REGISTRATION REPORT

Part B

Section 7

Metabolism and Residues

Detailed summary of the risk assessment

Product code: GLOB182F

Product name(s): SURRENDER

Chemical active substance:

Fludioxonil, 100 g/L

Interzonal

Zonal Rapporteur Member State: PL

CORE ASSESSMENT

Applicant: Globachem NV

Submission date: January 2021

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March 2022 (final Core Assessment)

Version history

When	What
01/2021	Initial dRR - Globachem NV.
09/2021	Dossier updated on request of izRMS.
10/2021	Initial izRMS assessment. The report in the dRR format has been prepared by the Applicant, therefore all comments, additional evaluations and conclusions of the izRMS are presented in grey commenting boxes. Minor changes are introduced directly in the text and highlighted in grey. Not agreed or not relevant information are ~~struck through and shaded for transparency~~.
03/2022	Final report (Core Assessment updated following the commenting period) Additional information/assessments included by the izRMS in the report in response to comments recieved from the cMS and the Applicant are highlighted in yellow. Information no longer relevant ~~is struck through and shaded~~.

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7 Metabolism and residue data (KCA section 6)

7.1 Summary and zRMS Conclusion

zRMS comments:

The application is submitted for GLOB182F, a FS formulation containing 100 g/L Fludioxonil for use as a seed treatment with fungicidal activity in maize seeds at a dose rate of 0.5 L/ton seeds and sunflower seeds at a dose rate of 1.5 L/ton seeds.

Maize and sunflower are the major crops in northern Europe (SANTE/2019/12752). Seed treatments in general lead to lower residues in the harvested crops and often residues are below the LOQ.
According to the SANTE/2019/12752 when a non-systemic active substance is applied to seeds, no quantifiable residues are expected in plants or plant products (zero residue situation). In case of zero residue situation for seed treatments 3 residue trials are required for major crops.
In accordance with SANTE/2019/12752 for seed treatments 3 residue trials on immature maize can be extrapolated to sweet corn (minor crop, <LOQ situation). Therefore the immature maize data cover the use on sweet corn.

No new data were submitted in the framework of this application by the Applicant.

Fludioxonil
Storage stability
The stability of fludioxonil residues in plant matrices under storage conditions prior to analysis was assessed during the peer review under Directive 91/414/EEC (EFSA, 2007). According to the EFSA Scientific Report (2007) 110, 1-85, Conclusion on the peer review of fludioxonil:
Storage stability studies demonstrating that fludioxonil residues are stable in various matrices including water-, oil, protein-, and starch-containing materials, under deep freeze storage conditions for up to 24 months.
Fludioxonil residues in animal product samples, determined as CGA 192155, are stable for at least 12 months when stored at ≤−16° C.
All available residue trials samples were stored for not more than 24 months and are valid with regard to storage stability.
No additional data are required.

Metabolism in plant and in animal
The metabolism of fludioxonil in primary crops was evaluated in the framework of the peer review under Directive 91/414/EEC (EFSA, 2007) using foliar application on fruit crops, leafy crops and root and tuber crops as well as for seed treatment on root and tuber crops, pulses/oilseeds and cereals.
Based on these metabolism studies, the residue definition was proposed as fludioxonil for monitoring and as 'sum of fludioxonil and its metabolites oxidized to metabolite 2,2-difluoro-benzo[1,3] dioxole-4 carboxylic acid (CGA 192155), expressed as fludioxonil' for risk assessment. These residue definitions apply to all crop categories for all kind of treatments. The current residue definition set in Regulation (EC) No 396/2005 is identical to the residue definition for enforcement derived in the peer review.
For cereals (seed treatment), fruits and leafy vegetables, pulses and oilseeds, the conversion factor of 1 between residue definitions for enforcement and risk assessment was derived which reflects the fact that no significant concentrations of metabolites containing the 2,2-difluoro-benzo[1,3]dioxole-4 carboxylic moiety are expected.
According to the EFSA Journal 2011;9(8):2335 a conversion factor of 2.8 should be applied for root and tuber vegetables.
According to the EFSA Journal 2011;9(8):2335:
Metabolism in lactating ruminants and poultry was sufficiently investigated and findings can be extrapolated to pigs as well. The relevant residue definition for enforcement and risk assessment was defined as the sum of fludioxonil and its metabolites oxidized to metabolite 2,2-difluoro-benzo[1,3]dioxole-4 carboxylic acid, expressed as fludioxonil. A validated analytical method for enforcement of the residue definition is also available with a LOQ of 0.01 mg/kg in milk and meat and a LOQ of 0.05 mg/kg in liver, kidney, fat and eggs.

The data are sufficient to support the intended uses of GLOB182F / Surrender on seed treatment for sunflower, maize and sweet corn. No further data are required.

Definition:
<u>The residue in plant commodities</u>
- for enforcement: fludioxonil
- risk assessment: sum of fludioxonil and its metabolites oxidized to metabolite 2,2-difluoro-benzo[1,3]

dioxole-4 carboxylic acid (CGA 192155), expressed as fludioxonil

Enforcement and risk assessment residue definition for animal commodities:

sum of fludioxonil and its metabolites oxidized to metabolite 2,2-difluoro-benzo[1,3]dioxole-4 carboxylic acid, expressed as fludioxonil

The conversion factor of 1 between residue definitions for enforcement and risk assessment was derived which reflects the fact that no significant concentrations of metabolites containing the 2,2-difluoro-benzo[1,3]dioxole-4carboxylic moiety are expected.

