

# REGISTRATION REPORT

## Part B

### Section 10

#### **Assessment of the relevance of metabolites in groundwater**

Detailed summary of the risk assessment

Product code: FLORAS 50 SC

Product name(s): Floras 50 SC, HerbiFlo 50 SC

Chemical active substance(s):

Florasulam, 50 g/L

Central

Zonal Rapporteur Member State: POLAND

#### CORE ASSESSMENT

(authorization)

Applicant: Elvita Sp. z o.o.

Submission date: 30/11/2023, updated March 2024

MS Finalisation date: April 2024 (initial Core Assessment)

June 2024 (final Core Assessment)

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### Version history

When	What
November 2023	Initial dRR – Elvita Sp. z o.o.
March 2024	Applicants' update.
April 2024	Initial zRMS assessment  The report in the dRR format has been prepared by the Applicant, therefore all comments, additional evaluations and conclusions of the zRMS are presented in grey commenting boxes. Minor changes are introduced directly in the text and <b>highlighted in grey</b> . Not agreed or not relevant information are <del>struck through</del> and <b>shaded</b> for transparency.
June 2024	Final report (Core Assessment updated following the commenting period)  No additional information or assessments after the commenting period.

## 10 Relevance of metabolites in groundwater

### Reviewer comments:

This part of dossier has been submitted to support registration of the plant protection product Floras 50 SC (HerbiFlo 50 SC) containing 50 g/L florasulam, according art. 33 of 1107/2009. Document refers data related to the forming of metabolites in the environment (see dRR B8). dRR Part B10 has been reviewed for the purposes of ongoing registration and also checked its compliance with the current guidelines. Information has been considered as sufficient and appropriate for concluding.

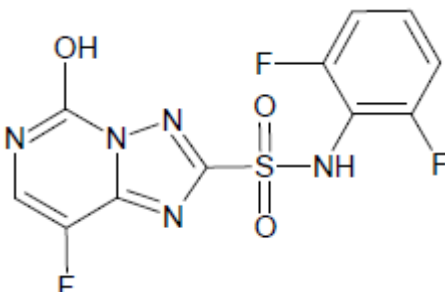
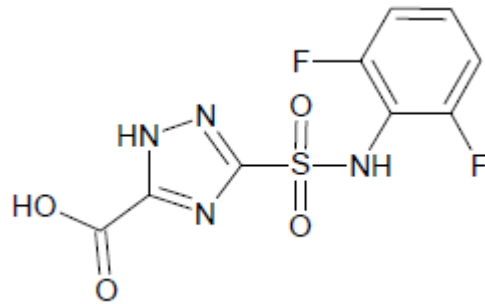
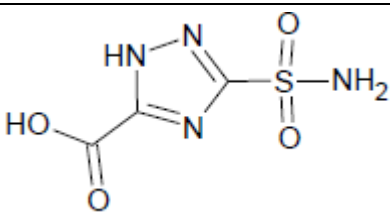
### 10.1 General information

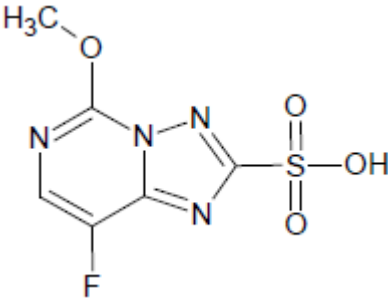
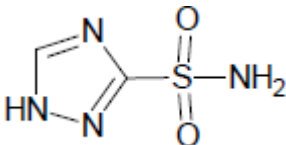
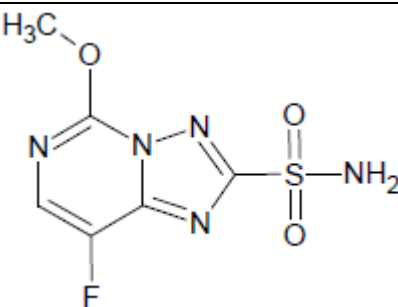
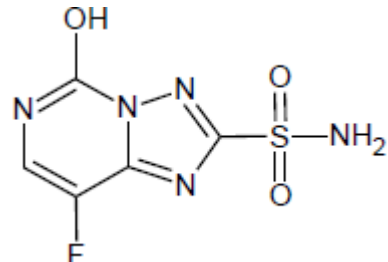
No metabolite is predicted to occur in groundwater at concentration above 0.1 µg/L (see reference to dRR Part B Section B8). No further assessment according to the stepwise procedure of the EC guidance document SANCO/221/2000 – rev.10 is therefore required.

