-field	*T. pyri*	40.8	N/A	N/A	>384	<0.11
	A. rhopalosiphi	40.8	N/A	N/A	0.0062	**6581**
Off-field, spray drift at 1 m (2.38%)	*T. pyri*	0.971	10	10	>384	<0.003
	A. rhopalosiphi	0.971	10	10	0.0062	**157**

N/A: not applicable
VDF: Vegetation distribution factor
* Application rate = 2 x 24 g a.s./ha; MAF = 1.7
Note: Correction factor of 10 is applied to off-field exposure in HQ calculation to account for unknown species of greater sensitivity (ESCORT 2).
HQs shown in **bold** are greater than the trigger value of 2

The in-field and off-field HQs for *T. pyri* are below the trigger value of 2, indicating an acceptable risk, and no further testing is required on this species. The in-field and off-field HQs for *A. rhopalosiphi* are greater than the trigger value of 2, indicating the need for a higher tier risk assessment.

Higher tier risk assessment

Under ESCORT 2, given that for one indicator species the in-field and off-field first tier HQ of 2 has been breached, in addition to further higher tier testing with the standard 'Tier I' indicator species, two additional crop relevant species are required to be tested. This requirement has been addressed by providing details of extended laboratory studies with the standard indicator species *A. rhopalosiphi*, plus the foliar dwelling predator *Chrysoperla carnea* and the ground dwelling parasitoid *Aleochara bilineata*. It is noted that, the studies on *C. carnea* and *A. bilineata* were conducted with different formulations (GF-2626 and GF-2032, respectively). However, in line with the approach taken in the DAR (2013), since similar levels of toxicity to non-target arthropods were proved in the laboratory studies then the results for GF-2626 and GF-2032 can be extrapolated to GF-2372.

In addition, details have been provided for an aged residue study with *A. rhopalosiphi* and GF-2372, for two non-target arthropod field studies with GF-2372 conducted in cereals in south-west France and in Netherlands and a field study with GF-2626 simulating drift events on non-target arthropod communities of grassy field margins in south-west France.

Extended laboratory studies

The extended laboratory data for *A. rhopalosiphi*, *A. bilineata* and *C. carnea* have been used in a higher tier risk assessment.

Under ESCORT 2, lethal and sublethal effects in extended laboratory of ≥ 50% following exposure at predicted in-field and off-field exposure rates, indicate the need for a further

assessment of the impact on non-target arthropod populations. The in-field and off-field predicted exposure rates (PER) and corresponding risk assessment are presented in the table below.

Table 10.5-4: Risk to non-target arthropods from applications of GF-2372 – Extended laboratory data – lethal and sublethal effects

Species	Endpoints (g a.s./ha)	In-field		Off-field				
		PER (g a.s./ha)	Risk acceptable ?	Off-field spray drift	CF	VDF	PER (g a.s./ha)	Risk acceptable ?
A. rhopalosiphi	LR_{50} = 1.95 ER_{50} = 1	40.8 *	**N**	2.38% (1 m)	5	1	4.855	**N**
C. carnea	LR_{50} > 48 ER_{50} > 48		Y			10	0.486	Y
A. bilineata	LR_{50} > 24 ER_{50} > 24		**N**			10	0.486	Y

* Application rate = 2 x 24 g a.s./ha; MAF = 1.7
VDF: Vegetation distribution factor. Only included for studies with a 2-D exposure system
CF: Correction factor
Note: Correction factor of 5 is applied to off-field exposure to account for interspecies variability

By comparison of these values to the extended laboratory endpoints an unacceptable in-field and off-field risk is indicated to *A. rhopalosiphi* but acceptable off-field risk was indicated to the two crop relevant arthropods *C. carnea* and *A. bilineata*. An acceptable in-field risk was also indicated to *C. carnea*. However, an acceptable in-field risk could not be not concluded for *A. bilineata* as the product GF-2032 was not tested at a high enough rate, i.e. 24 g a.s./ha. This indicates that applications of GF-2372 may be harmful to certain sensitive groups of non-target arthropod. Consequently further consideration is necessary for both in-field and off-field communities of non-target arthropods.

Aged residue studies and field tests

Laboratory and extended laboratory toxicity studies determined *A. rhopalosiphi* to be the most sensitive (and the only adversely affected) tested species. These findings were confirmed by the results of the field studies.

Two field studies were conducted in cereals in south-west France and in Netherland using GF-2372, and another field study simulating drift events on non-target arthropod communities of grassy field margins was carried out in south-west France using GF-2626. Since similar levels of toxicity of GF-2626 and GF-2372 to NTA were proved in laboratory toxicity studies, an extrapolation of toxicity data may be made between the two formulations.

I) In-field risk assessment for NTA

Under ESCORT 2, lethal and sublethal effects in aged residue studies of ≤ 50% following exposure at predicted in-field and off-field exposure rates, indicate an acceptable risk. In an aged residue test on the most sensitive species, *A. rhopalosiphi*, carried out with GF-2372 at test rates representative of in-field exposure (48 and 24 g a.s./ha), less than 50% effects were noted on mortality and parasitism when aged for 21 days. In comparison with 100% mortality when exposed to freshly treated foliage, a distinct decline in potential adverse effects with time after treatment is demonstrated. These findings are also supported by the results of the cereals field studies.

Two field tests were conducted to investigate in-field effect on non-target arthropods in commercial cereal field. One test was located in the Netherlands and the other in south-west France. In both cases the test item was GF-2372 and was tested according to three different application scenarios. One treatment was applied twice with approximately a 3 week spray interval at a rate of 24 g a.s./ha. In addition two single application treatments were tested, at 24 g and at 48 g a.s./ha. The first applications for each test were performed in spring 2010 for all three treatment scenarios.

Effects were similar in both tests. GF-2372 applied once at a rate of 24 or 48 g a.s./ha, or twice at 24 g a.s/ha with a spray interval of 21 days, induced moderate and transient but statistically significant adverse effects on populations of certain orders (mainly Homopetera, Hymenoptera, Diptera and Collembola). Recovery was seen for all these taxa within one or two months after the first application. There was no clear differentiation in effects related to test rate or application frequency. For few hymenopteran taxa the recovery period was slightly longer in the 2 x 24 g a.s./ha rate. In the southern test one mite taxon (Stigmaeidae) showed a delayed but persistent adverse effect in the 2 x 24 g a.s./ha treatment, but differences compared to the control were statistically significant only on one sampling moment (*ca.* 3 months after the second application). This was not observed in the northern test. Stronger effects were observed on aphids and a few associated specialist predators (Coccinellidae) and parasitoids (e.g. Aphelinidae). Aphid populations recovered within one month after application, before natural decline (migration). Related predators and parasitoids also disappeared from the field. It is expected that adverse effects observed for the specialist predators and parasitoids were at least partly due to indirect effects of reduced host availability. Multivariate analyses confirmed that recovery of the entire community occurred within approximately two months after the first application in all three GF-2372 treatments for both tests.

Based on the results of two cereal field studies, and given the lack of persistence of effect from exposure to treated foliage (as demonstrated in the above mentioned aged residue studies with *Aphidius*), long-term adverse effects persisting to the following season are considered unlikely.

It is concluded that although the proposed use of sulfoxaflor may adversely affect some ‘in-field‘ non-target arthropod populations, such affects are unlikely to be long-term, and the potential for re-colonisation and recovery within a year was demonstrated.

