

# **REGISTRATION REPORT**

## **Part B**

### **Section 7**

#### **Metabolism and Residues**

Detailed summary of the risk assessment

Product name(s): **INTUITY PLUS**

**(Mandestrobin 40 SC)**

Chemical active substance:  
Mandestrobin, 400 g/L

Central Zone

Zonal Rapporteur Member State: Poland

#### **CORE ASSESSMENT**

(authorization)

Applicant: XXXX

Submission date: February 2024

Evaluation date: January 2025

Finalisation date: August 2025

## Version history

When	What
February 2024	Article 33 – Initial Applicant’s version
May 2024	<ul style="list-style-type: none"> <li>- Update of the cover page with the product trade name ‘Intuity Plus’. Mandestrobin 40 SC is the internal unique name. The internal name Mandestrobin 40 SC is the one used across the dRR content. Additional, update of the applicant with the missing word ‘XXXX’</li> <li>- Update of Appendix 1: studies source and owner updated</li> </ul>
January 2025	Initial RR by zRMS
August 2025	Final RR

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## 7 Metabolism and residue data (KCA section 6)

### 7.1 Summary and zRMS Conclusion

The applicant's dRR was not rewritten. In the resulting zRMS' RR all comments /corrections/ add-ons were placed on the grey background.

#### 7.1.1 Critical GAP(s) and overall conclusion

##### Selection of critical uses and justification

The critical GAP with respect to consumer intake and risk assessment for the preparation Intuity Plus is presented in Table 7.1-1. They have been selected from the individual GAPs in the Central Zone for oilseed rape. The document SANTE/11647/2015/rev 23 from 25 March 2021 presents the EU representative GAP which is practically the same GAP as the intended critical one:

Crop and/ or situation  (a)	Member State or Country	Product name	F G or I (b)	Pests or Group of pests controlled  (c)	Formulation		Application					Application rate per treatment						PHI (days)  (l)
					Type	Conc. of as	method kind	growth stage & season (j)	number (k)		interval between applications (min)	g a.s./hL		water L/ha		g a.s./ha		
(d-f)	(i)	(f-h)		min	max	min	max	min	max	min		max						
Winter Oilseed rape	N & S	S-2200 25SC	F	Sclerotinia	SC	250 g/L	HVS	63-67	1	n.a.	n.a.	67	200	100	300	200	200	-*

A list of all intended uses within the Central Zone is given in Part B, Section 0.

##### Overall conclusion

The data available are considered sufficient for risk assessment. An exceedance of the current MRL of 0,01 mg/kg for mandestrobin in oilseed rape as laid down in Reg. (EU) 2021/1247 is not expected. According to the data provided by the applicant the current MRL of 0,05 mg/kg for mandestrobin in honey is not expected to be exceeded when the PPP is applied consistently with the intended critical GAP. The chronic and the short-term intakes of mandestrobin residues are unlikely to present a public health concern.

As far as consumer health protection is concerned, PL agrees with the authorization of the intended use. According to available data, no specific mitigation measures should apply.

##### Data gaps

Noticed data gaps are: none

Mandestrobin 40SC

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**Table 7.1-1: Acceptability of critical GAPs (and respective fall-back GAPs, if applicable)**

1	2	3	4	5	6	7		8				9			10	11
GAP number (see part B.0)*	Crop and/or situation **	Zone	Product code	F, Fn, Fpn G, Gn, Gpn or I***	Pests or Group of pests controlled	Formulation		Application				Application rate per treatment			PHI (days)	Conclusion
						Type	Conc. of as	method kind	growth stage & season	number min max	interval between applications (min)	PPP/ha min max	water L/ha min max	kg as/ha min max		
1	Winter and Spring Oilseed Rape <b>0401060</b>	CEU (PL, AT, HU, RO, DE, NL, CZ, SK, SI)	Mandestrobin 40 SC	F	<i>Sclerotinia sclerotiorum</i>	SC	400 g/L	Foliar	BBCH 60-69	1	-	0.5 L	100-300	0.2	-	The PHI is covered by the time remaining between application and harvest

\* Use number(s) in accordance with the list of all intended GAPs in Part B, Section 0 should be given in column 1

\*\* Use also code numbers according to Annex I of Regulation (EU) No 396/2005

\*\*\* F: professional field use, Fn: non-professional field use, Fpn: professional and non-professional field use, G: professional greenhouse use, Gn: non-professional greenhouse use, Gpn: professional and non-professional greenhouse use, I: indoor application

Explanation for Column 11 “Conclusion”

A	Exposure acceptable without risk mitigation measures, safe use
R	Further refinement and/or risk mitigation measures required
N	Exposure not acceptable, no safe use

### 7.1.2 Summary of the evaluation

The preparation Mandestrobin 40SC is composed of mandestrobin (400 g/L).

**Table 7.1-2: Toxicological reference values for the dietary risk assessment of mandestrobin**

Reference value	Source	Year	Value	Study relied upon	Safety factor
ADI	EFSA	2015	0.19 mg/kg bw/day	52-week dog study	100
ARfD	EFSA	2015	Not required		

#### 7.1.2.1 Summary for mandestrobin

**Table 7.1-3: Summary for mandestrobin**

Use-No.*	Crop	Plant metabolism covered?	Sufficient residue trials?	PHI sufficiently supported?	Sample storage covered by stability data?	MRL compliance	Chronic risk for consumers identified?	Acute risk for consumers identified?
1	Oilseed rape	Yes	Yes (8 NEU, 4 SEU trials)	Yes	Yes	Yes	No	No

\* Use number(s) in accordance with the list of all intended GAPs in Part B, Section 0 should be given in column 1

After applying the GAP this is the no-residue situation.

As residues of mandestrobin do not exceed the trigger values defined in Reg (EU) No 544/2011, there is no need to investigate the effect of industrial and/or household processing.

Residues in succeeding crops have been sufficiently investigated taking into account the specific circumstances of the cGAP uses being considered here. It is very unlikely that residues will be present in succeeding crops.

Considering dietary burden and based on the intended uses, no significant modification of the intake was calculated for livestock. Further investigation of residues as well as the modification of MRLs in commodities of animal origin is therefore not necessary.

#### 7.1.2.2 Summary for Intuity Plus (Mandestrobin 40SC)

**Table 7.1-4: Information on Mandestrobin 40SC (KCA 6.8)**

Crop	PHI for Mandestrobin 40SC proposed by applicant	PHI/ Withholding period* sufficiently supported for	PHI for Mandestrobin 40SC proposed by zRMS	zRMS Comments (if different PHI proposed)
		Mandestrobin		
Oilseed rape	F**	NR		

NR: not relevant

\* Purpose of withholding period to be specified

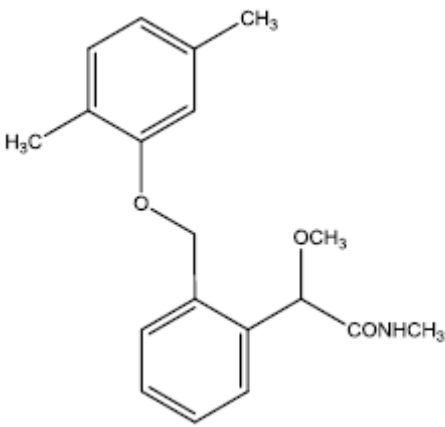
\*\* F: PHI is defined by the application stage at last treatment (time elapsing between last treatment and harvest of the crop).

## Assessment

### 7.2 Mandestrobin

General data on mandestrobin are summarized in the table below (last updated 2015/04/22)

**Table 7.2-1: General information on mandestrobin**

Active substance (ISO Common Name)	Mandestrobin
IUPAC	( <i>RS</i> )-2-methoxy-N-methyl-2-[ $\alpha$ -(2,5-xylyloxy)-otolyl]acetamide
Chemical structure	
Molecular formula	C <sub>19</sub> H <sub>23</sub> NO <sub>3</sub>
Molar mass	313.39 g/mol
Chemical group	Methoxyacetamide fungicides (strobilurin fungicides)
Systemic	Yes
Company (ies)	XXXX
Rapporteur Member State (RMS)	Austria
Approval status	Approved (09/12/2015) Reg. (EU) 2015/2085
Review Report	SANTE/11647/2015 rev 1 09 October 2015 25 March 2021 (rev.3)
Current MRL regulation	Regulation (EU) 2021/1247
Peer review of MRLs according to Article 12 of Reg No 396/2005 EC performed	No
EFSA Journal : Conclusion on the peer review	Yes (EFSA Journal 2015;13(5):4100)
EFSA Journal: conclusion on article 12	No
Current MRL applications on intended uses	None



## 7.2.1 Stability of Residues (KCA 6.1)

### 7.2.1.1 Stability of residues during storage of samples

#### Available data

Two new stability studies have been submitted by the applicant in the framework of this application. Results are summarized in the table below. The detailed assessment of these studies are presented in Appendix 2.

**Table 7.2-2: Summary of stability data achieved at  $\leq -18^{\circ}\text{C}$  (unless stated otherwise)**

Matrix	Characteristics of the matrix	Acceptable Maximum Storage duration	Reference
<b>Data relied on in EU</b>			
<b>Plant products</b>			
Oilseed Rape	High oil content	12 months (mandestrobin, De-Xy-S-2200, 4-OH-S-2200 and 2-CH <sub>2</sub> OH-S-2200)	EFSA, 2015
Lettuce	High water content	12 months (mandestrobin, De-Xy-S-2200, 4-OH-S-2200, 5-CH <sub>2</sub> OH-S-2200 and 2-CH <sub>2</sub> OH-S-2200)	EFSA, 2015
Barley grain and straw	High starch content (grain), Other (straw)	12 months (mandestrobin, De-Xy-S-2200, 4-OH-S-2200, 5-CH <sub>2</sub> OH-S-2200 and 2-CH <sub>2</sub> OH-S-2200)	EFSA, 2015
<b>New data</b>			
<b>Plant products</b>			
Orange (whole fruit)	High acid content	12 months (mandestrobin, De-Xy-S-2200), 26 months ( 4-OH-S-2200 and 2-CH <sub>2</sub> OH-S-2200)	Lindner M., Grewe D., Leischow, J., 2017 (ROR-0286)
Dry bean	High protein content	12 months (mandestrobin, De-Xy-S-2200, 4-OH-S-2200 and 2-CH <sub>2</sub> OH-S-2200)	
Honey	--	5 months (mandestrobin, De-Xy-S-2200, 4-OH-S-2200, 5-CH <sub>2</sub> OH-S-2200 and 2-CH <sub>2</sub> OH-S-2200)	Antón, B., 2022 (ROR-0307)

#### Conclusion on stability of residues during storage

Residues of mandestrobin (S-2200, R & S-isomers), De-Xy-S-2200, 4-OH-S-2200, 2-CH<sub>2</sub>OH-S-2200 are stable for at least 12 months in oilseed rape (seeds), lettuce and barley (grain and straw), dry bean and orange (whole fruit), when stored frozen at  $-18^{\circ}\text{C}$  or below. Additionally, storage stability of 4-OH-S-2200 and 2-CH<sub>2</sub>OH-S-2200 residues was demonstrated in orange (whole fruit) for at least 26 months.

Residues of 5-CH<sub>2</sub>OH-S-2200 are stable for at least 12 months in lettuce and barley (grain and straw) when stored frozen at -18°C or below.