General information on the metabolites are provided in Table 10.1-1. The impact of the relevance assessment on whether a particular GAP use leads to acceptable risk or not is presented in the summary of the cGAP evaluation in chapter 8.8 of the dRR Part B, Section 8 (Environmental fate and behaviour).

General information on the metabolites are provided in Table 10.1-1.

**Table 10.1-1: General information on the metabolite(s)**

Name of active substance	Metabolite name and code	Structural/molecular formula	Trigger for relevance assessment	
Florasulam	<b>5-OH Florasulam;</b> N-(2,6-difluorophenyl)-8-fluoro-5-oxo-5,6-dihydro[1,2,4]triazolo[1,5-c]pyrimidine-2-sulfonamide		Max PEC <sub>gw</sub> Based on:	Not applicable, (max PEC <sub>gw</sub> < 0.1 µg/L)
Florasulam	<b>DFP-ASTCA;</b> 3-[(2,6-difluorophenyl)sulfamoyl]-1H-1,2,4-triazole-5-carboxylic acid		Max PEC <sub>gw</sub> Based on:	Not applicable, (max PEC <sub>gw</sub> < 0.1 µg/L)
Florasulam	<b>ASTCA;</b> 3-sulfamoyl-1H-1,2,4-triazole-5-carboxylic acid		Max PEC <sub>gw</sub> Based on:	Not applicable, (max PEC <sub>gw</sub> < 0.1 µg/L)

Name of active substance	Metabolite name and code	Structural/molecular formula	Trigger for relevance assessment	
Florasulam	<b>TPSA;</b> 8-fluoro-5-methoxy[1,2,4]triazolo[1,5-c]pyrimidine-2-sulfonic acid		Max PEC <sub>gw</sub> Based on:	Not applicable, (max PEC <sub>gw</sub> < 0.1 µg/L)
Florasulam	<b>TSA;</b> 1H-1,2,4-triazole-3-sulfonamide		Max PEC <sub>gw</sub> Based on:	Not applicable, (max PEC <sub>gw</sub> < 0.1 µg/L)
Florasulam	<b>ASTP;</b> 8-fluoro-5-methoxy[1,2,4]triazolo[1,5-c]pyrimidine-2-sulfonamide		Max PEC <sub>gw</sub> Based on:	Not applicable, (max PEC <sub>gw</sub> < 0.1 µg/L)
Florasulam	<b>5-OH ASTP;</b> 8-fluoro-5-oxo-5,6-dihydro[1,2,4]triazolo[1,5-c]pyrimidine-2-sulfonamide		Max PEC <sub>gw</sub> Based on:	Not applicable, (max PEC <sub>gw</sub> < 0.1 µg/L)

## 10.2 Relevance assessment of metabolite 5-OH Florasulam.

The relevance of the groundwater metabolite 5-OH Florasulam has already been assessed and the assessment agreed at EU level (see EFSA journal 2015; 13(1):3984), and the relevance assessment is applicable as well for the GAP and groundwater scenarios considered in this dRR. 5-OH Florasulam is not considered relevant according to the criteria laid down in the EC guidance document SANCO/221/2000 –rev.10. A summary of the relevance assessment is given in Table 10.2-1.