II) Off-field risk assessment for NTA

The impact of simulated drift events on arthropod populations and communities typical of grassy field margins in Southern Europe was carried out with GF-2626 at exposures equivalent to 0.3,

0.6, 1.2, 2.4, 4.8 and 9.6 g sulfoxaflor/ha. At the community level no consistent rate related response was noted. For some test item rates faint and transient responses could be observed, but the magnitude was not related to the dose rate. At the population level no consistent dose related adverse effects from GF-2626 treatments were found, except for the collembolan taxon Bourletiellidae and for aphids. The aphids are target pest organisms for using of GF-2626, therefore the adverse effects are expected. In all rates populations of the family Bourletiellidae were recovered within one or two months after application. Moreover, the effects of GF-2626 on Collembola are covered by the field study on micro-arthropods, as well (see IIIA 10.6.4), that concluded a lack of adverse effects on micro-arthropod field community, including Collembola, after proposed uses of formulated sulfoxaflor.

In an aged residue test on the most sensitive species, *A. rhopalosiphi*, carried out with GF-2372 at test rates representative of off-field exposure 14 mL GF-2372/ha (7 g a.s./ha), less than 50% effects were noted on mortality and parasitism when aged for 7 days. In comparison with 100% mortality when exposed to freshly treated foliage, a distinct decline in potential adverse effects with time after treatment is demonstrated. These findings are in compliance with the results of the off-field study.

It is concluded that the risk to off-field communities of non-target arthropods due to applications of Sulfoxaflor is considered acceptable.

ZRMS conclusions:

According to ESCORT 2 guidance, no effects on arthropods in off-field areas are tolerated. Then, the study of Bakker, F. 2011 show potential adverse effects on some arthropods populations at the lower tested rate (0.3 g Sulfoxaflor/ha) with a recovery of two months..As states in the EFSA Journal of Sulfoxaflor “No sustained adverse effects on familylevels of arthropod communities prevailing in grasslands in South-West France are likely to occur, when GF-2626 (active ingredient Sulfoxaflor) is applied at rates of up to 9.6 g Sulfoxaflor/ha. Then, zRMS choose to use this endpoint as a NOAER = 9.6 g Sulfoxaflor/ha associated with an assessement factor.

An assessement factor of 3 is considered necessary to take into account

- the toxicity of the prepraration (HQ for *A. rhopalosiphi* = 6581),
- the fact that many arthropods populations observed in the study need a recovery period including Aphidiinae (these effects are not clearly dose related up to and including 2.4g a.s./ha).

The off-field risk assessement for non-target arthopods, based on the endpoint NOAER = 9.6 g Sulfoxaflor/ha corrected with a factor 3 is presented in the following table: .

Dose (g/ha)	Distance	Drift%	MAF*	Exposure	NOAER corr	HQ	Trigger
24	1/3 m	2.77	1.9	1.26	3.2	0.39	1

*As worst case a MAF soil by default is considered.

No vegetation distribution factor has been taking into account in the exposure calculation since the exposure in the off-field study is 3D and made on vegetalized fields.
Therefore, the off-risk assessement presented above is considered relevant for non vegetalized off-field areas.

The off-field risk to non-target arthopods is acceptable when GF-2372 is applied without mitigations measures for Cereals, Cotton and Oilseed rape.

IIIA 10.5.1 Using artificial substrates

The following *Aphidius rhopalosiphi* glass-plate toxicity study performed on GF-2372 was assessed in the EU review and is available in the DAR (2013) Annex B.9.

Report:	**IIIA 10.5.1/01, Stevens, J. (2011a)**
Title:	A rate-response laboratory test to determine the effects of GF-2372 on the parasitic wasp, *Aphidius rhopalosiphi* (Hymenoptera: Braconidae).
Document No:	Dow Study ID: 101320
Guidelines:	Mead-Briggs *et al.* (2000)
GLP	Yes

Study Comments: IIIA 10.5.1/01	Already reviewed in the EU DAR for Sulfoxaflor (2013).
Agreed Endpoints: IIIA 10.5.1/01	48-h LR_{50} = 0.0124 g GF-2372 /ha (nominally 6.2 mg Sulfoxaflor/ha)

The following *Typhlodromus pyri* glass-plate toxicity study performed on GF-2372 was assessed in the EU review and is available in the DAR (2013) Annex B.9.

Report:	**IIIA 10.5.1/02, Fallowfield, L. (2010b)**
Title:	A rate-response laboratory test to determine the effects of GF-2372 on the predatory mite, *Typhlodromus pyri* (Acari: Phytoseiidae).
Document No:	Dow Study ID: 101319
Guidelines:	Blümel *et al.* (2000)
GLP	Yes

Study Comments:	Already reviewed in the EU DAR for Sulfoxaflor (2013).

IIIA 10.5.1/02	
Agreed Endpoints: IIIA 10.5.1/02	7-day -LR50 > 768 g formulation/ha (equivalent to 384 g sulfoxaflor/ha) NOER = 768 g formulation/ha (equivalent to 384 g sulfoxaflor/ha)

IIIA 10.5.2 Extended laboratory studies

The following extended laboratory toxicity study with *Aphidius rhopalosiphi* performed on GF-2372 was assessed in the EU review and is available in the DAR (2013) Annex B.9.

Report:	**IIIA 10.5.2/01, Stevens, J. (2011b)**
Title:	A rate-response extended laboratory bioassay to determine the effects of GF-2372 on the parasitic wasp, *Aphidius rhopalosiphi* (Hymenoptera, Braconidae).
Document No:	Dow Study ID: 101916
Guidelines:	Mead-Briggs *et al.* (2009)
GLP	Yes

Study Comments: IIIA 10.5.2/01	Already reviewed in the EU DAR for Sulfoxaflor (2013).
Agreed Endpoints: IIIA 10.5.2/01	48-h LR_{50} =3.90 g product/ha

The following extended laboratory toxicity study with *Aleochara bilineata* performed on GF-2032 was assessed in the EU review and is available in the DAR (2013) Annex B.9.

Report:	**IIIA 10.5.2/02, Spincer, D. (2009)**
Title:	An extended laboratory test to determine the effects of fresh residues of GF-2032 on the rove beetle, *Aleochara bilineata* (Coleoptera; Staphylinidae).
Document No:	Dow Study ID: 080089
Guidelines:	Grimm *et al.* (2000)
GLP	Yes

Study Comments: IIIA 10.5.2/02	Already reviewed in the EU DAR for Sulfoxaflor (2013).
Agreed Endpoints: IIIA 10.5.2/02	LR_{50} >100 mL GF-2032/ha, ER_{50} of >100 mL GF- 2032/ha (equivalent to 24 g sulfoxaflor/ha)

The following extended laboratory toxicity study with *Chrysoperla carnea* performed on GF-2626 was assessed in the EU review and is available in the DAR (2013) Annex B.9.

Report:	**IIIA 10.5.2/03, Spincer, D. (2011)**
Title:	A rate-response extended laboratory test to determine the effects of GF-2626 on the green lacewing, *Chrysoperla carnea* (Neuroptera, Chrysopidae).
Document No:	Dow Study ID: 101310;
Guidelines:	Vogt *et al.* (2000)
GLP	Yes

Study Comments: IIIA 10.5.2/03	Already reviewed in the EU DAR for Sulfoxaflor (2013).
Agreed Endpoints: IIIA 10.5.2/03	LR_{50} >400 mL GF-2626/ha (equivalent to 48 g sulfoxaflor/ha)

Aged residue study

The following aged residue study with *Aphidius rhopalosiphi* performed on GF-2372 was assessed in the EU review and is available in the DAR (2013) Annex B.9.