The freezer storage stability of mandestrobin (isomers S-2167 and S-2354) and metabolites De-Xy-S-2200, 4-OH-S-2200, 2-CH<sub>2</sub>OH-S-2200 and 5-CH<sub>2</sub>OH-S-2200 was also determined in honey samples. *Storage stability was demonstrated to be at least 5 months for mandestrobin and all metabolites tested in honey* This investigation was done in conjunction with the field studies carried out to determine the magnitude of residues in honey.

### 7.2.1.2 Stability of residues in sample extracts (KCA 6.1)

#### Available data

No new data submitted in the framework of this application.

#### Conclusion on stability of residues in sample extracts

The stability of residues in sample extracts was demonstrated by acceptable procedural recoveries analysed concurrently with residue trial samples.

zRMS agrees with the above consideration of the applicant.

## 7.2.2 Nature of residues in plants, livestock and processed commodities

### 7.2.2.1 Nature of residue in primary crops (KCA 6.2.1)

#### Available data

No new data submitted in the framework of this application.

**Table 7.2-3: Summary of plant metabolism studies**

Crop Group	Crop	Label position	Application and sampling details					Reference
			Method, F or G (a)	Rate (kg a.s./ha)	No	Sampling (DAT)	Remarks	
EU data								
Fruits and fruiting vegetable	-	-	-	-	-	-	-	-
Leafy vegetables	Lettuce	[Phenoxy- <sup>14</sup> C] and [benzyl- <sup>14</sup> C]-mandestrobin	Foliar treatment, F	0.8	2	Immature leaves: 5 DAA1 Mature leaves: 5 DAA2	-	EFSA, 2015
Root and tuber vegetables	-	-	-	-	-	-	-	-
Pulses and	Oilseed	[Phenoxy-	Foliar	0.4	1	Seed: 54	-	EFSA, 2015

oilseeds	rape	<sup>14</sup> C] and [benzyl- <sup>14</sup> C]-mandestrobin	treatment, F			days		
					2	Forage: 14 DAA2 Seed: 40 DAA2		
Cereals	Wheat	[Phenoxy- <sup>14</sup> C] and [benzyl- <sup>14</sup> C]-mandestrobin	Foliar treatment, F	0.3	1	Forage: 7 days Hay: 14 days Grain and straw: 104 days	-	EFSA, 2015

DAA1 – Days after application 1

DAA2 – Days after application 2

### Conclusion on metabolism in primary crops

See reference to the DAR (Austria, 2014): “Mandestrobin (S-2200) is extensively metabolised in crops. The route of the metabolism of Mandestrobin (S-2200) has been shown to be similar in all three crop groups. The main route of metabolism in crops is via hydroxylations and oxidations, and subsequent glycoside conjugation, to yield the metabolites 4-OH-S-2200, 2-CH<sub>2</sub>OH-S-2200, 5-CH<sub>2</sub>OH-S-2200 and 5-COOH-S-2200 and their conjugates. Minor metabolic pathways involved demethylation of the methoxy group of the side chain to form MCBX, and cleavage of the ether linkage to form De-Xy-S-2200. S-2200 was a major component of the residue in all crops. The R/S ratio of [<sup>14</sup>C]S-2200 remained approximately 1:1 indicating no R/S isomerization in all tested crops. The major metabolites found at levels >10% TRR were 4-OH-S-2200 (conjugated), 2-CH<sub>2</sub>OH-S-2200 (conjugated) and De-Xy-S-2200. All the free metabolites found in crops are also found in the rat, however only 4-OH-S-2200 and 5-COOH-S-2200 are major metabolites in the rat (found at >10% of dose).”

Data evaluated during the peer review are sufficient to support the intended uses of Mandestrobin 40SC.

### 7.2.2.2 Nature of residue in rotational crops (KCA 6.6.1)

#### Available data

No new data submitted in the framework of this application.

**Table 7.2-4: Summary of metabolism studies in rotational crops**

Crop group	Crop	Label po- sition	Application and sampling details					Reference
			Method, F or G *	Rate (kg a.s./ha)	Sowing intervals (DAT)	Harvest Inter- vals (DAT)	Remarks	
EU data								
Fruits and fruiting vegeta- ble	-	-	-	-	-	-	-	-
Leafy vegeta- bles	Lettuce	[phenoxy- <sup>14</sup> C] and [benzyl- <sup>14</sup> C]-S-	Spray application to bare soil, F	1.6	30, 120 and 365	NCH	Immature leaves (50% size) and mature	EFSA 2015

		2200					leaves (NCH)	
<b>Root and tuber vegetables</b>	Carrot	[phenoxy- <sup>14</sup> C] and [benzyl- <sup>14</sup> C]-S-2200	Spray application to bare soil, F	1.6	30, 120 and 365	NCH	Mature foliage and roots (NCH)	EFSA, 2015
<b>Pulses and oilseeds</b>	-	-	-	-	-	-	-	-
<b>Cereals</b>	Wheat	[phenoxy- <sup>14</sup> C] and [benzyl- <sup>14</sup> C]-S-2200	Spray application to bare soil, F	1.6	30, 120 and 365	NCH	Forage (6-8 inch stem elongation), hay (early flower to soft dough), mature grain and straw (NCH)	EFSA, 2015

\* Outdoor/field application (F) or glasshouse/protected/indoor application (G)

### Summary of plant metabolism studies reported in the EU

Refer to the DAR (Austria, 2014): (Following application to bare soil..) “*The dose level used in this study (1.6 kg as/ha) represents a highly exaggerated rate relative to the intended application rate of 0.2 kg as/ha for oilseed rape. The results of the study demonstrated that S-2200 and metabolites were taken up by rotational crops, extensively metabolized to polar metabolites and incorporated into the constituents of plant. The metabolism in rotational crops was considered to be essentially the same as in primary crops.*

The major metabolism pathway included:

- hydroxylation of the dimethylphenoxy ring to form 4-OH-S-2200 and subsequent formation of glycoside and malonyl glycoside conjugate
- oxidation of the methyl group attached to the 2- and the 5-positions of the dimethylphenoxy ring to form 2-CH<sub>2</sub>OH-S-2200, 5-CH<sub>2</sub>OH-S-2200 and the corresponding glycoside conjugate

Minor metabolic pathways included

- the demethylation of the methoxy group of the side chain to form MCBX and
- cleavage of the ether link to form De-Xy-S-2200 and
- further oxidation of 5-CH<sub>2</sub>OH-S-2200 to form 5-COOH-S-2200

Further metabolism occurred to form other minor metabolites and polar products.”

### Conclusion on metabolism in rotational crops

Refer to EFSA, 2015: “*The metabolism and distribution of mandestrobin has been studied in confined rotational crops (wheat, lettuce, carrots) at 30, 120 and 365 day plant-back intervals. There was moderate uptake of S-2200 residues from soil into rotational crops. The metabolism in rotational crops was essentially the same as in primary crops.*”

Data evaluated during the peer review are sufficient to support the intended uses of Mandestrobin 40SC.

### 7.2.2.3 Nature of residues in processed commodities (KCA 6.5.1)

#### Available data

No new data submitted in the framework of this application.

**Table 7.2-5: Nature of the residues in processed commodities**

Conditions (Duration, Temperature, pH)	Identified compound(s) (%)	Reference
<b>EU data</b>		
<b>Pasteurisation</b> (20 minutes, 90°C, pH 4)	Mandestrobin – 94.2% Unknowns – 0.8%	EFSA, 2015
<b>Baking, boiling, brewing</b> (60 minutes, 100°C, pH 5)	Mandestrobin – 99.8% Unknowns – 0.7%	EFSA, 2015
<b>Sterilisation</b> (20 minutes, 120°C, pH 6)	Mandestrobin – 99.6% Unknowns – 1.3%	EFSA, 2015

#### Conclusion on nature of residues in processed commodities

Refer to the DAR (Austria, 2014): “*The nature of the residue during processing showed that Mandestrobin (S-2200) was stable under conditions representing pasteurisation and baking/brewing/boiling and sterilisation. No degradation would be expected during food processing*”.

Data evaluated during the peer review are sufficient to support the intended uses of Mandestrobin 40SC.

### 7.2.2.4 Conclusion on the nature of residues in commodities of plant origin (KCA 6.7.1)

**Table 7.2-6: Summary of the nature of residues in commodities of plant origin**

<b>Endpoints</b>	
Plant groups covered	Pulses/Oilseeds (Oilseed rape) Cereals (Wheat) Leafy crops (Lettuce)
Rotational crops covered	Cereals (Wheat) Leafy crops (Lettuce) Root and Tuber crops (Carrot)
Metabolism in rotational crops similar to metabolism in primary crops?	Yes
Processed commodities	Studies on the nature of the residue during processing showed that Mandestrobin (S-2200) was stable under conditions representing pasteurisation and baking/brewing/boiling and sterilisation.
Residue pattern in processed commodities similar to pattern in raw commodities?	Yes
Plant residue definition for monitoring	Mandestrobin (Reg. (EU) 2021/1247)
Plant residue definition for risk assessment	Sum of mandestrobin, De-Xy-S-2200, 4-OH-S-2200 conjugate, 2-CH <sub>2</sub> OH-S-2200 conjugate, expressed as mandestrobin (EFSA, 2015)
Conversion factor from enforcement to RA	Oilseed Rape: 4 (EFSA, 2015)

zRMS agrees with the above consideration of the applicant.

### 7.2.2.5 Nature of residues in livestock (KCA 6.2.2-6.2.5)

#### Available data

No new data submitted in the framework of this application.

**Table 7.2-7: Summary of animal metabolism studies**

Group	Species	Label position	No of animal	Application details		Sample details		Reference
				Rate (mg/kg bw/d)	Duration (days)	Commodity	Time of sampling	
EU data								
Lactating ruminants	Goat	[phenoxy- <sup>14</sup> C] and [benzyl- <sup>14</sup> C]-S-2200	2	Phenoxy label: 0.31  Benzyl label: 0.59	7	Milk	Twice daily	EFSA, 2015
						Urine and faeces	Daily	
						Tissues	At sacrifice (6-7 hrs after final dose)	
Laying poultry	Hens	[phenoxy- <sup>14</sup> C] and [benzyl- <sup>14</sup> C]-S-2200	20	Phenoxy label: 1.04  Benzyl label: 0.87	14	Eggs	Twice daily	EFSA, 2015
						Excreta	Daily	
						Tissues	At sacrifice (6 hrs after final dose)	

#### Summary of animal metabolism studies reported in the EU

Refer to DAR (Austria, 2014): “The available metabolism studies on laying hens and lactating goats showed that the metabolic pathways in livestock were similar to that found in the rat. Mandestrobin (S-2200) is extensively metabolised and mainly excreted in the hen (83-98% of the dose) and goat (78 % of the dose). The route of the metabolism of S-2200 has been shown to be similar and proceeds via a series of hydroxylations and oxidations, N-demethylation, O-demethylation and ether hydrolysis.

Parent S-2200 was the main component of the residue in eggs, milk fat, muscle (goat) and fat (hen and goat). The main metabolites were 5-COOH-S-2200 (goat kidney and liver), 4-OH-S-2200 (in hen liver and as the glucuronide in goat kidney) and De-Xy-S-2200 (hen liver). The primary metabolites are further metabolised by conjugation, thus S-2200, De-Xy-S-2200, 4-OH-S-2200 and 5-CA-2-HM-S-2200 were present in liver in bound/conjugated form.

