REGISTRATION REPORT

Part B

Section 10

Assessment of the relevance of metabolites in groundwater

Detailed summary of the risk assessment

Product code: F7B-39-30

Product name: Rinpode

Chemical active substance: Florpyrauxifen-benzyl 25 g/l

Central Zone

Zonal Rapporteur Member State: Poland

CORE ASSESSMENT/

Applicant: Corteva Agriscience

Submission date: March 2023

MS Finalisation date: 15/11/2023

Following commenting round: 18/03/2024

References correction: 31/07/2024

Version history

When	What
March 2023	Submission to zRMS and concerned Member States
November 2023	zRMS assessment
March 2024	Following commenting round
July 2024	References correction

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This application was submitted by Corteva Agriscience in March 2023.
The application is for the first approval of the formulation F7B-39-30 (trademark: Rinpode) as new post-emergence herbicide developed by Corteva Agriscience. The formulation is an EC (emulsion concentrate) containing 25 g/L of florpyrauxifen-benzyl (19.870 g a.e./L) for use as an herbicide in sugar beets.
F7B-39-30 is submitted to Southern and Central zones with France and Poland acting as zRMS respectively. Concerned Member States are Spain, Italy, Portugal, Greece, Croatia in Southern zone and Belgium, The Netherlands, Luxembourg, Hungary, Germany, Austria, Romania, Czech Republic, Romania, Slovakia in Central zone.

Florpyrauxifen-benzyl (trademark: Rinskor® active) is a New Active Substance (NAS), developed by Corteva Agrisciences, approved in accordance with Regulation (EC) No 1107/2009 on July 3rd, 2019. Details of the approval Regulation, Commission Review Report and EFSA R.O. are provided in the below table:

Active Substance	*Approval Regulation*	*SANCO/SANTE Review Report*	*EFSA Scientific Report*
Florpyrauxifen-benzyl (trademark: Rinskor® active)	Commission Implementing Regulation (EU) 2019/1138 of 3 July 2019	SANTE/10658/2019 rev2 of 21 May 2019	EFSA Journal 2018;16(8):5378. doi: 10.2903/j.efsa.2018.5378.

The Regulation (EU) 2019/1138 for Florpyrauxifen-benzyl (trademark: Rinskor® active) provides specific provisions under Part B which need to be considered by the applicant in the preparation of their submission and by the MS prior to granting an authorisation: "*For the implementation of the uniform principles as referred to in Article 29(6) of Regulation (EC) No 1107/2009, the conclusions of the review report on 21 March 2019, and in particular Appendices I and II thereof, shall be taken into account. In this overall assessment Member States shall pay particular attention to: — the protection of aquatic and terrestrial non-target plants. Conditions of use shall include risk mitigation measures such as buffer zones and/or drift reduction nozzles, where appropriate*."
These concerns have been addressed within the current submission, where not otherwise stated.

Florpyrauxifen-benzyl (trademark: Rinskor® active) is a foliar post-emergence herbicide effective to control the most import weeds present in rice paddies; it is not yet authorized for sugar beets. Florpyrauxifen-benzyl is a member of the arylpicolinate family of chemistry, a new structural class of synthetic auxin herbicides, Group O (according to HRAC MOA classification). F7B-39-30 is active at low use rates in post-emergence applications against broadleaf weeds in sugar-beet.

F7B-39-30 (trademark: Rinpode) is very similar to GF-3206 (trademark Loyant 25 Neo EC), with the addition of a food-grade dye, included in the composition at 0.0005% w/w. F7B-39-30 and GF-3206 are the same formulation type (emulsion concentrate) and contain equal amounts of active ingredient, antifoam, emulsifiers, solvents and adjuvant. The minimal difference in composition between F7B-39-30 and GF-3206 lead to toxicological and ecotoxicological properties that can be considered equivalent and in comparable performance on crop safety or efficacy. Based on comparability of both formulations, data generated with GF-3206 are used in support of the claim for F7B-39-30. GF-3206, which is authorized formulation since 2019 in all Southern Europe rice countries, is the representative formulation considered for the florpyrauxifen-benzyl (trademark: Rinskor® active) approval, so it was fully evaluated in the active substance European process.

Information on the detailed composition of F7B-39-30 or of the GF-3206 formulation used as read-across can be found in the CONFIDENTIAL dossier of this submission (draft Registration Report - Part C).
F7B-39-30 critical and Country GAP within the zones is given in Part B, Section 0.