Report:	**IIIA 10.5.2/04, Stevens, J. (2011c)**
Title:	An aged-residue extended laboratory test to determine the effects of GF-2372 on the parasitic wasp, *Aphidius rhopalosiphi* (Hymenoptera, Braconidae).
Document No:	Dow Study ID: 101990
Guidelines:	Mead-Briggs *et al.* (2009)
GLP	Yes

Study Comments: IIIA 10.5.2/04	Already reviewed in the EU DAR for Sulfoxaflor (2013).
Agreed Endpoints: IIIA 10.5.2/04	The effects of both fresh and field-aged foliar residues of GF-2372 on the parasitic wasp, *Aphidius rhopalosiphi*, were evaluated under extended laboratory test conditions. Although fresh residues of GF-2372 were harmful to the test insects at treatment rates of 14, 48 and 96 g GF-2372 /ha, the aged residues showed a clear decline in effects over time. At a treatment rate of 14 g GF-2372 /ha, residues were no longer unacceptable by 7 days after treatment. At a treatment rate of 48 g GF-2372 /ha, residues were no longer unacceptable by 14 days after treatment. At a treatment rate of 96 g GF-2372 /ha, residues were no longer unacceptable by 28 days after treatment.

IIIA 10.5.3 Semi-field tests

No semi-field data submitted.

IIIA 10.5.4 Field tests

The following field test performed on GF-2626 in SW France was assessed in the EU review and is available in the DAR (2013) Annex B.9.

Report:	**IIIA 10.5.4/01, Bakker, F. (2011)**
Title:	A "terrestrial mesocosm study" to assess the effects of GF-2626 (a 12 % SC formulation of Sulfoxaflor) on the non-target, surface- and plant-dwelling arthropod fauna of a grassland habitat in SW France, when exposed to low concentrations during spring.
Document No:	Dow Study ID: 101029;
Guidelines:	De Jong 2010 *et al.* (2010)
GLP	Yes

Study Comments: IIIA 10.5.4/01	Already reviewed in the EU DAR for Sulfoxaflor (2013)
Agreed Endpoints: IIIA 10.5.4/01	The reported study is GLP compliant and conducted to a standard study protocol without any significant deviation. The test results are in compliance with the guideline's validity criteria. It is acceptable for regulatory use. At the population level no consistent dose related adverse effects from GF-

	2626 treatments were found, except for the collembolan taxon Bourletiellidae and for aphids. The aphids are target pest organisms for using of GF-2626, therefore the adverse effects are expected. In all rates populations of the family Bourletiellidae were recovered within one or two months after application. Moreover, the effects of GF-2626 on Collembola are covered by the field study on micro-arthropods, as well (see B.9.7.1.2), that concluded a lack of adverse effects on micro-arthropod field community, including Collembola. Hence, no sustained adverse effects on arthropod communities prevailing in grasslands in South-West France are likely to occur, when GF-2626 (active ingredient Sulfoxaflor) is applied at rates of up to 9.6 g Sulfoxaflor/ha.

The following field test performed on GF-2372 in SW France was assessed in the EU review and is available in the DAR (2013) Annex B.9.

Report:	**IIIA 10.5.4/02, Roig, J. (2011)**
Title:	A field trial to determine the effects of GF-2372 (a 50% WG formulation of Sulfoxaflor) on the non-target arthropod fauna of arable land after one and two applications to a wheat crop South West France.
Document No:	Dow Study ID: 101030;
Guidelines:	IOBC (Hassan, 1992), Anonymous (1992), ESCORT (Barrett *et al.*, 1994), Brown (1998) and IOBC, BART and EPPO Joint Initiative (Candolfi et al., 2000), De Jong 2010 *et al.* (2010)
GLP	Yes

Study Comments: IIIA 10.5.4/02	Already reviewed in the EU DAR for Sulfoxaflor (2013)
Agreed Endpoints: IIIA 10.5.4/02	The reference item treatment (one application with dimethoate at 320 g a.s/ha and one application with lambdacyhalothrin at 40 g a.s./ha with a 21 day spray interval) induced severe and statistically significant effects on populations in all arthropod orders. At the end of the season the community as a whole had recovered, but at the population level some adverse effects persisted throughout the sampling period until spring next season. GF-2372 applied once at a rate of 24 or 48 g Sulfoxaflor/ha, or twice at 24 g Sulfoxaflor/ha with a spray interval of 21 days, induced moderate and transient but statistically significant adverse effects on populations of certain orders (mainly Homoptera, Hymenoptera and few Diptera and

	Collembola). Recovery was seen for all these taxa within one or two months after the first application. There was no clear differentiation in effects related to test rate or application frequency. For few hymenopteran taxa the recovery period was slightly longer in the 2 x 24 g Sulfoxaflor/ha rate. One mite taxon (Stigmaeidae) showed a delayed but persistent adverse effect in the 2 x 24 g Sulfoxaflor/ha treatment, but differences compared to the control were statistically significant only on one sampling moment (ca 3 months after the second application). These findings were confirmed by community analyses, although the observed responses of the arthropod communities were not statistically significant for any of the GF-2372 treatments tested. It is concluded, that no sustained adverse effects on arthropod communities prevailing in a commercial cereal field in Southern Europe (France) are likely to occur, when GF-2372 (active ingredient Sulfoxaflor) is applied at rates of up to 48 g Sulfoxaflor/ha.

The following field test performed on GF-2372 in the Netherlands was assessed in the EU review and is available in the DAR (2013) Annex B.9.

Report:	**IIIA 10.5.4/03, Bakker, F. (2011)**
Title:	A field trial to determine the effects of GF-2372 (a 50% WG formulation of Sulfoxaflor) on the non-target arthropod fauna of arable land after one and two applications to a wheat crop in the Netherlands
Document No:	Dow Study ID: 101031
Guidelines:	IOBC (Hassan, 1992), Anonymous (1992), ESCORT (Barrett et al., 1994), Brown (1998) and IOBC, BART and EPPO Joint Initiative (Candolfi et al., 2000), De Jong 2010 *et al.* (2010)
GLP	Yes

Study Comments: IIIA 10.5.4/03	Already reviewed in the EU DAR for Sulfoxaflor (2013)
Agreed Endpoints: IIIA 10.5.4/03	The reference item treatment (one application with dimethoate at 320 g a.s/ha and one application with lambdacyhalothrin at 40 g a.s./ha with a 21 day spray interval) induced severe and statistically significant effects on populations in all arthropod orders. At the end of the season the community as a whole had recovered, but at the population level some adverse effects

	persisted throughout the sampling period until spring next season. GF-2372 applied once at a rate of 24 or 48 g Sulfoxaflor/ha, or twice at 24 g Sulfoxaflor/ha with a spray interval of 21 days, induced moderate and transient but statistically significant adverse effects on populations of certain orders (mainly Homoptera, Hymenoptera and few Diptera and Collembola). Recovery was seen for all these taxa within one or two months after the first application. There was no clear differentiation in effects related to test rate or application frequency. For few hymenopteran taxa the recovery period was slightly longer in the 2 x 24 g Sulfoxaflor/ha rate. One mite taxon (Stigmaeidae) showed a delayed but persistent adverse effect in the 2 x 24 g Sulfoxaflor/ha treatment, but differences compared to the control were statistically significant only on one sampling moment (ca 3 months after the second application). These findings were confirmed by community analyses, although the observed responses of the arthropod communities were not statistically significant for any of the GF-2372 treatments tested. It is concluded, that no sustained adverse effects on arthropod communities prevailing in a commercial cereal field in Southern Europe (France) are likely to occur, when GF-2372 (active ingredient Sulfoxaflor) is applied at rates of up to 48 g Sulfoxaflor/ha.