Mandestrobin (S-2200) has a log Pow of 3.51 and is the main metabolite in milk fat (up to 35 % TRR,

0.012 mg/kg) and in fat (up to 50 % TRR, 0.016 mg/kg in poultry and 50 % TRR, 0.006 mg/kg in goat). However no significant accumulation of residues in tissues, particularly fatty tissues, has been observed.”

**According to Regulation (EU) No 283/2013, metabolism studies on fish** may be required where the plant protection product is used in crops whose parts or products, also after processing, are fed to fish and where residues in feed may result from the intended applications. This is further specified in the working document on the nature of pesticide residues in fish (SANCO/11187/2013, rev.3), according to which fish metabolism data are required when pesticide use may lead to residues >0.1 mg/kg of the total diet (dry weight basis) in fish feed AND when the active substances are fat soluble, i.e. have a log Po/w  $\geq 3$ . For mandestrobin the log Po/w is higher than 3 (3.51) and the substance is considered as fat soluble. Furthermore, rape seed meal is used as a fish feeding stuff. However, as residues of mandestrobin were consistently below the LOQ in rape seeds, residues above the trigger value of 0.1 mg/kg are not expected.

### Conclusion on metabolism in livestock

Refer to EFSA, 2015: “The available metabolism studies on laying hens and lactating goats showed that the metabolic pathways in livestock were similar to that found in the rat.”

The metabolism of Mandestrobin in livestock was considered sufficiently investigated to support the proposed use of Mandestrobin 40SC on oilseed rape.

### 7.2.2.6 Conclusion on the nature of residues in commodities of animal origin (KCA 6.7.1)

**Table 7.2-8: Summary on the nature of residues in commodities of animal origin**

	Endpoints
Animals covered	Lactating goats
	Laying hens
Time needed to reach a plateau concentration	7 days in milk
	7 days in eggs
Animal residue definition for monitoring	Mandestrobin (Reg. (EU) 2021/1247)
Animal residue definition for risk assessment	Mandestrobin (EFSA, 2015)
Conversion factor	Not required (EFSA, 2015)
Metabolism in rat and ruminant similar	Yes
Fat soluble residue	Yes (log PoW = 3.51 at 25 ± 1°C and pH 5) (EFSA, 2015)

zRMS agrees with the above consideration of the applicant.

## 7.2.3 Magnitude of residues in plants (KCA 6.3)

### 7.2.3.1 Summary of European data and new data supporting the intended uses

No new data are submitted in the framework of this application.

**Table 7.2-9: Summary of EU reported and new data supporting the intended uses of Mandestrobin 40SC and conformity to existing MRL**

Commodity	Source	Residue zone (N-EU, S-EU, EU, outside EU)	Evaluation GAP Residue levels (mg/kg) E = according to enforcement residue definition RA = according to risk assessment residue definition	STMR (mg/kg)	HR (mg/kg)	Unrounded OECD calculator MRL (mg/kg)	Current EU MRL (mg/kg) *	MRL compliance
Oilseed rape	EFSA, 2015	N-EU (8 trials)	GAP on which MRL/EU a.s. assessment is based: 1 x 0.2 kg as/ha, BBCH 63-67, PHI n/a, outdoor E: 8 x <0.01 RA: 8 x <0.04	Northern and Southern datasets similar. MRL derived from merged values (EFSA 2015).				
	EFSA, 2015	S-EU (4 trials)	GAP on which MRL/EU a.s. assessment is based: 1 x 0.2 kg as/ha, BBCH 63-67, PHI n/a, outdoor E: 4 x <0.01 RA: 4 x <0.04					
	Overall supporting data for cGAP	EU	E : 12 x <0.01 RA: 12 x <0.04	E: <0.01 RA: <0.04	E: <0.01 RA: <0.04	0.01	0.01*	Yes

\* Source of EU MRL: Reg. (EU) 2021/1247



### 7.2.3.2 Conclusion on the magnitude of residues in plants

A total of 12 supervised trials are available on oilseed rape that are supportive of the proposed GAP for Mandestrobin 40SC. The proposed GAP for Mandestrobin 40SC specifies applications up to BBCH 69, whereas the representative use in the DAR specified applications up to BBCH 67, since these are both within the same principal growth stage for oilseed rape (BBCH 67: decline of flowering, BBCH 69: end of flowering), then the trials conducted to support the DAR are considered supportive for the use of Mandestrobin 40SC.

All of the trials presented have been previously evaluated by the EU (EFSA, 2015). A total of 8 trials in NEU and 4 trials in SEU are available, with residues < LOQ in all trials (<0.01 mg/kg), therefore the combined NEU and SEU dataset has been used to support the GAP in CEU.

Samples of seed from all trials were analysed for residues of mandestrobin and metabolites De-Xy-S-2200, 4-OH-S-2200 (free and conjugated) and 2-CH<sub>2</sub>OH-S-2200 (free and conjugated). Residues of all analytes were <LOQ in all trials. The ratio of *R*- and *S*-isomers of S-2200 remained approximately 50:50 in the oilseed rape samples.

According to the available data, no exceedance of the MRL will occur. The uses are considered acceptable.

zRMS agrees with the above consideration of the applicant.

## 7.2.4 Magnitude of residues in livestock

### 7.2.4.1 Dietary burden calculation

In the DAR (Austria, 2014) a livestock dietary burden calculation was carried out as residues in oilseed rape presscake should be considered. According to the DAR “*With respect to an allocated yield of 40% oil and 60% press cake a theoretical transfer factor for Mandestrobin (S-2200) from rape seed (STMR < 0.01 mg/kg) to cake was calculated as 1.7.*” The dietary burden calculation in the DAR was performed according to the EFSA Pesticide Livestock Calculator as a worst case assumption based on the median residue levels (STMR) obtained from the supervised residue trials considering a conversion factor (CF) of 4 and a processing factor (PF) of 1.7.

More recently EFSA has published Reasoned Opinions to alter MRLs in stone fruits and strawberries and grapes (EFSA, 2018a and 2018b), however since the crops considered in those submissions do not form part of the livestock diet, then an updated dietary burden calculation was not required.

Therefore, to present a worst-case scenario for residues, the inputs used for the dietary burden calculation in this submission are the same as those used in the DAR. **The most recent EFSA Pesticide Livestock Calculator (2017) has been used.** The input values for the calculation are presented below.

**Table 7.2-10: Input values for the dietary burden calculation**

Feed Commodity	Median dietary burden		Maximum dietary burden	
	Input value (mg/kg)	Comment	Input value (mg/kg)	Comment
Risk assessment residue definition: Sum of mandestrobin, De-Xy-S-2200, 4-OH-S-2200 conjugate, 2-CH <sub>2</sub> OH-S-2200 conjugate, expressed as mandestrobin (EFSA, 2015)				

Feed Commodity	Median dietary burden		Maximum dietary burden	
	Input value (mg/kg)	Comment	Input value (mg/kg)	Comment
Oilseed rape	0.068	STMR x CF x PF (Austria, 2014)	0.068	STMR x CF x PF (Austria, 2014)

**Table 7.2-11: Results of the dietary burden calculation**

Animal species	Median dietary burden (mg/kg bw/d)	Maximum dietary burden (mg/kg bw/d)	Highest contributing commodity	Max dietary burden (mg/kg DM)	Trigger exceeded (Y/N)
Beef cattle*	0.0004	0.0004	Rape, meal	0.015	N
Dairy cattle*	0.0003	0.0003	Rape, meal	0.008	N
Ram/ewe	0.0004	0.0004	Rape, meal	0.012	N
Lamb	0.0005	0.0005	Rape, meal	0.012	N
Breeding swine	0.0004	0.0004	Rape, meal	0.015	N
Finishing swine*	0.0005	0.0005	Rape, meal	0.015	N
Broiler poultry	0.0010	0.0010	Rape, meal	0.014	N
Layer poultry*	0.0005	0.0005	Rape, meal	0.008	N
Turkey	0.0011	0.0011	Rape, meal	0.015	N

\* These categories correspond to those (formerly) assessed at EU level.

zRMS agrees with the above consideration of the applicant.

#### 7.2.4.2 Livestock feeding studies (KCA 6.4.1-6.4.3)

The maximum dietary burden does not exceed the trigger values of 0.1 mg/kg DM or 0.004 mg/kg bw/day, therefore livestock feeding studies are not required to support the use of Mandestrobin 40SC. No new data were submitted in the framework of this application.

zRMS agrees with the above consideration of the applicant.

#### 7.2.5 Magnitude of residues in processed commodities (Industrial Processing and/or Household Preparation) (KCA 6.5.2-6.5.3)

Residues of mandestrobin and its metabolites in oilseed rape seed were <LOQ (<0.01 mg/kg) in the supervised residue trials, therefore processing studies are not required to support the use of Mandestrobin 40SC. No new data were submitted in the framework of this application.

zRMS agrees with the above consideration of the applicant.

#### 7.2.6 Magnitude of residues in representative succeeding crops

The crops under consideration can be grown in rotation. Data dealing with magnitude of residues in succeeding crops are available and are summarized hereafter.

### 7.2.6.1 Field rotational crop studies (KCA 6.6.2)

#### Available data

No new data submitted in the framework of this application.

**Table 7.2-12: Summary of available studies in field rotational crops**

Primary crop	Rate (kg a.s./ha) (GS at application or PHI)	Residue levels in succeeding crops			
		Succeeding crop group	Succeeding crop	Sowing intervals (DAT)	Reference / Remarks
EU data					
Oilseed rape	0.2 (BBCH 65)	Leafy vegetables	Lettuce	14, 120 and 365	EFSA, 2015
		Root and tuber vegetables	Carrot leaves	14, 120 and 365	EFSA, 2015
			Carrot root	14, 120 and 365	EFSA, 2015
		Brassicas	Broccoli	14, 120 and 365	EFSA, 2015
		Cereals	Barley grain	14, 120 and 365	EFSA, 2015
			Barley straw	14, 120 and 365	EFSA, 2015

#### Conclusion on rotational crops studies

Refer to EFSA, 2015: *“In a field study on representative crops (carrots, lettuce, broccoli and barley) no detectable residues of mandestrobin or the metabolites 4-OH-S-2200, 2-CH<sub>2</sub>OH-S-2200 and 5-CH<sub>2</sub>OH-S-2200 were found in any of the succeeding crop samples at any plant back interval after application of 0.2 kg as/ha on the preceeding crop winter rapeseed.”*

Data evaluated during the peer review are sufficient to support the intended use of Mandestrobin 40SC on oilseed rape.

zRMS agrees with the above consideration of the applicant.

### 7.2.7 Other / special studies (KCA6.10, 6.10.1)

According to SANTE/11956/2016 rev.9, oilseed rape is considered a melliferous crop, therefore a new study is submitted as part of this application which investigates the potential residues in honey following the use of mandestrobin.

A summary of the residue data is presented below, however a detailed assessment of the data is provided in Appendix 2.