10 Relevance of metabolites in groundwater

zRMS comment: For the requested use on sugar beet the max. PECgw for florpyrauxifen-benzyl metabolite X12483137 (with FOCUS-PEARL, Thiva scenario) was 0.492 µg/L.
The metabolite does not have biological activity comparable to the parent ~~fluxapyroxad~~ florpyrauxifen-benzyl. It is considered as low risk compound for the environment (EFSA, 2018). From the results of the available gonotoxic studies it is concluded that X12483137 did not show any potential to induce micronuclei in cultured human peripheral blood lymphocytes, both in the absence and presence of metabolic activation system, is non-mutagenic in the Bacterial Reverse Mutation Assay using Salmonella typhimurium and Escherichia coli and does not have potential to induce gene mutations in in vitro mammalian cells both in the absence and presence of the metabolic activation system.
There is no health risk arising from use or drinking of ground water after application of the product in line with GAP. No further assessment needed.

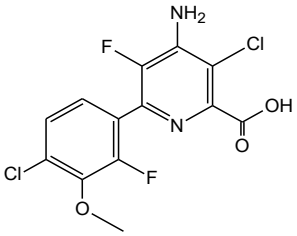
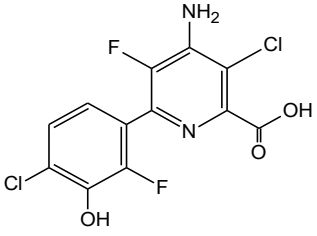
10.1 General information

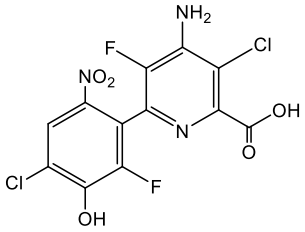
The florpyrauxifen-benzyl metabolite X12483137 is predicted to occur in groundwater at concentrations above 0.1 µg/L (see Part B, Section 8, Chapter ~~8.8~~ 8.7). Assessment of the relevance of this metabolites according to the stepwise procedure of the EC guidance document SANCO/221/2000 –rev.11 is therefore required.

General information on the metabolites is provided in 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 1 of the dRR Part B, Section 8 (Environmental fate and behaviour).

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 1 of the dRR Part B, Section 8 (Environmental fate and behaviour).

Table 10.1-1: General information on the metabolites evaluated for PECgw

Name of active substance	Metabolite name and code	Structural/molecular formula	Trigger for relevance assessment	
Florpyrauxifen-benzyl	X11438848		Max PEC_{gw} Based on:	<0.001 µg/L All FOCUS-GW scenarios, annual applications to sugar beet
Florpyrauxifen-benzyl	X11966341		Max PEC_{gw} Based on:	<0.001 µg/L All FOCUS-GW scenarios, annual applications to sugar beet

Name of active substance	Metabolite name and code	Structural/molecular formula	Trigger for relevance assessment	
Florpyrauxifen-benzyl	X12483137		Max PEC_{gw} Based on:	0.492 µg/L (sugar beet, 4 x 0.5 g a.s./ha) FOCUS-PEARL, Thiva scenario, applications every year

10.2 Relevance assessment of X12483137 metabolite

Summary:

The groundwater metabolite X12483137 is not considered as relevant according to the criteria laid down in the EC guidance document SANCO/221/2000 – rev.~~10~~ 11. A summary of the relevance assessment is given in
Table 10.2-1 and the corresponding studies are listed in the corresponding sections. Studies supporting PEC_{gw} data are evaluated in Section 8 (Environmental fate and behaviour), the genotoxicity studies are evaluated in Section 6 (Mammalian Toxicology).

Table 10.2-1: Summary of the relevance assessment for X12483137 metabolite

	Assessment step		Result of assessment	
	STEP 1		Metabolite of no concern?	no
Quantification of groundwater contamination	STEP 2		Max PEC_{gw}	0.492 µg/L
			Based on	FOCUS-PEARL, Thiva scenario, application every year to sugar beet, 4 x 0.5 g a.s./ha
Hazard assessment	STEP 3	Stage 1	Biological activity comparable to the parent?	No
		Stage 2	Genotoxic properties of metabolite	Non-genotoxic
		Stage 3	Toxic properties of metabolite;	
			Classification of parent	No classification
			Classification of metabolite	N/A
Consumer health risk assessment	STEP 4		Estimated consumer exposure via drinking water and other sources; threshold of concern approach	acceptable (<0.75 µg/L) with application / every year in sugar beet.
	STEP 5		Refined risk assessment	N/A*

	Assessment step	Result of assessment	
		Predicted exposure (% of ADI)	
		ADI based on	

10.2.1 STEP 1: Exclusion of degradation products of no concern

X12483137 does not meet the criteria for products of no concern as defined in step 1 of the guidance and therefore needs further assessment.

10.2.2 STEP 2: Quantification of potential groundwater contamination

PEC_{gw} calculations after leaching from soil for X12483137 were performed (see Part B, Section 8, chapter 8.8). The uses for which concentrations of X12483137 were considered to exceed 0.1 µg/L are listed in Table 10.2-1. Details are given in Part B, Section 8, chapter ~~8.8~~ 8.7.