IIIA 10.6 Effects on Earthworms and Other Soil Non-target Macro-organisms

Overall summary

GF-2372 was one of the representative formulations in the EU review of sulfoxaflor. However new risk assessment parameters are now considered in the assessment of risk to earthworms and soil macro-organisms and hence an appropriate risk assessment with the proposed use pattern is provided and is considered adequate. The risk assessment has been conducted in line with the Terrestrial Guidance Document (SANCO/10329/2002, rev. 2 final).

The critical endpoints employed in the risk assessment for earthworms and other soil non-target organisms are indicated in the tables below.

Table 10.6-1: EU Endpoints - Toxicity of sulfoxaflor and relevant soil metabolites X11719474 and X11519540 to earthworms and soil macro-organisms

Compound	Test species	Test design	EU agreed endpoints* (mg/kg soil)
Earthworms			
Sulfoxaflor	*Eisenia fetida*	acute, 14 days (10% peat in test soil)	**LC_{50} = 0.885**
X11719474		acute, 14 days (10% peat in test soil)	**LC_{50} >1000****
Sulfoxaflor	*Eisenia fetida*	chronic, 56 days (10% peat in test soil)	**NOEC = 0.1**
X11719474		chronic, 56 days (10% peat in test soil)	**NOEC = 10****
X11519540		chronic, 56 days (10% peat in test soil)	**NOEC = 10****
Other soil non-target organisms			
X11719474	*Folsomia candida*	chronic, 28 d (5% peat in test soil)	**NOEC = 10****
X11519540			**NOEC = 10****
X11519540	*Hypoaspis aculeifer*	chronic, 14 d (5% peat in test soil)	**NOEC = 10****

* EFSA Journal (2014); 12(5):3692
** The highest concentration tested.
Endpoints used in the risk assessment are in **bold**.
The EPPO correction factor (2) does not need to be applied to the endpoints as the log Pow of sulfoxaflor is < 2

The available data for GF-2372 are summarised in the following table.

Table 10.6-2: EU Endpoints - Toxicity of GF-2372 to earthworms and soil macro-invertebrates

Compound	Test species	Test design	EU agreed endpoints*
GF-2372	*Eisenia foetida*	acute, 14 days (10% peat in test soil)	LC_{50} = 1.050 mg GF-2372/kg **LC_{50} = 0.525 mg Sulfoxaflor/kg**
	Eisenia foetida	chronic, 56 days (10% peat in test soil)	NOEC = 0.16 mg GF-2372/kg **NOEC = 0.08 mg Sulfoxaflor/kg**
	Folsomia candida	chronic, 28 d (5% peat in test soil)	NOEC = 0.16 mg GF-2372/kg **NOEC = 0.08 mg Sulfoxaflor/kg**
	Hypoaspis aculeifer	chronic, 14 d (5% peat in test soil)	NOEC = 6.25 mg GF-2372/kg **NOEC = 3.125 mg Sulfoxaflor/kg**

Field study on earthworms:

An earthworm field study was conducted to investigate effects of GF-2626 (SC formulation containing 120 g/L of Sulfoxaflor) and its metabolite X11719474 on the earthworm fauna in Southern Germany.

Three application scenario were used in the study:

T1: first application of 4.8 g/ha X11719474 (plateau concentration 1) plus second application of 24 g Sulfoxaflor/ha applied as GF-2626 after one week

T2: first application of 9.6 g/ha X11719474 (plateau concentration 2) plus a second application of 24 g Sulfoxaflor/ha applied as GF-2626 after one week plus a third application of 24 g Sulfoxaflor/ha applied as GF-2626 four weeks after the first application

T3: first application of 9.6 g/ha X11719474 (plateau concentration 2) plus a second application of 48 g Sulfoxaflor./ha applied as GF-2626 after one week.

All validity criteria were met due to the high earthworm abundance, the presence of key earthworm species of different ecological types (epigeic, endogeic and anecic) and the homogeneity in abundance and species distribution at the field site. The effect of the toxic reference treatment indicated the sensitivity of the earthworm population. The time of applications during high activity of earthworms and additional irrigation in the time after the application guaranteed the exposure of earthworms to the test item and the toxic reference item.

After application of GF-2626 and its metabolite X11719474 applied to field plots no adverse effects on total earthworm numbers occurred in any of the samplings. No significant reductions in numbers and weights of earthworm species, groupings or totals were found in any of the samplings.

Hence, no sustained adverse effects on an earthworm field community are likely to occur, when GF-2626 (active ingredient Sulfoxaflor) and its metabolite X11719474 are applied at rates of up to 48 g Sulfoxaflor/ha and 9.6 g X11719474/ha, respectively.

Field study on soil micro-arthropods:

A field study was conducted to assess possible effects of GF-2626 (SC formulation containing 120 g/L of Sulfoxaflor) and its metabolite X11719474 on soil living invertebrates (Collembola, Acari) under field conditions on a grassland in Southern Germany. For this purpose community composition and abundance of selected soil living invertebrates were monitored over the period of one year.

Three application scenario were used in the study:

T1: first application of 4.8 g/ha X11719474 (plateau concentration 1) plus second application of 24 g Sulfoxaflor/ha applied as GF-2626 after one week

T2: first application of 9.6 g/ha X11719474 (plateau concentration 2) plus a second application of 24 g Sulfoxaflor/ha applied as GF-2626 after one week plus a third application of 24 g Sulfoxaflor/ha applied as GF-2626 four weeks after the first application

T3: first application of 9.6 g/ha X11719474 (plateau concentration 2) plus a second application of 48 g Sulfoxaflor./ha applied as GF-2626 after one week.

After application of GF-2626 and its metabolite X11719474 applied to field plots no adverse effects on soil living micro-arthropod numbers occurred in any of the samplings. No significant or persistent treatment related reductions were observed in any of the test item treatment.

Hence, no sustained adverse effects on soil micro-arthropod field communities are likely to occur, when GF-2626 (active ingredient Sulfoxaflor) and its metabolite X11719474 are applied at rates of up to 48 g Sulfoxaflor/ha and 9.6 g X11719474/ha, respectively.

* EFSA Journal (2014); 12(5):3692
Endpoints used in the risk assessment are in **bold**.
The EPPO correction factor (2) does not need to be applied to the endpoints as the log Pow of sulfoxaflor is < 2

In accordance with the GAP, application to cereals, oilseed rape and cotton are considered for this risk assessment. PEC_{soil} values for sulfoxaflor and for its potentially relevant metabolites (X11719474 and X11519540) following applications to cereals, oilseed rape and cotton are summarised in Section 5, Points IIIA 9.4 and IIIA 9.5, respectively.

IIIA 10.6.1 Toxicity exposure ratios, TER_A and TER_{LT}

Acute risk

Acute toxicity exposure ratios (TERs) for the proposed uses of GF-2372 in cereals, oilseed rape and cotton are presented in Table 10.6.1-1.

Table 10.6.1-1: Acute TER values for earthworms

Test compound	Crop	LC_{50} (mg a.s./kg)	Maximum instantaneous PECsoil (mg a.s./kg)	TER_A	Trigger value
GF-2372	Cereals	0.525	0.019	27.6	10
Sulfoxaflor		0.885	0.019	46.6	
X11719474		> 1000	0.041	> 24390	
GF-2372	Oilseed rape	0.525	0.009	58.3	
Sulfoxaflor		0.885	0.009	98.3	
X11719474		> 1000	0.026	> 38462	
GF-2372	Cotton	0.525	0.019	27.6	
Sulfoxaflor		0.885	0.019	46.6	
X11719474		> 1000	0.027	> 37037	

All the acute TER values are higher than the acute trigger value of 10, indicating that GF-2372 poses an acceptable acute risk to earthworms when applied according to the proposed uses of GF-2372 on cereals, oilseed rape and cotton.