**Table 7.2-13: Summary of residues in honey**

Crop	Rate (kg a.s./ha) (GS at appli- cation)	Residue levels in honey (mg/kg)					
		S-2167	S-2354	De-Xy- S- 2200	4-OH-S- 2200	2-CH <sub>2</sub> OH- S-2200	5-CH <sub>2</sub> OH- S-2200
New data (Report: S21-01066, ROR-0307)							
<i>Phacelia tanacetifolia</i>	1 x 0.2 (BBCH 63-65)	<0.005	<0.005	<0.01	<0.01	<0.01	<0.01
		0.01	0.01	<0.01	<0.01	<0.01	<0.01
		<0.005	<0.005	<0.01	<0.01	<0.01	<0.01
		<0.005	<0.005	<0.01	<0.01	<0.01	<0.01

**Table 7.2-14: Residues endpoints for honey**

Crop/ commodity [Code number] <sup>(a)</sup>	Region	Residue levels (mg/kg) observed in the residue trials representative for the intended GAP	STMR <sup>(b)</sup> (mg/kg)	HR <sup>(b)</sup> (mg/kg)	Calculated MRL (mg/kg)
Honey and other apiculture products [1040000]	EU	RD <sub>(ENF)</sub> : 3 x < 0.01; 0.02 RD <sub>(RA)</sub> : 3 x < 0.04; 0.08	0.04	0.08	0.04

EU: Europe; NEU: northern Europe; SEU: southern Europe; STMR: supervised trials median residue; HR: highest residue; MRL: maximum residue level;

(a): Food commodity code as reported in Annex I of Regulation (EC) No 396/2005.

(b) According to the residue definition for risk assessment

(\*): Indicates that the MRL is set at the limit of analytical quantification (LOQ).

RD<sub>(RA)</sub>: Residue values calculated according to the residue definition for risk assessment: Sum of mandestrobin, De-Xy-S-2200, 4-OH-S-2200 conjugate and 2-CH<sub>2</sub>OH-S-2200 conjugate, expressed as mandestrobin.

RD<sub>(ENF)</sub>: Residue values calculated according to the residue definition for enforcement: Mandestrobin

### Conclusion on honey studies

A total of 4 trials are available to demonstrate residues of mandestrobin and its metabolites in honey. The data demonstrate that there would be no exceedance of a default 0.05\* mg/kg MRL value. The data are acceptable to support the use of Mandestrobin 40SC.

zRMS agrees with the above consideration of the applicant.

## 7.2.8 Estimation of exposure through diet and other means (KCA 6.9)

Toxicological reference values relevant for dietary risk assessment are reported in the summary of the evaluation (see 7.1.2).

As an ARfD was not deemed necessary, an acute risk assessment is not relevant.

### 7.2.8.1 Input values for the consumer risk assessment

The residue endpoints calculated in this submission, alongside the input values from the most recent EFSA Reasoned Opinions (EFSA, 2018a and 2018b) and all current EU MRLs for mandestrobin, have been used as input values for the consumer risk assessment. The input values are presented below.

**Table 7.2-15: Input values for the consumer risk assessment**

Commodity	Chronic risk assessment		Acute risk assessment	
	Input value (mg/kg)	Comment	Input value (mg/kg)	Comment
Risk assessment residue definition: Sum of mandestrobin, De-Xy-S-2200, 4-OH-S-2200 conjugate, 2-CH <sub>2</sub> OH-S-2200 conjugate, expressed as mandestrobin (EFSA, 2015)				
Oilseed rape seed [0401060]	0.04	STMR <sub>RA</sub> (EFSA, 2015 and this submission)	Not required	
Honey and other apiculture products [1040000]	0.04	STMR <sub>RA</sub> (this submission)		
Table and wine grapes	1.39	STMR <sub>RA</sub> (EFSA, 2018b)		
Strawberries	0.95	STMR <sub>Mo</sub> x CF (1.1) (EFSA, 2018b)		
Apricots, peaches/nectarines	0.53	STMR <sub>RA</sub> (EFSA, 2018a)		
Cherries	0.58	STMR <sub>RA</sub> (EFSA, 2018a)		
Plums	0.13	STMR <sub>RA</sub> (EFSA, 2018a)		
All other plant commodities	MRL <sup>(a)</sup>	Reg. (EU) 2021/1247		
All other animal commodities	MRL	Reg. (EU) 2021/1247		

<sup>(a)</sup> A conversion factor (CF) for enforcement to risk assessment was no necessary because currently all existing EU MRLs are set at the LOQ

zRMS agrees with the above consideration of the applicant.

### 7.2.8.2 Conclusion on consumer risk assessment

Extensive calculation sheets are presented in Appendix 3.

**Table 7.2-16: Consumer risk assessment**

TMDI (% ADI) according to EFSA PRIMo 3.1	See IEDI
IEDI (% ADI) according to EFSA PRIMo 3.1	2% (based on PT general diet)
IENTI (% ARfD) according to EFSA PRIMo*	Not required
NTMDI (% ADI) **	Not required
NEDI (% ADI)**	Not required
NESTI (% ARfD) **	Not required

\* include raw and processed commodities if both values are required for PRIMo

\*\* if national model is available

The proposed uses of mandestrobin in the formulation Mandestrobin 40SC do not represent unacceptable acute or chronic risks for the consumer.

zRMS agrees with the above consideration of the applicant.

### **7.3 Combined exposure and risk assessment**

Not relevant. The product contains only one active substance.

zRMS agrees with the above consideration of the applicant.

### **7.4 References**

Austria, 2014. Draft Assessment Report (DAR) on the active substance mandestrobin prepared by the rapporteur Member State Austria in the framework of Regulation (EU) No 1107/2009, January 2014.

Austria, 2015. Revised Assessment Report on mandestrobin, compiled by EFSA, March 2015.

EFSA (European Food Safety Authority), 2015. Conclusion on the peer review of the pesticide risk assessment of the active substance mandestrobin. EFSA Journal 2015;13(5):4100, 72 pp. doi:10.2903/j.efsa.2015.4100

EFSA (European Food Safety Authority), 2018a. Reasoned Opinion on the modification of the existing maximum residue levels for mandestrobin in apricots, cherries, peaches/nectarines and plums. EFSA Journal 2018;16(1):5148, 21 pp. <https://doi.org/10.2903/j.efsa.2018.5148>

European Food Safety Authority (EFSA), 2018b. Reasoned Opinion on the setting of import tolerances for mandestrobin in strawberries and table and wine grapes. EFSA Journal 2018; 16(8):5395, 22 pp. <https://doi.org/10.2903/j.efsa.2018.5395>

## Appendix 1 Lists of data considered in support of the evaluation

### List of data submitted by the applicant and relied on

Data point	Author(s)	Year	Title Company Report No. Source (where different from company) GLP or GEP status Published or not	Vertebrate study Y/N	Owner
KCA 6.1	Lindner M., Grewe D., Leischow, J.	2017	Storage Stability of Residues of Mandestrobin and its Metabolites De-Xy-S-2200, 4-OH-S-2200 and 2-CH <sub>2</sub> OH-S-2200 in Dried Beans and Orange Fruit Eurofins Report no. S15-01208 <del>Sumitomo Chemical Co., Ltd.</del> XXXX. ROR-0286 GLP, Unpublished	N	XXXX
KCA 6.1 KCA 6.10.1	Antón. B.	2022	Determination of Residues of Mandestrobin and its Metabolites in Honey, after One Application of Mandestrobin 25 SC in <i>Phacelia tanacetifolia</i> under semi-field conditions, at 4 Sites in Central and Southern Europe in 2021 Eurofins Trialcamp S.L.U., Report No.: S21-01066 <del>Sumitomo Chemical Co., Ltd.</del> XXXX. ROR-0307 GLP, Unpublished	N	XXXX

\* XXXX).

### List of data submitted or referred to by the applicant and relied on, but already evaluated at EU peer review

Data point	Author(s)	Year	Title Company Report No. Source (where different from company) GLP or GEP status Published or not	Vertebrate study Y/N	Owner
KCA 6.1	Daneva, E. & Taeufer, A.	2011a	Freezer Storage Stability Study of S-2200 (its optical isomers of S-2167 (R-isomer) and S-2354 (S-isomer)) in seeds of Oilseed Rape Eurofins Dr Specht GLP GmbH report no. SUM-1012	N	XXXX

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<b>Data point</b>	<b>Author(s)</b>	<b>Year</b>	<b>Title Company Report No. Source (where different from company) GLP or GEP status Published or not</b>	<b>Vertebrate study Y/N</b>	<b>Owner</b>
			XXXX. ROR-0007 GLP, unpublished		
KCA 6.1	Daneva, E. & Taeufer, A.	2011b	Freezer Storage Stability Study of S-2200 (its optical isomers of S-2167 (R-isomer) and S-2354 (S-isomer)) in/on High-Water and Dry Crops over 12 Months Eurofins Agroscience Services Chem GmbH report no. S10-01949 XXXX. ROR-0009 GLP, unpublished	N	XXXX
KCA 6.1	Daneva, E. & Taeufer, A.	2012a	Freezer Storage Stability Study of S-2200 Metabolite, De-Xy-S2200, in Lettuce (Head), Seeds of Oilseed Rape and Barley (Grain and Straw) over 12 Months Eurofins Agroscience Services Chem GmbH report no. SUM-1024 XXXX. ROR-0011 GLP, unpublished	N	XXXX
KCA 6.1	Daneva, E. & Taeufer, A.	2012a	Freezer Storage Stability Study of S-2200 Metabolite, 4-OH-S-2200, in Lettuce (Head), Seeds of Oilseed Rape and Barley (Grain and Straw) over 12 Months Eurofins Agroscience Services Chem GmbH report no. SUM-1025 XXXX. ROR-0012 GLP, unpublished	N	XXXX
KCA 6.1	Daneva, E. & Zetzsch, A.	2012b	Freezer Storage Stability Study of S-2200 Metabolite, 2-CH <sub>2</sub> OH-S-2200, in Lettuce (Head), Seeds of Oilseed Rape and Barley (Grain and Straw) over 12 months Eurofins Agroscience Services Chem GmbH Report No. SUM-1026 XXXX. ROR-0013 GLP, Unpublished	N	XXXX
KCA 6.1	Daneva, E. & Zetzsch, A.	2012a	Freezer Storage Stability Study of S-2200 Metabolite, 5-CH <sub>2</sub> OH-S-2200, in Lettuce (Head) and Barley (Grain and Straw) over 12 Months Eurofins Agroscience Services Chem GmbH report no. SUM-1028 XXXX. ROR-0014 GLP, unpublished	N	XXXX
KCA 6.2.1	Panthani, A. & Lentz, N R.	2010a	Metabolism of [ <sup>14</sup> C]S-2200 in Lettuce Plants Springborn Smithers Laboratories Report No: 13048.6631 XXXX. ROM-0008	N	XXXX



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<b>Data point</b>	<b>Author(s)</b>	<b>Year</b>	<b>Title Company Report No. Source (where different from company) GLP or GEP status Published or not</b>	<b>Vertebrate study Y/N</b>	<b>Owner</b>
			GLP, unpublished		
KCA 6.2.1	Panthani, A. & Lentz, N R.	2010b	Metabolism of [ <sup>14</sup> C]S-2200 in Wheat Springborn Smithers Laboratories Report No: 13048.6619 XXXX. ROM-0009 GLP, unpublished	N	XXXX
KCA 6.2.1	Panthani, A. & Connor, S.	2011	Metabolism of [14C]S-2200 in Rapeseed Plants Smithers Viscient Report No: 13048.6618 XXXX. ROM-0026 GLP, unpublished	N	XXXX
KCA 6.2.2	XXXX	2012a	Amended Final Report 1 and 2: [14C]S-2200 - Absorption, distribution, metabolism and excretion following repeated oral administration to the laying hen XXX Report No.: 8227547 XXXX. ROM-0040 GLP, unpublished	Y	XXXX
KCA 6.2.3	XXXX	2012b	Amended Final Report 1: [14C]S-2200 - Absorption, distribution, metabolism and excretion following repeated oral administration to the lactating ruminant XXXX Report No.: 8227546 XXXX. ROM-0039 GLP, unpublished	Y	XXXX
KCA 6.3	Delmotte, R.	2011	Magnitude of the Residue of S-2200 25% SC and its metabolites in Winter Rape Seed Raw Agricultural Commodity after foliar application – Northern and Southern Europe - 2010 Staphyt study no. FLN-10-6267 XXXX. ROR-0008 GLP, unpublished	N	XXXX
KCA 6.3	Lebrun, F.	2012	Magnitude of the Residue of S-2200 25% SC and its metabolites in Winter Rape Seed Raw Agricultural Commodity after foliar application – Northern and Southern Europe - 2011 SGS study no. IF-11/01898756 XXXX. ROR-0198 GLP, unpublished	N	XXXX