**Table 10.2-1: Summary of the relevance assessment for 5-OH Florasulam**

	Assessment step		Result of assessment	
	STEP 1		Metabolite of no concern?	no
Quantification of groundwater contamination	STEP 2		Max PEC <sub>gw</sub>	> 0.1 µg/L, < 0.75 µg/L
			Based on	FOCUS PEARL 5.5.5 FOCUS PELMO 6.6.4. FOCUS MACRO 5.5.4.
Relevance assessment	STEP 3	Stage 1	Biological activity comparable to the	No pesticidal activity

			parent?	
		Stage 2	Genotoxic properties of metabolite	Non-genotoxic
		Stage 3	Toxic properties of metabolite;	Not toxicologically relevant
			Classification of parent	Not classified
			Classification of metabolite	Not classified
Consumer health risk assessment	STEP 4		Estimated consumer exposure via drinking water and other sources; threshold of concern approach	Not needed since the threshold of <0.75 µg/L is not exceeded based on the intended uses
	STEP 5	Refined risk assessment		N/A *
		Predicted exposure (% of ADI)		N/A *
				ADI based on

\* N/A: not applicable

### 10.2.1 STEP 1: Exclusion of degradation products of no concern

SANCO/221/2000 –rev.10- final allows the exclusion of metabolites from consideration if they satisfy certain criteria that would allow the conclusion to be made that they are of no concern. These criteria are as follows:

- it is CO<sub>2</sub> or an inorganic compound, not containing a heavy metal; or,
- it is an organic compound of aliphatic structure, with a chain length of 4 or less, which consists only of C, H, N or O atoms and which has no "alerting structures" such as epoxide, nitrosamine, nitrile or other functional groups of known toxicological concern.
- it is a substance, which is known to be of no toxicological or ecotoxicological concern, and which is naturally occurring at much higher concentrations in the respective compartment.

The metabolite 5-OH Florasulam does not satisfy the above criteria and therefore needs further assessment.

### 10.2.2 STEP 2: Quantification of potential groundwater contamination

PEC<sub>gw</sub> calculations after leaching from soil for 5-OH Florasulam were performed (see Part B, Section 8, chapter 8.8). The results of the leaching model PELMO 6.6.4., PEARL 5.5.5. and MACRO 5.5.4 show that when used according to the intended uses in winter and spring cereals, the metabolite 5-OH Florasulam exceed the threshold of 0.1 µg/L in several scenarios. However they remain below the threshold of 0.75 µg/L set for metabolites in Sanco/221/2000 –rev.10.

### 10.2.3 STEP 3: Hazard assessment – identification of relevant metabolites

#### 10.2.3.1 STEP 3, Stage 1: screening for biological activity

This work was performed during the EU review of Florasulam. It was decided that 5-OH Florasulam has a lower biological activity than the parent.

Reference is made to the EFSA journal 2015; 13(1):3984 for more detailed information about this assessment of the relevance of the metabolite 5-OH Florasulam.

#### 10.2.3.2 STEP 3, Stage 2: screening for genotoxicity

5-OH Florasulam was screened for genotoxic activity by the following data package of in vitro genotoxicity studies: Ames test, gene mutation test with mammalian cells, and a chromosome aberration test. 5-OH Florasulam was non-genotoxic as shown by a negative Ames test, a negative gene mutation test with mammalian cells and a negative chromosome aberration test. 5-OH Florasulam is considered not relevant and is further evaluated in Stage 3.

Tests:

- Ames test (OECD 471; OPPTS 870.5100; method B14),
- Gene mutation test with mammalian cells (OECD 476; EC, B.17; OPPTS 870.5300),
- Chromosome aberration test (OECD 473; OPPTS 870.5375).

Reference: EFSA Conclusion 2015; 13(1):3984 + RAR of Florasulam.