Long-term risk

Long-term toxicity exposure ratios (TERs) for the proposed uses of GF-2372 in cereals, oilseed rape and cotton are presented in Tables 10.6.1-2 and 10.6.1-3.

Table 10.6.1-2: Chronic TER values for earthworms

Substance	Crop	NOEC (mg a.s./kg)	Maximum PECsoil (mg a.s./kg)	TER_{LT}	Trigger value
GF-2372	Cereals	0.08	0.019 (max. initial)	**4.21**	5
Sulfoxaflor		0.1	0.019 (max. initial)	5.26	
X11719474		10	0.053 (plateau)	189	
X11519540		10	0.008 (plateau)	1250	
GF-2372	Oilseed rape	0.08	0.009 (max. initial)	8.89	
Sulfoxaflor		0.1	0.009 (max. initial)	11.1	
X11719474		10	0.035 (plateau)	286	
X11519540		10	0.005 (plateau)	2000	
GF-2372	Cotton	0.08	0.019 (max. initial)	**4.21**	
Sulfoxaflor		0.1	0.019 (max. initial)	5.26	
X11719474		10	0.035 (plateau)	286	
X11519540		10	0.005 (plateau)	2000	

TERs in **bold** are below the trigger value

The resulting TER_{LT} values for sulfoxaflor and its soil metabolites are above the trigger value of 5 indicating an acceptable chronic risk to earthworms. However, the TER_{LT} values for GF-2372 are below the trigger value of 5 for the proposed uses in cereals and cotton indicating a potential long-term risk to earthworms.

The results of the earthworm field study indicated a lack of adverse effects on earthworm field community under field conditions when GF-2626 (active ingredient sulfoxaflor) and its metabolite X11719474 are applied at rates of up to 48 g sulfoxaflor/ha and 9.6 g X11719474/ha, respectively. Since similar levels of toxicity of GF-2626 and GF-2372 to earthworms were proved in laboratory toxicity studies, an extrapolation of toxicity data may be made between the two formulations. Therefore, it can be concluded that the proposed uses of GF-2372 on cereals, oilseed rape and cotton pose an acceptable risk to earthworms.

Table 10.6.1-3: Chronic TER values for soil macro-organisms

Substance	Crop	NOEC (mg a.s./kg)	Maximum PECsoil (mg a.s./kg)	TER_{LT}	Trigger value
Folsomia candida					
GF-2372	Cereals	0.08	0.019 (max. initial)	**4.21**	5
X11719474		10	0.053 (plateau)	189	
X11519540		10	0.008 (plateau)	1250	
GF-2372	Oilseed rape	0.08	0.009 (max. initial)	8.89	
X11719474		10	0.035 (plateau)	286	
X11519540		10	0.005 (plateau)	2000	
GF-2372	Cotton	0.08	0.019 (max. initial)	**4.21**	
X11719474		10	0.035 (plateau)	286	
X11519540		10	0.005 (plateau)	2000	
Hypoaspis aculeifer					
GF-2372	Cereals	3.125	0.019 (max. initial)	165	5
X11519540		10	0.008 (plateau)	1250	
GF-2372	Oilseed rape	3.125	0.009 (max. initial)	347	
X11519540		10	0.005 (plateau)	2000	
GF-2372	Cotton	3.125	0.019 (max. initial)	165	
X11519540		10	0.005 (plateau)	2000	

TERs in **bold** are below the trigger value

The resulting TER_{LT} values for sulfoxaflor soil metabolites are above the trigger value of 5 indicating that these metabolites pose an acceptable chronic risk to both soil macro-organisms species. The TER_{LT} for exposure of *Hypoaspis aculeifer* to GF-2372 also demonstrates an acceptable risk. However, the TER_{LT} values exposure of *Folsomia candida* to GF-2372 are below the trigger value of 5 for the proposed uses in cereals and cotton indicating a potential long-term risk.

The results of the field study on soil micro-arthropods (Collembola, Acari) indicated a lack of adverse effects on soil micro-arthropod field communities under field conditions when GF-2626 (active ingredient sulfoxaflor) and its metabolite X11719474 are applied at rates of up to 48 g sulfoxaflor/ha and 9.6 g X11719474/ha, respectively. Since similar levels of toxicity of GF-2626 and GF-2372 to *Folsomia candida* were proved in laboratory toxicity studies, an extrapolation of toxicity data may be made between the two formulations. Therefore, it can be concluded that the proposed uses of GF-2372 on cereals, oilseed rape and cotton pose an acceptable risk to soil macro-organisms.

IIIA 10.6.2 Acute toxicity

The following acute toxicity study with earthworms performed on GF-2372 was assessed in the EU review and is available in the DAR (2013) Annex B.9.

Report:	**IIIA 10.6.2/01, McCormac, A. (2010)**
Title:	Determination of acute toxicity of GF-2372 to the earthworm *Eisenia fetida* in an artificial soil substrate.
Document No:	Dow Study ID: 101914
Guidelines:	OECD 207
GLP	Yes

Study Comments: IIIA 10.6.2/01	Already reviewed in the EU DAR for Sulfoxaflor (2013)
Agreed Endpoints: IIIA 10.6.2/01	The regulatory endpoint is a 14-day LC_{50} 1.050 mg GF-2372/kg soil dry weight, equivalent to 0.525 mg Sulfoxaflor/kg soil.

IIIA 10.6.3 Sublethal effects

The following chronic toxicity study with earthworms performed on GF-2372 was assessed in the EU review and is available in the DAR (2013) Annex B.9.

Report:	**IIIA 10.6.3/01, McCormac, A. (2011)**
Title:	Determination of chronic (sub-lethal) toxicity of GF-2372 to the earthworm *Eisenia fetida* in an artificial soil substrate.
Document No:	Dow Study ID: 101915
Guidelines:	OECD 222
GLP	Yes

Study Comments: IIIA 10.6.3/01	Already reviewed in the EU DAR for Sulfoxaflor (2013)
Agreed Endpoints: IIIA 10.6.3/01	Based on nominal concentrations, the regulatory endpoint is a 56-day NOEC = 0.16 mg GF-2372/kg soil dry weight (equivalent to 0.08 mg Sulfoxaflor/kg soil).

IIIA 10.6.4 Field tests

The following field study with earthworms performed on GF-2626 was assessed in the EU review and is available in the DAR (2013) Annex B.9.

Report:	**IIIA 10.6.4/01, Klein, O. (2012)**
Title:	Field Study to Evaluate the Effects of Sulfoxaflor (as GF-2626 12% SC formulation) and its primary soil metabolite X11719474 on Earthworms in Southern Germany.
Document No:	Dow Study ID: 110844
Guidelines:	Kula & Kula (1994 - BBA guideline for testing the effects of pesticides on earthworms in the field), ISO Guideline 11268-3 (1999), ISO Guideline 23611-1 (2006)
GLP	Yes

Study Comments: IIIA 10.6.4/01	Already reviewed in the EU DAR for Sulfoxaflor (2013)
Agreed Endpoints: IIIA 10.6.4/01	After application of GF-2626 and its metabolite X11719474 applied to field plots no adverse effects on total earthworm numbers occurred in any of the samplings. No significant reductions in numbers and weights of earthworm species, groupings or totals were found in any of the samplings. No sustained adverse effects on an earthworm field community are likely to occur, when GF-2626 (active ingredient Sulfoxaflor) and its metabolite X11719474 are applied at rates of up to 48 g Sulfoxaflor/ha and 9.6 g X11719474/ha, respectively**.**

IIIA 10.6.5 Residue content of earthworms

Based on the acceptable risk to earthworms following the proposed uses of GF-2372 and on the low bioaccumulation tendency of Sulfoxaflor, studies to determine the residue content of earthworms are not required.