10.2.3 STEP 3: Hazard assessment – identification of relevant metabolites

10.2.3.1 STEP 3, Stage 1: screening for biological activity

The biological activity of the X12483137 metabolite does not have comparable target activity as the parent active compound as shown by biological data summarised in the EFSA Conclusions (EFSA Journal 2018; 16(7):5378) for highly susceptible species to florpyrauxifen-benzyl such as the aquatic plant *Myriophyllum spicatum* and the terrestrial plant *Daucus carota*. The E_rC_{50} for *M. spicatum* for X12483137 (i.e. 50.5 µg/L) is 420× higher than the corresponding E_rC_{50} for florpyrauxifen-benzyl (i.e. 0.12 µg/L). Similarly, for *D. carota*, the ER_{50} values for X12483137 are at least 40× and 370× higher than the corresponding ER_{50} for florpyrauxifen-benzyl in pre- and post-emergence studies, respectively. Overall X12483137 metabolite is considered not relevant for biological activity and is further evaluated in Stage 2.

10.2.3.2 STEP 3, Stage 2: screening for genotoxicity

X12483137 was screened for genotoxic activity by the following data package of *in vitro* genotoxicity studies: Ames test, in vitro micronucleus test, and a chromosome aberration test. The Ames test and an in vitro micronucleus test are in line with the requirements of the SANCO/221/2000 rev.11 guideline. X12483137 was non-genotoxic as shown in all studies. ~~by a negative Ames test, negative gene mutation test with mammalian cells, negative chromosome aberration test~~. X12483137 is considered not relevant.

10.2.3.3 STEP 3, Stage 3: screening for toxicity

The parent of X12483137, Florpyrauxifen-benzyl, is not classified as acutely or chronically toxic or very toxic / for reproductive toxicity / as a carcinogen (or corresponding classification in accordance to CLP 1272/2008). There are no reasons to expect that X12483137 may be toxic or highly toxic. X12483137 has not been subject to targeted testing. X12483137 is not considered relevant and is further evaluated in Step 4.

10.2.4 STEP 4: Exposure assessment – threshold of concern approach

X12483137 was not considered relevant in the hazard assessment of Step 3.
The PEC_{gw} for X12483137 was < 0.75 µg/L. There is no consumer exposure via other routes. X12483137 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

Step 5 is not warranted therefore is not conducted.

Appendix 1 Lists of data considered in support of the evaluation

Tables considered not relevant can be deleted as appropriate.

MS to blacken authors of vertebrate studies in the version made available to third parties/public.

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
CA 5.4.1/4	Xie, H.	2021	X12483137: In Vitro Mammalian Cell Micronucleus Assay in Human Peripheral Blood Lymphocytes (HPBL). Corteva Study No. 201936; Lab Study No. AG27GT.348.BTL BioReliance Corporation, Rockville, Maryland, USA GLP/GEP (Y/N): Yes Published (Y/N): No	N	Corteva Agriscience (bringing together the global heritage businesses of Pioneer, DuPont Crop Protection, and Dow AgroSciences)
CA 5.4.1/5	Davis, X.F.	2020	X12483137: Bacterial Reverse Mutation Test. Corteva Study No. 201938; Lab Study No. 22442-500 Haskell R&D Center, E.I. du pont de Nemours and Company, Member of Corteva Agriscience Group of Companies, Newark, Delaware, USA28 GLP/GEP (Y/N): Yes Published (Y/N): No	N	Corteva Agriscience (bringing together the global heritage businesses of Pioneer, DuPont Crop Protection, and Dow AgroSciences)
CA 5.4.1/6	Miller, A.	2021	X12483137: In Vitro Mammalian Cell Forward Gene Mutation (CHO/HPRT) Assay with Duplicate Cultures. Corteva Study No. 201937; Lab Study No. AG27GT.783.BTL BioReliance Corporation, Rockville, Maryland, USA GLP/GEP (Y/N): Yes Published (Y/N): No	N	Corteva Agriscience (bringing together the global heritage businesses of Pioneer, DuPont Crop Protection, and Dow AgroSciences)

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

None

~~The following tables are to be completed by MS~~

~~List of data submitted by the applicant and not 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~~
~~KCP XX~~	~~Author~~	~~YYYY~~	~~Title~~ ~~Company Report N~~ ~~Source~~ ~~GLP/non GLP/GEP/non GEP~~ ~~Published/Unpublished~~	~~Y/N~~	~~Owner~~

~~List of data relied on not submitted by the applicant but necessary for evaluation~~

~~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~~
~~KCP XX~~	~~Author~~	~~YYYY~~	~~Title~~ ~~Company Report N~~ ~~Source~~ ~~GLP/non GLP/GEP/non GEP~~ ~~Published/Unpublished~~	~~Y/N~~	~~Owner~~

Appendix 2 Additional information

None