### 10.2.3.3 STEP 3, Stage 3: screening for toxicity

One acute oral toxicity study was done on 5-OH florasulam:

- Acute oral toxicity (OECD 401; OPPTS 870.1100; EEC method B.1) - EFSA Conclusion 2015; 13(1):3984 + DAR & RAR of Florasulam.

The metabolite is not toxic, result: LD50>5000mg/kg bw.

### 10.2.4 STEP 4: Exposure assessment – threshold of concern approach

5-OH Florasulam was not considered relevant in the hazard assessment of Step 3.

The PEC<sub>gw</sub> for 5-OH Florasulam was < 0.75 µg/L for each scenarios. There is no consumer exposure via other routes. 5-OH Florasulam is not considered to exceed the toxicological threshold of concern as defined in EC guidance document SANCO/221/2000 –rev.10.

### 10.2.5 STEP 5: Refined risk assessment

Not required.

## 10.3 Relevance assessment of metabolite ASTCA.

The relevance of the groundwater metabolite ASTCA has already been assessed and the assessment agreed at EU level (see EFSA journal 2015; 13(1):3984), and the relevance assessment is applicable as well for the GAP and groundwater scenarios considered in this dRR. ASTCA is not considered relevant according to the criteria laid down in the EC guidance document SANCO/221/2000 –rev.10. A summary of the relevance assessment is given in Table 10.3-1.

**Table 10.3-1: Summary of the relevance assessment for ASTCA**

	Assessment step		Result of assessment	
	STEP 1		Metabolite of no concern?	no
Quantification of groundwater contamination	STEP 2		Max PEC <sub>gw</sub>	> 0.1 µg/L, < 0.75 µg/L
			Based on	FOCUS PEARL 5.5.5 FOCUS PELMO 6.6.4. FOCUS MACRO 5.5.4.
Hazard assessment	STEP 3	Stage 1	Biological activity comparable to the parent?	No pesticidal activity
		Stage 2	Genotoxic properties of metabolite	Non-genotoxic
		Stage 3	Toxic properties of metabolite;	Not toxicologically relevant
			Classification of parent	Not classified
			Classification of metabolite	Not classified
Consumer health risk assessment	STEP 4		Estimated consumer exposure via drinking water and other sources; threshold of concern approach	Not needed since the threshold of <0.75 µg/L is not exceeded based on the intended uses
	STEP 5		Refined risk assessment	N/A *

	Predicted exposure (% of ADI)	N/A *
	ADI based on	N/A *

\* N/A: not applicable

### 10.3.1 STEP 1: Exclusion of degradation products of no concern

SANCO/221/2000 –rev.10- final allows the exclusion of metabolites from consideration if they satisfy certain criteria that would allow the conclusion to be made that they are of no concern. These criteria are as follows:

- it is CO<sub>2</sub> or an inorganic compound, not containing a heavy metal; or,
- it is an organic compound of aliphatic structure, with a chain length of 4 or less, which consists only of C, H, N or O atoms and which has no "alerting structures" such as epoxide, nitrosamine, nitrile or other functional groups of known toxicological concern.
- it is a substance, which is known to be of no toxicological or ecotoxicological concern, and which is naturally occurring at much higher concentrations in the respective compartment.

The metabolite ASTCA does not satisfy the above criteria and therefore needs further assessment.

### 10.3.2 STEP 2: Quantification of potential groundwater contamination

PEC<sub>gw</sub> calculations after leaching from soil for ASTCA were performed (see Part B, Section 8, chapter 8.8). The results of the leaching model PELMO 6.6.4., PEARL 5.5.5. and MACRO 5.5.4 show that when used according to the intended uses in winter and spring cereals, the metabolite 5-OH Florasulam exceed the threshold of 0.1 µg/L in several scenarios. However they remain below the threshold of 0.75 µg/L set for metabolites in Sanco/221/2000 –rev.10.

### 10.3.3 STEP 3: Hazard assessment – identification of relevant metabolites

#### 10.3.3.1 STEP 3, Stage 1: screening for biological activity

This work was performed during the EU review of Florasulam. It was decided that ASTCA has a lower biological activity than the parent.