IIIA 10.6.6 Effects on other non-target macro-organisms

Data on effects on soil macro-organisms other than earthworms are only required where the field DT_{90} is > 100 days.

The maximum field DT_{90f} for sulfoxaflor is estimated to be 24.68 days (Section 5, Point IIIA 9.1). Therefore, studies on the effects of sulfoxaflor on other non-target macro-organisms are not triggered because the DT_{90f} is less than 100 days.

For the relevant soil metabolites X11719474 and X11519540 the maximum field DT_{90f} values are 1279 and 3838 days, respectively (Section 5, Point IIIA 9.1). Given that the DT_{90f} is > 100 days the need to address effects on other non-target macro-organisms is triggered and collembola (*Folsomia candida*) reproductive toxicity studies and gammasid mite (*Hypoaspis aculeifer*) reproductive toxicity studies for these metabolites have been provided. A study on the effects of metabolite X11719474 on the soil mite *Hypoaspis aculeifer* was not submitted as a higher tier litter bag study had been carried out with GF-2626 and metabolite X11719474 (ref to Section IIIA 10.6.7).

The following reproductive toxicity studies with collembola (*Folsomia candida*) and gammasid mite (*Hypoaspis aculeifer*) performed on GF-2372 were assessed in the EU review and areavailable in the DAR (2013) Annex B.9.

Report:	**IIIA 10.6.6/01, Witte, B. (2011a)**
Title:	Effects of GF-2372 on Reproduction of the Collembola *Folsomia candida* in Artificial Soil with 5% Peat.
Document No:	Dow Study ID: 102002.
Guidelines:	OECD 232 (2009), ISO 11267 (1999)
GLP	Yes

Study Comments: IIIA 10.6.6/01	Already reviewed in the EU DAR for Sulfoxaflor (2013)
Agreed Endpoints: IIIA 10.6.6/01	The LC_{50} was determined to be 0.68 mg GF-2372/kg soil and the EC_{50} was determined to be 0.52 mg GF-2372/kg soil (equivalent to 0.26 mg Sulfoxaflor/kg soil). The regulatory endpoint is a 28-day NOEC for the reproduction 0.16 mg GF-2372/kg soil dry weight (equivalent to 0.08 mg Sulfoxaflor/kg - based on the analysed content of a.s.).

Report:	**IIIA 10.6.6/02, Witte, B. (2011b)**
Title:	GF-2372: Effects of GF-2372 on Reproduction of the Predatory Mite *Hypoaspis aculeifer* in Artificial Soil with 5% Peat.
Document No:	Dow Study ID: 101999
Guidelines:	Römbke et al. (2003), OECD 56 (2006)
GLP	Yes

Study Comments: IIIA 10.6.6/02	Already reviewed in the EU DAR for Sulfoxaflor (2013)
Agreed Endpoints: IIIA 10.6.6/02	The NOEC is determined to be 6.25 mg GF-2372/kg soil dry weight (equivalent to 3.125 mg Sulfoxaflor/kg).

The following study on micro-arthropod field community performed on GF-2626 and the metabolite X11719474 was assessed in the EU review and is available in the DAR (2013) Annex B.9.

Report:	**IIIA 10.6.6/03, Mack, P. (2012)**
Title:	Field Study to Evaluate the Effects of Sulfoxaflor (as GF-2626 12% SC formulation) and its primary soil metabolite X11719474 on Soil Micro-Arthropods in Southern Germany.
Document No:	Dow Study ID: 110845
Guidelines:	ISO Guideline 23611-2 (2006), OECD 56 (2006)
GLP	Yes

Study Comments: IIIA 10.6.6/03	Already reviewed in the EU DAR for Sulfoxaflor (2013)
Agreed Endpoints: IIIA 10.6.6/03	After application of GF-2626 and its metabolite X11719474 applied to field plots no adverse effects on soil living micro-arthropod numbers occurred in any of the samplings. No significant or persistent treatment related reductions were observed in any of the test item treatment. Hence, no sustained adverse effects on soil microarthropod field communities are likely to occur, when GF-2626 (active ingredient Sulfoxaflor) and its metabolite X11719474 are applied at rates of up to 48 g Sulfoxaflor/ha and 9.6 g X11719474/ha, respectively.

IIIA 10.6.7 Effects on organic matter breakdown

Data on the impact on soil organic matter breakdown are only required where the field DT_{90} is >365 days.

The maximum field DT_{90f} for sulfoxaflor is estimated to be 24.68 days (Section 5, Point IIIA 9.1). Therefore, studies on the effects of sulfoxaflor on organic matter breakdown are not triggered because the DT_{90f} is less than 100 days.

For the relevant soil metabolites X11719474 and X11519540 the maximum field DT_{90f} values are 1279 and 3838 days, respectively (Section 5, Point IIIA 9.1). Given the high soil persistence of the metabolites X11719474 and X11519540 (DT_{90s} > 365 days), data on the impact on organic matter breakdown are required. A litter bag study carried out with GF-2626 and metabolite X11719474 has been submitted. Since no impact on the organic matter breakdown was determined in this study (conducted up to 48 g sulfoxaflor/ha plus 9.6 g X11719474/ha), and given no effects of the metabolite X11519540 on the reproduction of Collembola and gammasid mites were reported, no further studies are needed.

The following study on effects on organic matter breakdown performed on GF-2626 and the metabolite X11719474 was assessed in the EU review and is available in the DAR (2013) Annex B.9.

Report:	**IIIA 10.6.7/01, Mack, P. (2011)**
Title:	Field Study to Evaluate the Effects of Sulfoxaflor (as GF-2626 12% SC formulation) and its primary soil metabolite X11719474 on the Decomposition of Organic Matter in the Field.
Document No:	Dow Study ID: 110602
Guidelines:	"EPFES" workshop, Lisbon, April 2002 (RÖMBKE et al. 2003), OECD 56 (2006)
GLP	Yes

Study Comments: IIIA 10.6.7/01	Already reviewed in the EU DAR for Sulfoxaflor (2013)
Agreed Endpoints: IIIA 10.6.7/01	Sulfoxaflor (as GF-2626) and its metabolite X11719474 had no adverse effects on the breakdown of buried organic material (straw) compared to a water treated control after exposure of about 1, 3, 6 and 9 months

IIIA 10.7 Effects on Soil Microbial Activity

Overall summary

Effects on soil microbial activity of GF-2372 were evaluated as part of the EU review of sulfoxaflor. An appropriate risk assessment has been conducted in line with the Terrestrial Guidance Document (SANCO/10329/2002, rev. 2 final) and is considered adequate.

The endpoints employed in the risk assessment for effects on soil microbial activity are indicated in Table 10.7-1.

Table 10.7-1: EU Endpoints – Effects of sulfoxaflor, GF-2372 and relevant soil metabolites on soil microbial activity

Compound	Test type	EU agreed endpoints*
Sulfoxaflor	N transformation	< 25 % effect at day 28 at 0.33 mg a.s./kg d.w. soil (240 g a.s./ha)
	C transformation	< 25 % effect at day 28 at 0.33 mg a.s./kg d.w. soil (240 g a.s./ha)
GF-2372	N transformation	< 25 % effect at day 28 at 0.32 mg prep./kg d.w. soil 0.16 mg a.s./kg d.w. soil (120 g a.s./ha)
	C transformation	< 25 % effect at day 28 at 0.32 mg prep./kg d.w. soil 0.16 mg a.s./kg d.w. soil (120 g a.s./ha)
X11719474	N transformation	< 25 % effect at day 28 at 0.16 mg a.s./kg d.w. soil (120 g a.s./ha)
	C transformation	< 25 % effect at day 28 at 0.16 mg a.s./kg d.w. soil (120 g a.s./ha)
X11519540	N transformation	< 25 % effect at day 28 at 0.32 mg a.s./kg d.w. soil (240 g a.s./ha)
	C transformation	< 25 % effect at day 28 at 0.32 mg a.s./kg d.w. soil (240 g a.s./ha)

* EFSA Journal (2014); 12(5):3692

In accordance with the GAP, application to spring cereals is used as worst case scenario. PEC_{soil} values for sulfoxaflor and for metabolites (X11719474 and X11519540) following applications to spring cereals (worst-case scenario) are summarised in Section 5, Points IIIA 9.4 and IIIA 9.5, respectively.