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<b>Data point</b>	<b>Author(s)</b>	<b>Year</b>	<b>Title Company Report No. Source (where different from company) GLP or GEP status Published or not</b>	<b>Vertebrate study Y/N</b>	<b>Owner</b>
KCA 6.5.1	Dixon, K. & Gilbert, J.	2011	[14C]S-2200: Nature of the Residue (High Temperature Hydrolysis) Study Covance Laboratories Ltd Report No.: 8239214 XXXX. ROM-0027 GLP, unpublished	N	XXXX
KCA 6.6.1	Panthani, A., Connor, S. & Malekani, K.	2011	Confined Rotational Crop Study with [ <sup>14</sup> C]S-2200 Smithers Viscient Report No.: 13048.6630 XXXX. ROM-0032 GLP, unpublished	N	XXXX
KCA 6.6.2	Roussel, Ch. H	2012	Rotational Field-Crops Residue Study after Application of S-2200 25 SC (25% w/v) to Winter Rapeseed STAPHYT, Report No: FLN-10-6268 XXXX. ROR-0202 GLP, unpublished	N	XXXX

\* XXXX).

## Appendix 2 Detailed evaluation of the additional studies relied upon

### A 2.1 Mandestrobin

#### A 2.1.1 Storage stability of residues in plant products

##### A 2.1.1.1 Study 1

Comments of zRMS:	<p>The study has been accepted.</p> <p>The study is very well documented. The objective of the study was to obtain data about the storage stability of mandestrobin and its metabolites De-Xy-S-2200, 4-OH-S-2200 and 2-CH<sub>2</sub>OH-S-2200 in dried beans (white seeds) and orange (whole fruit) under deep frozen conditions (<math>\leq -18\text{ }^{\circ}\text{C}</math>) over storage periods of up to 26 months.</p> <p>Storage samples allow assessment of storage stability, while procedural recoveries demonstrate the analytical performance of the method throughout the study. Sample extraction and determination of residues of mandestrobin, De-Xy-S-2200, 4-OH-S-2200 and 2-CH<sub>2</sub>OH-S-2200 was performed according to validated methods with quantification by use of LC-MS/MS. The LOQ of the analytical methods was 0.01 mg/kg for all analytes and matrices. The mean recoveries for samples extracted without any storage (i. e. day 0 storage samples) and the procedural recoveries performed on each testing date were within 70 % to 110 % with relative standard deviations <math>\leq 20\text{ }%</math> for all analytes and matrices. These values demonstrate satisfying analytical performance for all analytes and matrices while analysing the storage samples.</p> <p>For dried beans from the third month for analysis of 4-OH-S-2200 and 2-CH<sub>2</sub>OH-S-2200 the recovery data represent a successfully performed reduced validation set. The mean recovery at each fortification level was in the range of 70 - 110 % with a relative standard deviation of <math>\leq 20\text{ }%</math> for one evaluated LC-MS/MS mass transition for 4-OH-S-2200 and 2-CH<sub>2</sub>OH-S-2200 in dried beans.</p> <p>Furthermore, a full validation for De-Xy-S-2200, 4-OH-S-2200 and 2-CH<sub>2</sub>OH-S-2200 in orange (whole fruit) is included in this study. Recovery data of day 0 testing (n = 3) and procedural recoveries of 3 months and 6 months testing (n = 1, each) represent the validation data at the level of 10x LOQ (0.1 mg/kg). For recovery data at LOQ level (0.01 mg/kg) a separate analytical set was run within the study. The mean recovery at each fortification level was in the range of 70 - 110 % with a relative standard deviation of <math>\leq 20\text{ }%</math> for 2 evaluated LC-MS/MS mass transitions. For all combinations of analytes and matrices the average amount of analyte recovered relative to the initial recovery at day 0 was <math>\geq 70\text{ }%</math>, which can be seen as criterion for sufficient storage stability.</p> <p>Thus, stability was demonstrated for mandestrobin, De-Xy-S-2200, 4-OH-S-2200 and 2-CH<sub>2</sub>OH-S-2200 in homogenates of dried beans and orange (whole fruit) upon storage at <math>\leq -18\text{ }^{\circ}\text{C}</math> for 12 months and the stability of 4-OH-S-2200 and 2-CH<sub>2</sub>OH-S-2200 in homogenates of orange (whole fruit) was demonstrated upon storage at <math>\leq -18\text{ }^{\circ}\text{C}</math> for even 26 months.</p>
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Reference: KCA 6.1

Report Storage Stability of Residues of Mandestrobin and its Metabolites De-Xy-S-2200, 4-OH-S-2200 and 2-CH<sub>2</sub>OH-S-2200 in Dried Beans and Orange Fruit, Lindner M., Grewe D., Leischow, J., 2017, Eurofins Report no. S15-01208,

	XXXX reference no. ROR-0286
Guideline(s):	EC working document 7032/VI/95 (rev. 5): Appendix H - Storage Stability of Residue Samples OECD 506 - Stability of Pesticide Residues in Stored Commodities (16.10.2007) EPA OPPTS 860.1380 - Storage Stability Data (August 1996)
Deviations:	No
GLP:	Yes
Acceptability:	Yes (New data not previously reviewed at EU level, but submitted and accepted in support of the Mandestrobin 25SC product authorisation (SEU zRMS: France, 2019))

## Materials and methods

The freezer storage stability of mandestrobin and its metabolites De-Xy-S-2200, 4-OH-S-2200 and 2-CH<sub>2</sub>OH-S-2200 residues was determined for dried beans and orange (whole fruit). Aliquots of homogenised matrix material (5 - 20 g) were transferred into a glass bottle with screw cap (De-Xy-S-2200, 4-OH-S-2200 and 2-CH<sub>2</sub>OH-S-2200) or a 50 mL Sarstedt tube (mandestrobin) and fortified with the test item at a level of 0.1 mg/kg. Stored samples of mandestrobin and De-Xy-S-2200 were fortified individually whereas 4-OH-S-2200 and 2-CH<sub>2</sub>OH-S-2200 were combined. The samples were stored at ≤-18°C for intervals of 1, 3, 6, 9, 12 and 26 (analysis of 4-OH-S-2200 and 2-CH<sub>2</sub>OH-S-2200 in orange only) months until analysis.

Analysis was undertaken using the validated analytical methods SCA-1203V (mandestrobin), SUM-1023V (De-Xy-S-2200), SUM-1021V (4-OH-S-2200) and SUM-1022V (2-CH<sub>2</sub>OH-S-2200). The methods have been validated with an LOQ of 0.01 mg/kg and procedural recoveries for all of the analyses, using a fortification level of 0.1 mg/kg were in the range of 92-109% for mandestrobin, 72-97% for De-Xy-S-2200, 79-107% for 4-OH-S-2200 and 80-96% for 2-CH<sub>2</sub>OH-S-2200.

## Results and discussions

The stability of residues of mandestrobin and its metabolites De-Xy-S-2200, 4-OH-S-2200 and 2-CH<sub>2</sub>OH-S-2200 under frozen storage conditions (≤ -18°C) is summarised in the Table below.

**Table A 1:** Summary of storage stability data for mandestrobin and the metabolites De-Xy-S-2200, 4-OH-S-2200 and 2-CH<sub>2</sub>OH-S-2200 in dried bean and whole orange at ≤ -18°C

Matrix	Fortification level (mg/kg)	Storage period (months)	Stored residues (mg/kg)	Individual recoveries (%)	Mean stored recovery (%)	Procedural recoveries (%)	Recovery of day-0
<b>Mandestrobin</b>							
Dried bean white seed	0.1	0	0.087, 0.094, 0.096	87, 94, 96	92	-	100
		1	0.097, 0.099	97, 99	98	95	107
		3	0.107, 0.105	107, 105	106	109	115
		6	0.088, 0.082	88, 82	85	95	92
		9	0.086, 0.082	86, 82	84	97	91
		12	0.097, 0.097	97, 97	97	106	105
Orange whole fruit	0.1	0	0.088, 0.091, 0.087	88, 91, 87	89	-	100
		1	0.093, 0.101	93, 101	97	97	109
		3	0.088, 0.085	88, 85	87	92	98

Matrix	Fortification level (mg/kg)	Storage period (months)	Stored resi- dues (mg/kg)	Individual recoveries (%)	Mean stored recovery (%)	Procedural recoveries (%)	Recovery of day-0
		6	0.092, 0.094	92, 94	93	101	104
		9	0.102, 0.102	102, 102	102	106	115
		12	0.105, 0.106	105, 106	106	108	119
De-Xy-S-2200							
Dried bean white seed	0.1	0	0.088, 0.090, 0.087	88, 90, 87	88	-	100
		1	0.072, 0.075	72, 75	74	78	84
		3	0.074, 0.076	74, 76	75	73	85
		6	0.091, 0.089	91, 89	90	72	102
		9	0.112, 0.112	112, 112	112	94	127
		12	0.107, 0.108	107, 108	108	90	122
Orange whole fruit	0.1	0	0.090, 0.084, 0.087	90, 84, 87	87	-	100
		1	0.072, 0.077	72, 77	75	78	86
		3	0.082, 0.074	81, 74	78	83	90
		6	0.104, 0.099	104, 99	102	76	117
		9	0.107, 0.112	107, 112	110	97	126
		12	0.108, 0.104	108, 104	106	90	122
4-OH-S-2200							
Dried bean white seed	0.1	0	0.076, 0.064, 0.073	76, 64, 73	71	-	100
		1	(a)	(a)	(a)	(a)	(a)
		3	0.082, 0.072	82, 72	77	81, 79, 83	108
		6	0.086, 0.086	86, 86	86	85	121
		9	0.084, 0.079	84, 79	82	94	115
		12	0.084, 0.080	84, 80	82	101	115
Orange whole fruit	0.1	0	0.074, 0.081, 0.089	74, 81, 89	81	-	100
		1	(a)	(a)	(a)	(a)	(a)
		3	0.086, 0.086	86, 86	86	89	106
		6	0.084, 0.082	84, 82	83	97	102
		9	0.095, 0.077	95, 77	86	107	106
		12	0.073, 0.077	73, 77	75	90	93
		26	0.091, 0.092	91, 92	92	100	113
2-CH <sub>2</sub> OH-S-2200							
Dried bean white seed	0.1	0	0.097, 0.094, 0.098	97,94, 98	96	-	100
		1	(a)	(a)	(a)	(a)	(a)
		3	0.092, 0.088	92, 88	90	95, 83, 92	94
		6	0.098, 0.099	98, 99	99	96	103
		9	0.086, 0.092	86, 92	89	80	93
		12	0.089, 0.088	89, 88	89	94	93
Orange whole fruit	0.1	0	0.090,0.089, 0.094	90, 89, 94	91	-	100
		1	(a)	(a)	(a)	(a)	(a)
		3	0.088, 0.080	88, 80	84	80	92
		6	0.081, 0.092	81, 92	87	89	95

Matrix	Fortification level (mg/kg)	Storage period (months)	Stored residues (mg/kg)	Individual recoveries (%)	Mean stored recovery (%)	Procedural recoveries (%)	Recovery of day-0
		9	0.083, 0.077	83, 77	80	90	88
		12	0.092, 0.092	92, 92	92	90	101
		26	0.097, 0.090	97, 90	94	90	103

<sup>(a)</sup> Because of a mistake in the lab, procedural recoveries were outside the acceptance criteria and one month data cannot be used for assessment of storage stability

## Conclusion

The storage stability data show that mandestrobin and its metabolites De-Xy-S-2200, 4-OH-S-2200 and 2-CH<sub>2</sub>OH-S-2200 are stable in representative high protein (dry bean) and high acid (orange whole fruit) content commodities for at least 12 months when stored frozen at -18°C. Additionally, storage stability was demonstrated for residues of 4-OH-S-2200 and 2-CH<sub>2</sub>OH-S-2200 in orange (whole fruit) when stored frozen (< -18°C) for at least 26 months.