Reference is made to the EFSA journal 2015; 13(1):3984 for more detailed information about this assessment of the relevance of the metabolite ASTCA.

#### 10.3.3.2 STEP 3, Stage 2: screening for genotoxicity

ASTCA was screened for genotoxic activity by the following data package of in vitro genotoxicity studies: Ames test, gene mutation test with mammalian cells, and a chromosome aberration test. ASTCA was non-genotoxic as shown by a negative Ames test, a negative gene mutation test with mammalian cells and a negative chromosome aberration test. ASTCA is considered not relevant and is further evaluated in Stage 3.

Tests:

- Ames test (OECD 471; OPPTS 870.5100; method B14),
- Gene mutation test with mammalian cells (OECD 476; EC, B.17; OPPTS 870.5300),
- Chromosome aberration test (OECD 473; OPPTS 870.5375).

Reference: EFSA Conclusion 2015; 13(1):3984 + RAR of Florasulam.

#### 10.3.3.3 STEP 3, Stage 3: screening for toxicity

The parent, Florasulam is not classified as acutely or chronically toxic, neither is florasulam classified for reproductive toxicity or as a carcinogen (or corresponding classification in accordance to CLP 1272/2008). There are no reasons to expect that the groundwater metabolites ASTCA would be toxic or highly toxic. A complete in vitro genotoxicity data package has been generated by the main Notifier on both ASTCA to complete Stage 2 Step 3 of Sanco/221/2000-rev 10. The applicant is currently in the pro-



cess of data matching these data. ASTCA is not considered relevant and is further evaluated in Stage 3 Step 3, Step 4 is not considered necessary as the parent is not acutely or chronically toxic nor is it deemed to be carcinogen, mutagen or reproductive toxicant.

### 10.3.4 STEP 4: Exposure assessment – threshold of concern approach

ASTCA was not considered relevant in the hazard assessment of Step 3.

The PEC<sub>gw</sub> for ASTCA was < 0.75 µg/L for each scenarios. There is no consumer exposure via other routes. ASTCA is not considered to exceed the toxicological threshold of concern as defined in EC guidance document SANCO/221/2000 –rev.10.

### 10.3.5 STEP 5: Refined risk assessment

Not required.

## 10.4 Relevance assessment of metabolite TSA.

The relevance of the groundwater metabolite TSA has already been assessed and the assessment agreed at EU level (see EFSA journal 2015; 13(1):3984), and the relevance assessment is applicable as well for the GAP and groundwater scenarios considered in this dRR. TSA is not considered relevant according to the criteria laid down in the EC guidance document SANCO/221/2000 –rev.10. A summary of the relevance assessment is given in Table 10.4-1.

**Table 10.4-1: Summary of the relevance assessment for TSA**

	Assessment step		Result of assessment	
	STEP 1		Metabolite of no concern?	no
Quantification of groundwater contamination	STEP 2		Max PEC <sub>gw</sub>	> 0.1 µg/L, < 0.75 µg/L
			Based on	FOCUS PEARL 5.5.5 FOCUS PELMO 6.6.4. FOCUS MACRO 5.5.4.
Hazard assessment	STEP 3	Stage 1	Biological activity comparable to the parent?	No pesticidal activity
		Stage 2	Genotoxic properties of metabolite	Non-genotoxic
		Stage 3	Toxic properties of metabolite;	Not toxicologically relevant
			Classification of parent	Not classified
			Classification of metabolite	Not classified
Consumer health risk assessment	STEP 4		Estimated consumer exposure via drinking water and other sources; threshold of concern approach	Not needed since the threshold of <0.75 µg/L is not exceeded based on the intended uses
	STEP 5		Refined risk assessment	N/A *
			Predicted exposure (% of ADI)	N/A *
				ADI based on