Conclusion

TERs are summarised in Table 10.7-2.

Table 10.7-2: Minimum TERs for soil microbial activity after use of GF-2372 in cereals (worst-case scenario)

Substance	Test type	Timescale	Maximum PECsoil (mg/kg soil)	NOEC (mg/kg soil)	TER
GF-2372	N transformation	28 days	0.019 (max. initial)	0.16	8.42
	C transformation	28 days			
Sulfoxaflor	N transformation	28 days	0.019 (max. initial)	0.33	17.4
	C transformation	28 days			
X11719474	N transformation	28days	0.053 (plateau)	0.16	3.02
	C transformation	28 days			
X11519540	N transformation	28 days	0.008 (plateau)	0.32	40.0
	C transformation	28 days			

The TER values are all above 1, indicating that the predicted environmental concentrations of GF-2372, Sulfoxaflor and the metabolites X11719474 and X11519540 from the proposed uses of GF-2372 in cereals, oil seed rape and cotton will have no unacceptable effects on soil microorganisms.

IIIA 10.7.1 Laboratory testing

The following soil microbial toxicity study performed on GF-2372 was assessed in the EU review and is available in the DAR (2013) Annex B.9.

Report:	**IIIA 10.7.1/01, Feil, N. (2011)**
Title:	Effects of GF-2372 on the Activity of the Soil Microflora in the Laboratory
Document No:	Dow Study ID: 101317
Guidelines:	OECD 216, 217
GLP	Yes

Study Comments: IIIA 10.7.1/01	Already reviewed in the EU DAR for Sulfoxaflor (2013)
Agreed Endpoints: IIIA 10.7.1/01	The results indicate a lack of adverse effects on soil microbial respiration and nitrogen transformation at the maximum test dose of 0.32 mg GF-2372/kg soil dry weight (corresponding to the application rate of 240 g GF-2372/ha, i.e. 120 g Sulfoxaflor/ha).

IIIA 10.7.2 Additional testing

No additional studies with GF-2372 are required.

IIIA 10.8 Effects on Non-Target Plants

IIIA 10.8.1 Terrestrial plants

Overall summary

GF-2372 was the one of the representative formulations in the EU review of sulfoxaflor. However new risk assessment parameters are now considered in the assessment of risk to terrestrial plants and hence an appropriate risk assessment with the proposed use pattern is provided and is considered adequate. The risk assessment has been conducted in line with the Terrestrial Guidance Document (SANCO/10329/ 2002, rev. 2 final).

The critical endpoints employed in the risk assessment for non-target plants are indicated in the table below.

Table 10.8.1-1: EU Endpoints - Toxicity of GF-2372 to terrestrial non-target plants

Compound	Most sensitive species	Endpoint	EU agreed endpoints*
GF-2372	All plant species tested	Vegetative vigour	ER_{50} > 150 g a.s./ha**
GF-2372	All plant species tested	Seedling emergence	ER_{50} > 150 g a.s./ha**

* EFSA Journal (2014); 12(5):3692
** The highest rate tested

Sulfoxaflor is not a herbicide, nor shows phytotoxic or growth regulating effects. The non-target plant study carried out with GF-2372 indicates that no significant adverse effects on 11 species of non-target plants were observed at a nominal application rate of up to 150 g Sulfoxaflor/ha (formulated as GF-2372) in seedling emergence and vegetative vigour tests. The maximum field single application rate proposed for GF-2372 is 24 g sulfoxaflor/ha. Since there is no data indicating > 50 % phytotoxic effects on any test species at the maximum application rate a an acceptable risk to non-target plants can be concluded for the uses of GF-2372 on cereals, oil seed rape and cotton.

Conclusion

An acceptable risk to non-target terrestrial plants has been demonstrated for the proposed uses of GF-2372 on cereals, oil seed rape and cotton.

IIIA 10.8.1.1 Seed germination

This is not an EC data requirement.

IIIA 10.8.1.2 Vegetative vigour

The following vegetative vigour study performed on GF-2372 was assessed in the EU review and is available in the DAR (2013) Annex B.9.

Report:	**IIIA 10.8.1.2/01, Rockliff, C. (2011a)**
Title:	Effects of GF-2372 (Sulfoxaflor, 500 g as/kg, WG) on the vegetative vigour of non target terrestrial plants (Tier II) (based on U.S. EPA FIFRA subdivision 122-1 & 123-1, OPPTS850.4400) – 2011.
Document No:	Dow Study ID: 101953
Guidelines:	USEPA OPPTS 850.4250, OECD 227
GLP	Yes

Study Comments: IIIA 10.8.1.2/01	Already reviewed in the EU DAR for Sulfoxaflor (2013)
Agreed Endpoints: IIIA 10.8.1.2/01	The regulatory endpoint is EC50 for visual injury, shoot length and foliar fresh weight >150 g GF-2372/ha (the highest rate tested) for all plant species tested.

IIIA 10.8.1.3 Seedling emergence

The following seedling emergence study performed on GF-2372 was assessed in the EU review and is available in the DAR (2013) Annex B.9.

Report:	**IIIA 10.8.1.3/01, Rockliff, C. (2011b)**
Title:	Effects of GF-2372 (Sulfoxaflor, 500 g as/kg, WG) on the seedling emergence of non target terrestrial plants (Tier II) (Based on U.S. EPA FIFRA subdivision J section 123-1, OPPTS 850.4225)- 2011.
Document No:	Dow Study ID: 101954
Guidelines:	USEPA OPPTS 850.4225, OECD 208
GLP	Yes

In the Seedling Emergence and Growth Test, GF-2372 + 0.05% Silwet L-77 applied at rates of 9.38 to 150 g Sulfoxaflor/ha did not reduce seedling emergence, shoot length or cause visual injury in any test species at >25%. A statistically significant effect on shoot length in ryegrass at all treatment levels was apparently due to the adjuvant which also caused a significant decrease in shoot length when tested alone. Foliar fresh weight was unaffected by treatment except for ryegrass which was also affected by treatment with adjuvant alone and also sporadically and

without a rate-response pattern for cucumber and oil seed rape. No treatment caused greater than 50% effect on any endpoint. Therefore, the EC_{50} for fresh weight, shoot length, seedling emergence and visual injury was >150 g Sulfoxaflor/ha for all test species.

Study Comments: IIIA 10.8.1.3/01	Already reviewed in the EU DAR for Sulfoxaflor (2013)
Agreed Endpoints: IIIA 10.8.1.3/01	The regulatory endpoint is EC50 for fresh weight, shoot length, seedling emergence and visual injury >150 g Sulfoxaflor/ha (the highest rate tested) for all plant species tested.

IIIA 10.8.1.4 Field testing

No additional studies with GF-2372 are required.

IIIA 10.8.2 Aquatic plants

Please refer to Point IIIA 10.2.1.12

IIIA 10.8.2.1 *Lemna* growth test

No *Lemna* toxicity study has been performed with the formulation GF-2372.

IIIA 10.8.2.2 Field tests

Field studies are not required and have not been submitted.