### A 2.1.1.2 Study 2

Comments of zRMS:	<p>The study has been accepted.</p> <p>To determine mandestrobin (isomers S-2167 and S-2354) and metabolites De-Xy-S-2200, 4-OH-S-2200, 2-CH<sub>2</sub>OH-S-2200 and 5-CH<sub>2</sub>OH-S-2200 stability in honey samples were fortified with each analyte at 0.1 mg/kg, placed into frozen storage (≤ -18°C) and analysed for residues of each analyte following 150-155 days of frozen storage. This determination was done in conjunction with the field studies carried out to determine the magnitude of residues in honey. The procedural recoveries performed on each testing date were within acceptable range with relative standard deviations ≤ 20 % for all analytes.</p> <p>The detailed data is presented below by the applicant.</p>
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Reference:	KCA 6.1
Report	<p>Antón, B. (2022)</p> <p>Determination of Residues of Mandestrobin and its Metabolites in Honey, after One Application of Mandestrobin 25 SC in <i>Phacelia tanacetifolia</i> under semi-field conditions, at 4 Sites in Central and Southern Europe in 2021</p> <p>Report No. S21-01066</p> <p>XXXX ref: ROR-0307</p>
Guideline(s):	<p>EC Guidance document 7029/VI/95 rev. 5</p> <p>SANTE/11956/2016 rev. 9</p> <p>SANTE/2020/12830 rev. 1</p>
Deviations:	No
GLP:	Yes (conducted under GLP/Officially recognised testing facilities)
Acceptability:	Yes (New data not previously reviewed at EU level, but submitted for mandestrobin renewal of approval (AIR6 dossier) in December 2022)

## Executive summary

The freezer storage stability of mandestrobin (isomers S-2167 and S-2354) and metabolites De-Xy-S-2200, 4-OH-S-2200, 2-CH<sub>2</sub>OH-S-2200 and 5-CH<sub>2</sub>OH-S-2200 was determined in honey samples. This investigation was done in conjunction with the field studies carried out to determine the magnitude of residues in

honey.

Samples were fortified with each analyte at 0.1 mg/kg and placed in to frozen storage ( $\leq -18^{\circ}\text{C}$ ). Samples of honey were analysed for residues of each analyte following 150-155 days of frozen storage. Analysis was conducted according to the analytical methods validated in the same study, with the LOQ of 0.005 mg/kg for mandestrobin (S-2167 and S-2354), and 0.01 mg/kg for metabolites De-Xy-S-2200, 4-OH-S-2200, 2-CH<sub>2</sub>OH-S-2200 and 5-CH<sub>2</sub>OH-S-2200.

Under the conditions of the study, residues of mandestrobin (S-2167 and S-2354) and metabolites De-Xy-S-2200, 4-OH-S-2200, 2-CH<sub>2</sub>OH-S-2200 and 5-CH<sub>2</sub>OH-S-2200 in honey were shown to be stable for at least 150 days when stored at  $-18^{\circ}\text{C}$  or below.

## Materials and methods

Test material 1:	S-2200 (R-isomer – S-2167)
Description:	Analytical standard
Lot/Batch#:	060020652
Purity:	100%
CAS#:	Not reported
Fortification level:	0.1 mg/kg

Test material 2:	S-2200 (S-isomer – S-2354)
Description:	Analytical standard
Lot/Batch#:	060020653
Purity:	99.8%
CAS#:	Not reported
Fortification level:	0.1 mg/kg

Test material 3:	De-Xy-S-2200
Description:	Analytical standard
Lot/Batch#:	CTS08001
Purity:	100%
CAS#:	Not reported
Fortification level:	0.1 mg/kg

Test material 4:	4-OH-S-2200
Description:	Analytical standard
Lot/Batch#:	CTS10004
Purity:	99.9%
CAS#:	Not reported
Fortification level:	0.1 mg/kg

Test material 5:	2-CH <sub>2</sub> OH-S-2200
Description:	Analytical standard
Lot/Batch#:	CTS10005
Purity:	98.3%
CAS#:	Not reported
Fortification level:	0.1 mg/kg

Test material 6: 5-CH<sub>2</sub>OH-S-2200  
 Description: Analytical standard  
 Lot/Batch#: 118-110422-1  
 Purity: 99.9%  
 CAS#: Not reported  
 Fortification level: 0.1 mg/kg

Test commodity:  
 Crop: Honey  
 Sample size: 2-2.5 g

Homogenised samples were fortified with mandestrobin (isomers S-2167 and S-2354) and metabolites De-Xy-S-2200, 4-OH-S-2200, 2-CH<sub>2</sub>OH-S-2200 and 5-CH<sub>2</sub>OH-S-2200 at 0.1 mg/kg, and deep frozen at ≤ -18°C. Samples were analysed for each analyte in triplicate on the day of storage initiation and following 150-155 days of storage at -18°C or below.

Samples were analysed using the analytical method validated as part of this study. The limit of quantitation (LOQ) was 0.005 mg/kg for S-2167 and S-2354, and 0.01 mg/kg for De-Xy-S-2200, 4-OH-S-2200, 2-CH<sub>2</sub>OH-S-2200 and 5-CH<sub>2</sub>OH-S-2200.

## Results and discussions

The data indicate that when frozen samples of honey, intended for residue analyses, are stored for 150-155 days at -18°C or below, acceptable storage stability can be expected for all analytes. Results are presented in the table below.

**Table A 2: Storage Stability mandestrobin (enantiomers S-2167 and S-2354) and its metabolites (De-Xy-S-2200, 4-OH-2200, 2-CH<sub>2</sub>OH-S-2200 and 5-CH<sub>2</sub>OH-S-2200) metabolites in honey samples at ≤ -18°C**

Storage Period	Procedural Recoveries		Storage Samples			
	Single Values (%)	Mean (%) <sup>a</sup> in brackets: RSD (%)	Percentage of analyte found relative to the nominal fortification level (%)		Percentage recovered <sup>a</sup> [corrected for the (mean) procedural recovery of the individual date of extraction]	Percentage recovered <sup>a</sup> [relative to the mean percentage recovered at Day 0]
			Single Values <sub>b</sub>	Mean <sup>a</sup> in brackets: RSD (%)		
S-2167						
0 days	-	-	80, 82, 84	82 (2.3)	-	-
Testing Interval (155 days)	91, 94, 91*	92 (2.2)	88, 85, 86	87 (1.8)	94	105
S-2354						
0 days	-	-	86, 85, 86	85 (0.7)	-	-
Testing Interval (155 days)	89, 92, 87*	89 (2.5)	90, 83, 85	86 (4.5)	96	101
De-Xy-S-2200						
0 days	-	-	100, 100, 99	100 (1.0)	-	-
Testing Interval (155 days)	104, 102, 102	103 (1.2)	109, 109, 113	110 (1.9)	107	111
4-OH-S-2200						
0 days	-	-	102, 95, 98	98 (3.9)	-	-



Testing Interval (154 days)	99, 102, 96	99 (2.7)	101, 102, 102	102 (0.7)	103	103
<b>2-CH<sub>2</sub>OH-S-2200</b>						
0 days	-	-	79, 80, 78	79 (1.1)	-	-
Testing Interval (154 days)	100, 99, 97	98 (1.7)	101, 100, 96	99 (2.7)	101	125
<b>5-CH<sub>2</sub>OH-S-2200</b>						
0 days	-	-	83, 81, 81	82 (1.4)	-	-
Testing Interval (150 days)	98, 98, 97	98 (0.7)	101, 103, 103	102 (0.9)	105	125

<sup>a</sup> calculated from unrounded values; <sup>b</sup> not corrected for procedural recoveries

\* procedural recoveries were fortified at 0.05 mg/kg

### Conclusion

The storage stability of Mandestrobin (isomers S-2167 and S-2354) and metabolites De-Xy-S-2200, 4-OH-S-2200, 2-CH<sub>2</sub>OH-S-2200 and 5-CH<sub>2</sub>OH-S-2200 was investigated in honey samples.

Residues of all analytes were found to be stable in honey when stored frozen (< -18°C) for at least 150 days.

#### A 2.1.2 Storage stability of residues in animal products

No new data were submitted in the framework of this submission.

#### A 2.1.3 Nature of residue in primary crops

No new data were submitted in the framework of this submission.

#### A 2.1.4 Nature of residue in rotational crops

No new data were submitted in the framework of this submission.

#### A 2.1.5 Nature of residues in processed commodities

No new data were submitted in the framework of this submission.

#### A 2.1.6 Nature of residues in livestock

No new data were submitted in the framework of this submission.

#### A 2.1.7 Magnitude of residues in plants

No new data were submitted in the framework of this submission.

#### A 2.1.8 Magnitude of residues in livestock

No new data were submitted in the framework of this submission.

## **A 2.1.9 Magnitude of residues in processed commodities (Industrial Processing and/or Household Preparation)**

### **A 2.1.9.1 Distribution of the residue in peel/pulp**

No new data were submitted in the framework of this submission.

### **A 2.1.9.2 Processing studies on a core set of representative processes**

No new data were submitted in the framework of this submission.

### **A 2.1.10 Magnitude of residues in representative succeeding crops**

No new data were submitted in the framework of this submission.