\* N/A: not applicable

### 10.4.1 STEP 1: Exclusion of degradation products of no concern

SANCO/221/2000 –rev.10- final allows the exclusion of metabolites from consideration if they satisfy certain criteria that would allow the conclusion to be made that they are of no concern. These criteria are as follows:

a) it is CO<sub>2</sub> or an inorganic compound, not containing a heavy metal; or,

b) it is an organic compound of aliphatic structure, with a chain length of 4 or less, which consists only of C, H, N or O atoms and which has no "alerting structures" such as epoxide, nitrosamine, nitrile or other functional groups of known toxicological concern.

c) it is a substance, which is known to be of no toxicological or ecotoxicological concern, and which is naturally occurring at much higher concentrations in the respective compartment.

The metabolite TSA does not satisfy the above criteria and therefore needs further assessment.

#### **10.4.2 STEP 2: Quantification of potential groundwater contamination**

PEC<sub>gw</sub> calculations after leaching from soil for TSA were performed (see Part B, Section 8, chapter 8.8). The results of the leaching model PELMO 6.6.4., PEARL 5.5.5. and MACRO 5.5.4 show that when used according to the intended uses in winter and spring cereals, the metabolite TSA exceed the threshold of 0.1 µg/L in several scenarios. However they remain below the threshold of 0.75 µg/L set for metabolites in Sanco/221/2000 – rev.10.

#### **10.4.3 STEP 3: Hazard assessment – identification of relevant metabolites**

##### **10.4.3.1 STEP 3, Stage 1: screening for biological activity**

This work was performed during the EU review of Florasulam. It was decided that TSA has a lower biological activity than the parent.

Reference is made to the EFSA journal 2015; 13(1):3984 for more detailed information about this assessment of the relevance of the metabolite TSA.

##### **10.4.3.2 STEP 3, Stage 2: screening for genotoxicity**

TSA was screened for genotoxic activity by the following data package of in vitro genotoxicity studies: Ames test, gene mutation test with mammalian cells, and a chromosome aberration test. TSA was non-genotoxic as shown by a negative Ames test, a negative gene mutation test with mammalian cells and a negative chromosome aberration test. TSA is considered not relevant and is further evaluated in Stage 3.

Tests:

- Ames test (OECD 471; OPPTS 870.5100; method B14),
- Gene mutation test with mammalian cells (OECD 476; EC, B.17; OPPTS 870.5300),
- Chromosome aberration test (OECD 473; OPPTS 870.5375).

Reference: EFSA Conclusion 2015; 13(1):3984 + RAR of Florasulam.

##### **10.4.3.3 STEP 3, Stage 3: screening for toxicity**

The parent, Florasulam is not classified as acutely or chronically toxic, neither is florasulam classified for reproductive toxicity or as a carcinogen (or corresponding classification in accordance to CLP 1272/2008). There are no reasons to expect that the groundwater metabolites TSA would be toxic or highly toxic. A complete in vitro genotoxicity data package has been generated by the main Notifier on both TSA to complete Stage 2 Step 3 of Sanco/221/2000-rev 10. The applicant is currently in the process of data matching these data. TSA is not considered relevant and is further evaluated in Stage 3 Step 3, Step 4 is not considered necessary as the parent is not acutely or chronically toxic nor is it deemed to be carcinogen, mutagen or reproductive toxicant.

#### **10.4.4 STEP 4: Exposure assessment – threshold of concern approach**

TSA was not considered relevant in the hazard assessment of Step 3.

The PEC<sub>gw</sub> for TSA was < 0.75 µg/L for each scenarios. There is no consumer exposure via other routes. TSA is not considered to exceed the toxicological threshold of concern as defined in EC guidance document SANCO/221/2000 –rev.10.

## **10.4.5          STEP 5: Refined risk assessment**

Not required.

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

No studies submitted by applicant.

## Appendix 2 Additional information

No additional information submitted by applicant.

Comments of zRMS:	No further comments.
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