IIIA 10.9 Other Non-Target Species (Flora and Fauna)

IIIA 10.9.1 Available preliminary data on other non-target species (flora and fauna)

No additional relevant data available.

IIIA 10.9.2 Critical assessment of relevance of preliminary test data

The potential impact on non-target organisms following the application of GF-2372 on the crops listed in the GAP can be assessed adequately based on the information presented in the preceding Annex points.

IIIA 10.10 Other/Special Studies

IIIA 10.10.1 Laboratory studies

No additional relevant data available.

IIIA 10.10.2 Field studies

No additional relevant data available.

IIIA 10.11 Summary and Evaluation of Points 9 and 10.1-10.10

IIIA 10.11.1 Predicted distribution and fate in the environment and time courses involved

The predicted distribution and fate of GF-2372 in the environment is described in Part B, Section 5.

IIIA 10.11.2 Non-target species at risk and extent of potential exposure

Birds and mammals

The avian and mammalian risk assessment, conducted in accordance with the EFSA Bird and Mammal Guidance Document (2009), indicated acceptable acute and chronic risk to birds for GF-2372, based on a worst-case screening assessment, when applied to cereals, oilseed rape and cotton. However, for completeness a refined risk assessment was conducted (DF & PD) which demonstrated an acceptable risk to mammals for GF-2372 when applied to cereals, oilseed rape and cotton, based on a screening risk assessment.

In addition, the screening risk assessment for exposure *via* drinking water demonstrated an acceptable risk for the proposed uses of GF-2372 on cereals, oilseed rape and cotton.

Since sulfoxaflor does not have a log P_{ow} value ≥ 3, risk assessments for birds and mammals feeding on fish and earthworms are not necessary for this active substance.

Aquatic organisms

The risk to aquatic organisms was assessed based on the Aquatic Guidance Document (Sanco/ 3268/2001). In the first instance TERs for the active substance and potentially relevant metabolites (X11719474 and X11519540) were calculated using the overall maximum initial PECsw from the proposed use from FOCUS Step 1. Where this indicated a concern TERs were calculated using FOCUS Step 2 PECsw values. TERs were also calculated for the formulated product (GF-2372) using spray drift PECsw values at the default distance of 1 m.

Overall, an acceptable risk to aquatic invertebrates was demonstrated, without the need for any risk mitigation measures.

Effects on bees

It is concluded that the risk to honeybees is acceptable when the product is applied before flowering. Pre-flowering application made 5 days before flowering is considered sufficiently protective by ZRMS. The following mitigation measure must be applied: Do not use where bees are actively foraging/ Do not apply 5 days before and during flowering.

Therefore, considering flowering plants other than crops, a mitigation measure is considered needed: “Do not apply when flowering weeds are present”

Finally, no information has been provided concerning the honeydew production and the possible way of transfert and exposure of Sulfoxaflor to bees. Then the following mitigation measure

must be applied for all intended uses: “To protect bees and pollinating insects do not apply to crop plants when in flower or during the honeydew production period”. This conclusion is considered to be conservative for bumble bees.

Effects on other non-target arthropod species

The risk assessment for non-target arthropods was conducted in line with ESCORT 2 (Candolfi *et al*., 2001), based on data for the proposed formulated product (GF-2372) as well as GF-2626 and GF-2032. It was considered appropriate to extrapolate toxicity data for these products to GF-2372, due to the comparable toxicity to non-target arthropods. The first tier risk assessment demonstrated acceptable off-field and in-field risks to *T. pyri* for the proposed uses of GF-2372 on cereals, oilseed rape and cotton at the maximum proposed application rate of 48 g product/ha. However, the in-field and off-field HQs for *A. rhopalosiphi* indicated the need for a further risk assessment.

Field studies conducted with GF-2372 and GF-2626 demonstrated the potential for recovery of arthropod populations within a year. On this basis the in-field risk to non-target arthropods was considered acceptable.

The off-field risk to non-target arthopods is acceptable when GF-2372 is applied without mitigations measures for Cereals, Cotton and Oilseed rape.

Effects on earthworms and other soil macro-organisms

The risk to earthworms and other soil macro-invertebrates was assessed in line with the Guidance Document on Terrestrial Ecotoxicology (SANCO/10329/2002). The calculated TER_A and TER_{LT} values were greater than the respective trigger values for sulfoxaflor and the potentially relevant metabolites X11719474 and X11519540, indicating acceptable acute and chronic risks to soil macro-organisms from the proposed uses of GF-2372. However, the TER_{LT} values for GF-2372 were below the trigger value of 5 indicating a potential long-term risk to earthworms and *Folsomia candida.*

Based on the results of the field study on earthworms and soil micro-arthropods (Collembola, Acari) it was be concluded that the proposed uses of GF-2372 on cereals, oilseed rape and cotton posed an acceptable risk to soil macro-organisms.

Effects on soil micro-organisms

The risk to soil micro-organisms was assessed in line with the Guidance Document on Terrestrial Ecotoxicology (SANCO/10329/2002). When applying GF-2372 according to the proposed representative GAPs on cereals, oilseed rape and cotton no negative effects on microbial activities are to be expected.

Effects on non-target plants

The potential risk to non-target terrestrial plants from the proposed uses of GF-2372 was evaluated using the recommendations presented in the Guidance Document on Terrestrial Ecotoxicology (SANCO/10329/2002, rev. 2 final).

Since there were no data indicating > 50 % phytotoxic effects on any test species at the maximum application rate an acceptable risk to non-target plants was concluded for the uses of GF-2372 on cereals, oilseed rape and cotton.

IIIA 10.11.3 Short and long term risks for non-target species, populations, communities and processes

There are no additional European requirements for formulated products.

IIIA 10.11.4 Risk of fish kills and fatalities in large vertebrates or terrestrial predators

There are no additional European requirements for formulated products.

IIIA 10.11.5 Precautions necessary to avoid/minimise environmental contamination and to protect non-target species

Please see IIIA 10.11.12

Appendix 1: List of data submitted in support of the evaluation

The submitted studies are reported in the DAR of the Sulfoxaflor (2013)

Annex Point/ Reference Number	Author(s)	Year	Title Source (where different from the Company), Company, Report Number, GLP or GEP status (where relevant), Published or not	Data Protection claimed (Y/N)	Relied On ? Y/N	Owner
IIIA 10.4.7/04	Liepold, K.	2011	A Semi-field Study to Investigate Residues in Honeybee Products (Apis mellifera carnica L.; (Hymenoptera, Apidae) in Phacelia tanacetifolia in Germany in 2010. Eurofins Agroscience Services GmbH Eutinger Str. 24 D-75223 Niefern-Öschelbronn Germany DAS Study ID: 110414 GLP/GEP (Y/N): Y Published (Y/N): N	Y	Y	DAS
IIIA 10.4.7/05	Anonymous	2016	Pre-Flowering Applications of Sulfoxaflor: Exposure and Effects on Honey bees Dow AgroSciences DAS Study ID: - GLP/GEP (Y/N): n.a. Published (Y/N): N	Y	Y	DAS

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 applications are possible.
Cereal (Wheat, Barley, Oats, Rye, Spelt, Triticale) [W,	South (FR, IT)	GF-2372	F	Aphids	WG	500 g/kg	Ground applied foliar spray, broadcast	BBCH 12-29 Sep-Dec BBCH 30 –	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.

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		
S]								87 Mar-Jul							If no autumn application, 2 spring applications are possible.

Remarks:
(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 plants - 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) The minimum and maximum number of application possible under practical conditions of use must be provided
(l) PHI - minimum pre-harvest interval
(m) Remarks may include: Extent of use/economic importance/restrictions