### **A 2.1.11 Other/Special Studies**

#### **A 2.1.11.1 Effect on the residue level in pollen and bee products**

Comments of zRMS:	<p>The study has been accepted.</p> <p>The methodologies for residues extraction and analysis (detection by LC-MS/MS) were adjusted and validated according to SANTE/2020/12830 Rev.1. for the determination of mandestrobin (enantiomers S-2167 and S-2354) and its metabolites (De-Xy-S-2200, 4-OH-2200, 2-CH<sub>2</sub>OH-S-2200 and 5-CH<sub>2</sub>OH-S-2200) in honey matrix. The LOQ of the analytical method for S-2167 and S-2354 was 0.005 mg/kg, with a LOD set at 0.001 mg/kg (20 % of the LOQ). The LOQ of the analytical method for De-Xy-S-2200, 4-OH-2200, 2-CH<sub>2</sub>OH-S-2200 and 5-CH<sub>2</sub>OH-S-2200 was 0.01 mg/kg, with a LOD set at 0.002 mg/kg (20 % of the LOQ).</p> <p>No residues of mandestrobin and its metabolites were detected at or above the LOD in any of the untreated specimens.</p> <p>A sufficient study description by the applicant is presented below.</p>
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Reference: 6.10.1

Report Antón, B. (2022)  
Determination of Residues of Mandestrobin and its Metabolites in Honey, after One Application of Mandestrobin 25 SC in *Phacelia tanacetifolia* under semi-field conditions, at 4 Sites in Central and Southern Europe in 2021  
Report No. S21-01066  
XXXX ref: ROR-0307

Guideline(s): EC Guidance document 7029/VI/95 rev. 5  
SANTE/11956/2016 rev. 9  
SANTE/2020/12830 rev. 1

Deviations: trial -04 : Sampling of treated honey could not be performed. There was insufficient honey production to complete the analysis due to adverse weather conditions. The trial was repeated with new phase code S21-01066-05, for which a sufficient sample was obtained to complete the analysis. Deviation has no impact on the integrity of the study.

GLP: Yes

Acceptability: Yes (New data not previously reviewed at EU level, but submitted for mandestrobin renewal of approval (AIR6 dossier) in December 2022)

### Executive summary

A total of four residue trials were conducted on *Phacelia tanacetifolia* in tunnels under semi-field conditions across northern and southern Europe (2 trials in Spain and 2 trials in Germany), in 2021. In each trial, a single foliar spray application of the formulation Mandestrobin 25 SC (250 g/L Mandestrobin) was made at a nominal application rate of 0.2 kg as/ha. The application was made at BBCH 63-65. Honeybee colonies were used to produce the requisite amounts of honey and samples of mature honey were collected at honey maturity (10 to 30 days after application (DAA)), or at the end of the flowering, once the honey matured at the monitoring site (6 days after application).

Samples were frozen on dry ice shortly after the sampling, and were stored deep frozen ( $\leq -18\text{ }^{\circ}\text{C}$ ) until analysis. Samples were stored for a maximum of 147 days prior to analysis.

Residues of mandestrobin (enantiomers S-2167 and S-2354) and its metabolites (De-Xy-S-2200, 4-OH-2200, 2-CH<sub>2</sub>OH-S-2200 and 5-CH<sub>2</sub>OH-S-2200) were analysed individually using LC-MS/MS. The analytical methods used were fully validated as part of this study. The limit of quantification (LOQ) of the analytical method for S-2167 and S-2354 residues determination in honey was 0.005 mg/kg, with a limit of detection (LOD) set at 0.001 mg/kg. The LOQ of the analytical method for De-Xy-S-2200, 4-OH-2200, 2-CH<sub>2</sub>OH-S-2200 and 5-CH<sub>2</sub>OH-S-2200 residues determination in honey was 0.01 mg/kg, with a LOD set at 0.002 mg/kg.

No residues of mandestrobin and its metabolites were detected at or above the LOD in any of the untreated samples.

Residues of mandestrobin (enantiomers S-2167 and S-2354) above the LOQ were found only in one of the treated samples. Residues ranged between  $< \text{LOD}$  to 0.01 mg/kg.

No residues of metabolites De-Xy-S-2200, 4-OH-2200, 2-CH<sub>2</sub>OH-S-2200 or 5-CH<sub>2</sub>OH-S-2200 were detected at or above the LOD in any of the treated samples.

### Materials and methods

Test material 1:	Mandestrobin 25 SC
Description:	Soluble concentrate
Lot/Batch#:	B9120962
Active substance content:	250 g/L (nominal), $249.9 \pm 0.9$ g/L (certified)
Expiry date:	08 July 2022
Development code	S-2200 (mandestrobin)
Test commodity:	
Crop:	<i>Phacelia tanacetifolia</i>
Type:	Flowering plant
Variety:	Stala and Angelia
Botanical name:	<i>Phacelia tanacetifolia</i> , EPPO: PHCTA
Crop part:	Honey from honeybee colonies ( <i>Apis mellifera</i> L.)
Sample size:	Honey: 25-86 g

A total of four residue trials were conducted on *Phacelia tanacetifolia* in northern (2 trials) and southern Europe (2 trials). The minimum distance between test sites was 24 km. All trials were performed in tunnels under semi-field conditions. Each trial consisted of two plots: a control (untreated) plot and a treated plot receiving one foliar application of Mandestrobin 25SC at a nominal rate of 0.2 kg as/ha. Applications were made at BBCH 63-65, with target water volumes of 400 L/ha. No adjuvants or spray additives were added to the spray mixture.

In all trials, the plot area covered by tunnels was 200 m<sup>2</sup> (40 m x 5 m). The crop area was approximately 163-169 m<sup>2</sup>. The tunnel design and dimensions are presented in the figure below.

**Figure A 1: Design of tunnels used to generate honey samples following application of Mandestrobin on *phacelia tanacetifolia* under semi-field conditions**

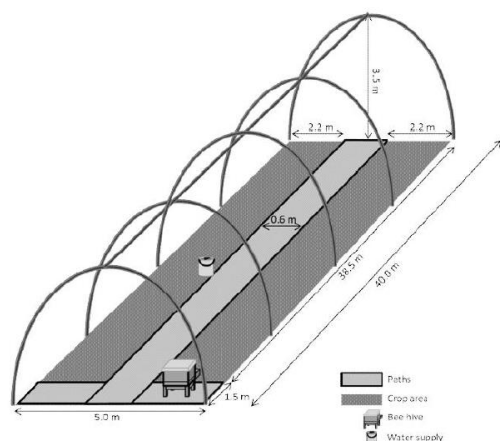


Figure 1. Tunnels design trials -01 and -02

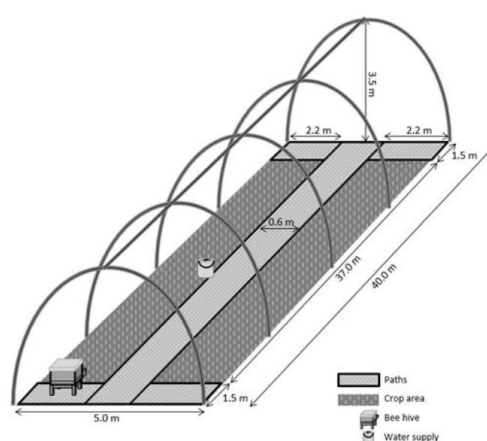


Figure 2. Tunnels design trials -03 and -05

Honeybee colonies (*Apis mellifera* L.) with a sufficient number of forager bees were used as a sampling device to produce the requisite amounts of honey.

All hives were equipped with a queen exclusion chamber to decrease brood production and to increase the space for honey storage. For all hives a colony assessment was performed prior to setup (0-3 days before setup of hives; assessment 1) and at the end of the trial (0-5 days after sampling of honey; assessment 2) recording the following parameters:

- Strength of the colony (percent area covered with bees)
- Presence of a healthy queen (i.e. presence of eggs or presence of queen cells)
- Visual assessment – number of cells containing pollen, nectar and brood
- Presence/absence of Varroa and/or other bee diseases

The colony strength across all trials varied from 7085 to 13787 bees (assessment 1) and 3,770 to 11,570 bees (assessment 2).

Hives were setup inside tunnels the evening before application. The water containers were removed from the tunnels during application and the honeybee colonies were covered with a plastic sheet until the end of application to avoid direct contamination. For trials -01, -02 and -05 sampling was performed at the field sites, before the end of the flowering. For trial -03, the colonies remained in the tunnels until the end of the flowering period due to fast crop development, therefore, the colonies were moved to the monitoring site 5 DAA during the early morning. On the next day, the water content of the honey was checked to be < 20 % (determined using a digital refractometer), and the mature honey was collected.

Honey was collected 6-30 DAA as a separate sample from each tunnel of each trial. Honey was sampled by gently pushing a spoon into the walls of the storage cells and allowing the honey to flow onto the spoon. Treated and untreated specimens were chilled on dry ice directly after sampling, and were transported to the freezer at the Test Facility/Test Site within a period < 5 hours after sampling.

Residues of mandestrobin (enantiomers S-2167 and S-2354) and its metabolites (De-Xy-S-2200, 4-OH-2200, 2-CH<sub>2</sub>OH-S-2200 and 5-CH<sub>2</sub>OH-S-2200) were analysed individually using LC-MS/MS. The analytical methods used were validated according to EU guidance (SANTE/2020/12830 rev.1) for the determination of residues in honey as part of this study. The analytical method was applied successfully for each analytical set when analysing the samples of the study (S21-01066-L1 (TRC-2101)). The validated LOQ was 0.005 mg/kg for each enantiomer S-2167 and S-2354, and 0.01 mg/kg for De-Xy-S-2200, 4-OH-2200, 2-CH<sub>2</sub>OH-S-2200 and 5-CH<sub>2</sub>OH-S-2200. The performance of the method was verified by obtaining procedural recoveries which were in the acceptable range of 70-120%.

A summary of the procedural recovery results is presented in the table below.

**Table A 3:** Summary of procedural recoveries in honey for mandestrobin (enantiomers S-2167 and S-2354) and its metabolites (De-Xy-S-2200, 4-OH-2200, 2-CH<sub>2</sub>OH-S-2200 and 5-CH<sub>2</sub>OH-S-2200)

Mass transition ( <i>m/z</i> )	Fortification level (mg/kg)	Summary of recoveries			
		Number of samples (n)	Range (%)	Mean (%)	RSD (%)
Mandestrobin <i>R</i> - isomer (S-2167)					
m/z 314→192*	0.005	5	90-94	92	1.8
	0.05	5	83-89	87	2.7
m/z 314→132	0.005	5	88-99	92	4.5
	0.05	5	83-88	86	2.1
Mandestrobin <i>S</i> -isomer (S-2354)					
m/z 314→192*	0.005	5	87-92	90	2.0
	0.05	5	83-89	86	3.3
m/z 314→132	0.005	5	86-92	89	2.7
	0.05	5	83-89	86	3.3
De-Xy-S-2200					
m/z 210→119*	0.01	5	92-104	97	5.6
	0.1	5	96-101	98	2.4
m/z 210→192	0.01	5	99-102	101	1.0
	0.1	5	95-102	100	2.9
4-OH-S-2200					
m/z 330→192*	0.01	5	104-109	107	2.1
	0.1	5	94-112	102	7.7
m/z 330→160	0.01	5	102-110	106	2.7
	0.1	5	95-116	103	10
2-CH <sub>2</sub> OH-S-2200					
m/z 312→192*	0.01	5	84-101	94	6.5
	0.1	5	79-103	88	12
m/z 12→119	0.01	5	81-100	89	8.6
	0.1	5	70-95	83	12
5-CH <sub>2</sub> OH-S-2200					
m/z 312→192*	0.01	5	80-92	86	5.9
	0.1	5	70-92	76	13
m/z 312→119	0.01	5	90-103	94	5.7
	0.1	5	74-94	81	10

\* Proposed to be used for quantification

All calculations are based on unrounded values

Recoveries are corrected for the (mean) peak area(s) of the control sample extract(s)

Samples were stored for a maximum of 147 days prior to analysis. Storage stability data for mandestrobin and its metabolites in honey was also generated as part of the study.

## Results and discussions

A summary of the residue results is given in the table below.

Residues of mandestrobin and its metabolites were all below the LOD (and < LOQ) in all untreated control samples.

Residues of mandestrobin (enantiomers S-2167 and S-2354) above the LOQ were found only in one of the treated samples. Residues ranged between < LOD to 0.01 mg/kg.

No residues of metabolites De-Xy-S-2200, 4-OH-2200, 2-CH<sub>2</sub>OH-S-2200 and 5-CH<sub>2</sub>OH-S-2200 were detected at or above the LOD in any of the treated samples.

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**Table A 4: Summary of residue trials for honey following application of Mandestrobin on *phacelia tanacetifolia* under semi-field conditions**

Trial No./ Location/ EU zone/ Year	Commodity/ Variety	Date of 1.Sowing or planting 2.Flowering 3. Harvest	Application rate per treatment			Dates of treatment or no. of treatments and last date (inter- val)	Growth stage at last treat- ment or date	Portion ana- lysed	Residues (mg/kg)						PHI (days)	Details on trial
			kg as/ha	Water (L/ha)	kg as/hL				S-2167	S-2354	De-Xy- S- 2200	4-OH-S- 2200	2-CH <sub>2</sub> OH- S-2200	5-CH <sub>2</sub> OH- S-2200		
(a)		(b)				(c)								(f)	(d)	(e)
Trial S21-01066-01 46220, Picassent, Valencia, Spain SEU 2021	<i>Phacelia tanacetifolia</i> / Stala	1. Naturally emergent 2. Apr-May 2021 3. Not re-ported	0.200	401	0.05	14 Apr 2021	BBCH 63	Honey	< 0.005	< 0.005	< 0.01	< 0.01	< 0.01	< 0.01	30	Semi-field (plastic tunnel) trial LOQ of mandestrobin (S-2167 and S-2354): 0.005 mg/kg for each enantiomer LOQ of metabolites (De-Xy-S-2200, 4-OH-S-2200, 2-CH <sub>2</sub> OH-S-2200 and 5-CH <sub>2</sub> OH-S-2200): 0.01 mg/kg for each compound Max. storage:
Trial S21-01066-02 02640, Almansa, Albacete, Spain SEU 2021	<i>Phacelia tanacetifolia</i> / Stala	1. 07 May 2021 2. Jun-Jul 2021 3. Not re-ported	0.211	422	0.05	02 Jul 2021	BBCH 63	Honey	0.01	0.01	< 0.01	< 0.01	< 0.01	< 0.01	7	
Trial S21-01066-03 76297, Stutensee, Baden-Württemberg, Germany NEU 2021	<i>Phacelia tanacetifolia</i> / Stala	1. 03 Mar 2021 2. May-Jun 2021 3. Not re-ported	0.201	402	0.05	10 Jun 2021	BBCH 65	Honey	< 0.005	< 0.005	< 0.01	< 0.01	< 0.01	< 0.01	6	147 days for sample 6 days for extracts

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Trial No./ Location/ EU zone/ Year	Commodity/ Variety	Date of 1.Sowing or planting 2.Flowering 3. Harvest	Application rate per treatment			Dates of treatment or no. of treatments and last date (inter- val)	Growth stage at last treat- ment or date	Portion ana- lysed	Residues (mg/kg)						PHI (days)	Details on trial
			kg as/ha	Water (L/ha)	kg as/hL				S-2167	S-2354	De-Xy- S- 2200	4-OH-S- 2200	2-CH <sub>3</sub> OH- S-2200	5-CH <sub>3</sub> OH- S-2200 (f)		
	(a)	(b)				(c)									(d)	(e)
Trial S21-01066-05 75177, Pforzheim, Baden-Württem- berg, Germany NEU 2021	<i>Phacelia tanacetifolia</i> / Angelia	1. 28 May 2021 2. Jul-Aug 2021 3. Not re- ported	0.204	407	0.05	27 Jul 2021	BBCH 63	Honey	< 0.005	< 0.005	< 0.01	< 0.01	< 0.01	< 0.01	10	

(a): According to CODEX Classification / Guide

(b): Only if relevant

(c): Year must be indicated

(d): Days after last application (Label pre-harvest interval, PHI, underline)

(e): Remarks may include: Climatic conditions; Reference to analytical method and information which metabolites are included



## Conclusion


A total of four independent residue trials across northern and southern Europe have been performed to measure residues in honey after foraging of bees on treated *Phacelia tanacetifolia*.

In accordance with EU technical guidelines (SANTE/11956/2016 rev. 9) a minimum of four trials is required, which is the case here.

All trials were conducted according to the intended cGAP application rate (1 x 0.2 kg as/ha) for the melliferous crops under consideration (i.e. oilseed rape). Therefore, these trials can be used to support the intended GAP.

## Appendix 3 Pesticide Residue Intake Model (PRIMo)

### A 3.1 IEDI calculations



European Food Safety Authority  
EFSA PRIMo revision 3.1; 2019/03/19

**Mandestrobin (F)**

LOQs (mg/kg) range from: **0.01** to: **0.05**

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**Toxicological reference values**

ADI (mg/kg bw/day): **0.19** ARID (mg/kg bw): **insert valid entry**

Source of ADI: **EFSA** Source of ARID:

Year of evaluation: **2015** Year of evaluation:

Input values

Details - chronic risk assessment

Supplementary results - chronic risk assessment

Details - acute risk assessment/children

Details - acute risk assessment/adults

Comments:

Normal mode

Chronic risk assessment: JMPR methodology (IEDI/TMDI)

				No of diets exceeding the ADI : ---					Exposure resulting from		
	Calculated exposure (% of ADI)	MS Diet	Exposure (µg/kg bw per day)	Highest contributor to MS diet (in % of ADI)	Commodity / group of commodities	2nd contributor to MS diet (in % of ADI)	Commodity / group of commodities	3rd contributor to MS diet (in % of ADI)	Commodity / group of commodities	MRLs set at the LOQ (in % of ADI)	commodities not under assessment (in % of ADI)
TMDI(NED) calculation (based on average food consumption)	2%	PT general	4.28	2%	Wine grapes	0.2%	Table grapes	0.1%	Peaches	0.1%	
	2%	NL toddler	4.03	1%	Table grapes	0.3%	Milk: Cattle	0.2%	Strawberries	0.6%	0.0%
	2%	FR adult	3.80	2%	Wine grapes	0.1%	Table grapes	0.1%	Strawberries	0.1%	0.0%
	2%	DE child	3.58	1%	Table grapes	0.3%	Strawberries	0.1%	Cherries (sweet)	0.3%	0.0%
	2%	RO general	3.18	1%	Wine grapes	0.1%	Table grapes	0.1%	Milk: Cattle	0.2%	
	2%	GEMS/Food G07	3.11	1%	Wine grapes	0.2%	Table grapes	0.0%	Peaches	0.2%	0.0%
	1%	IE adult	2.84	0.9%	Wine grapes	0.2%	Table grapes	0.1%	Strawberries	0.2%	
	1%	NL child	2.66	0.8%	Table grapes	0.2%	Strawberries	0.1%	Milk: Cattle	0.3%	0.0%
	1%	GEMS/Food G08	2.56	0.8%	Wine grapes	0.2%	Table grapes	0.1%	Peaches	0.2%	0.0%
	1%	GEMS/Food G11	2.56	0.7%	Wine grapes	0.3%	Table grapes	0.0%	Strawberries	0.2%	
	1%	GEMS/Food G15	2.48	0.7%	Wine grapes	0.2%	Table grapes	0.0%	Milk: Cattle	0.2%	0.0%
	1%	DE women 14-50 yr	2.26	0.6%	Wine grapes	0.2%	Table grapes	0.1%	Milk: Cattle	0.2%	0.0%
	1%	GEMS/Food G06	2.23	0.8%	Table grapes	0.1%	Peaches	0.0%	Wine grapes	0.2%	0.0%
	1%	DE general	2.15	0.6%	Wine grapes	0.2%	Table grapes	0.1%	Milk: Cattle	0.2%	0.0%
	1%	FR child 3-15 yr	1.90	0.3%	Wine grapes	0.3%	Table grapes	0.1%	Milk: Cattle	0.3%	0.0%
	1.0%	DK adult	1.83	0.7%	Wine grapes	0.1%	Table grapes	0.0%	Strawberries	0.1%	
	0.9%	UK adult	1.77	0.8%	Wine grapes	0.0%	Table grapes	0.0%	Strawberries	0.1%	
	0.9%	NL general	1.62	0.4%	Wine grapes	0.2%	Table grapes	0.0%	Milk: Cattle	0.2%	0.0%
	0.8%	GEMS/Food G10	1.61	0.3%	Wine grapes	0.2%	Table grapes	0.1%	Strawberries	0.2%	0.0%
	0.8%	UK vegetarian	1.48	0.6%	Wine grapes	0.1%	Table grapes	0.0%	Strawberries	0.1%	
	0.6%	FR toddler 2-3 yr	1.08	0.2%	Wine grapes	0.2%	Milk: Cattle	0.1%	Strawberries	0.3%	0.0%
	0.6%	UK toddler	1.07	0.2%	Table grapes	0.1%	Milk: Cattle	0.1%	Strawberries	0.2%	
	0.6%	ES adult	1.07	0.3%	Wine grapes	0.1%	Peaches	0.0%	Table grapes	0.1%	
	0.5%	FI adult	1.03	0.2%	Wine grapes	0.1%	Coffee beans	0.1%	Strawberries	0.2%	0.0%
	0.5%	UK infant	1.00	0.2%	Milk: Cattle	0.1%	Strawberries	0.0%	Apricots	0.3%	
	0.5%	FI 3 yr	0.93	0.2%	Strawberries	0.2%	Table grapes	0.0%	Peaches	0.1%	0.0%
	0.5%	DK child	0.87	0.1%	Table grapes	0.1%	Strawberries	0.1%	Milk: Cattle	0.2%	0.0%
	0.4%	FI 6 yr	0.72	0.1%	Strawberries	0.1%	Table grapes	0.0%	Peaches	0.1%	0.0%
	0.4%	IT toddler	0.72	0.1%	Peaches	0.1%	Table grapes	0.1%	Strawberries	0.1%	
	0.4%	ES child	0.68	0.1%	Milk: Cattle	0.1%	Peaches	0.0%	Strawberries	0.2%	
	0.3%	PL general	0.66	0.2%	Table grapes	0.0%	Cherries (sweet)	0.0%	Potatoes	0.0%	
	0.3%	IT adult	0.65	0.1%	Peaches	0.1%	Table grapes	0.0%	Apricots	0.1%	
	0.3%	SE general	0.64	0.1%	Strawberries	0.1%	Milk: Cattle	0.0%	Peaches	0.2%	
	0.3%	FR infant	0.53	0.1%	Milk: Cattle	0.1%	Strawberries	0.0%	Wine grapes	0.2%	0.0%
	0.1%	LT adult	0.23	0.0%	Milk: Cattle	0.0%	Strawberries	0.0%	Potatoes	0.1%	
0.1%	IE child	0.19	0.0%	Table grapes	0.0%	Milk: Cattle	0.0%	Strawberries	0.0%		

**Conclusion:**  
The estimated long-term dietary intake (TMDI(NED)/IEDI) was below the ADI.  
The long-term intake of residues of Mandestrobin (F) is unlikely to present a public health concern.

### **A 3.2            IESTI calculations**

Not required.