Magnitude of residues in plants

No new magnitude of residues in plant studies have been submitted by the applicant in the framework of this application.

Applicant makes reference to existing data that had supported the registration of a seed treatment PPPs (Fludioxonil 025 FS and Maxim ML 035 FS) containing fludioxonil.

Information submitted by the Applicant is sufficient and zRMS-Poland agrees with conclusions presented in point 7.2.3.1:

„*Residue trials in sweet corn, maize and rape seed (extrapolation to sunflower seeds possible according to SANTE/2019/12752) for seed dressing with Fludioxonil in Northern and Southern EU countries were evaluated and accepted during the EU review of the maximum residue levels (MRLs) for Fludioxonil according to Article 12 of regulation (EC) No 396/2005. A suitable number of trails for both Northern and Southern EU according to the GAP were evaluated. Fludioxonil residues were always found to be below 0.02 mg/kg. A summary of the data evaluated during the EU review of the maximum residue levels (MRLs) for Fludioxonil according to Article 12 of regulation (EC) No 396/2005 is provided in table 7.2-9 below. These trials can we referred for GLOB182F since they have been used to support the intended uses of the reference products (Fludioxonil 025 FS and Maxim ML 035 FS) in the zRMS and all CMs for more than 10 years and are therefore out of protection.”*

Sufficient residue trials are available to suport the intended uses for Surrender on seed treatment for sunflower, maize and sweet corn. According to the EFSA Journal 2011;9(8):2335 - „*Review of the existing MRLs for fludioxonil*”:

1. Maize grain:
Trials GAP: 10 x GAP compliant (5.0 g a.s./100 kg seed)
~~7~~ 10 x <0.02 mg/kg,
2. Sweet corn:
Trials GAP: 3 x GAP compliant (5.0 g a.s./100 kg seed)
3 x <0.02 mg/kg,
3. Sunflower seed (extrapolation from rape seed)
Trials GAP: 7 x GAP compliant (15.00 g a.s./100 kg seed)
7 x <0.02 mg/kg.

The studies on the magnitude of residues are valid with regard to storage stability.

In the EFSA Journal 2011;9(8):2335 it is concluded that oilseeds, cereals grains and sweet corn: *there is a lack of residues trials compliant with the LOQ for enforcement (0.01 mg/kg). However, residues resulting from the seed treatment are expected to be below this LOQ (supported by the metabolism studies). In these cases MRLs are set at 0.01* mg/kg.*

Available results show that the in force MRL on sunflower seed, maize and corn of 0.01* mg/kg (~~Reg. 2021/1098~~ Reg. 2021/1807) will not be exceeded.

Since fludioxonil was applied to oilseed rape, maize and sweet corn seeds before sowing, a PHI is not considered to be relevant.

No additional data are required.

Industrial Processing and/or Household Preparation

In the EFSA Journal 2011;9(8):2335 it is stated that *The effect of processing on the nature of fludioxonil was investigated in the framework of the peer review. A study was conducted simulating representative hydrolytic conditions for pasteurisation (20 minutes at 90 C, pH 4), boiling/brewing/baking (60 minutes at 100 C pH 5) and sterilisation (20 minutes at 120 C, pH 6). This study showed that fludioxonil is stable under these conditions and that no formation of toxicologically relevant metabolites occurs (Denmark, 2005). Thus, for processed commodities the same enforcement residue definition as for raw agricultural commodities (RAC) is applicable. Also for risk assessment, considering that all metabolites are oxidized to a common moiety, it is unlikely that new metabolites will occur.*

As residues of fludioxonil exceeding 0.1 mg/kg are not expected in the treated crops, there is no need to investigate the effect of industrial and/or household processing.
No additional data are required.

Magnitude of residues in livestock
No new data submitted in the framework of this application.
Fludioxonil is authorised for use on several crops that might be fed to livestock. Livestock dietary burden calculations were performed by EFSA in the framework of Art. 12 evaluation (2011). Significant intakes were calculated for all groups of livestock in the review of MRLs. In EFSA Journal 2011;9(8):2335 it is stated that *The calculated dietary burdens for ruminants and pigs were found to exceed the trigger value of 0.1 mg/kg DM. Further investigation of residues is therefore only required in these groups of livestock.*
During the peer review under Directive 91/414/EEC the magnitude of fludioxonil residues in livestock was investigated in a feeding study with lactating cows (Denmark, 2005). Three groups of lactating cows, each consisting of three animals, were dosed for 28-30 days with fludioxonil at levels of 0.02, 0.06 and 0.20 mg fludioxonil/kg bw/day. The samples were analyzed for parent fludioxonil and its metabolites determined as 2,2-difluoro-benzo[1,3]dioxole-4 carboxylic acid (CGA 192155) and expressed as fludioxonil equivalents.
At the highest dose level, no residues above the LOQ (0.01 or 0.05 mg/kg) were observed in animal tissues and further analysis was not carried out on the lower dose samples. Residues were found in six out the eighteen milk samples obtained at the highest dose level. Residue concentrations ranged from 0.010 mg/kg to 0.019 mg/kg. The highest residue was observed 14 days after the first dose administration. No residues (<0.01 mg/kg) were found in any milk samples from the two lower dose levels.
Based on the available livestock feeding study, MRLs and risk assessment values in ruminant and pig products were calculated in compliance with the latest international recommendations on this matter (FAO, 2009). Significant residues in milk or any edible matrix of pigs are not expected and MRLs for these commodities can be established at the LOQ. However, livestock dietary intake for meat ruminants exceeds the highest dose level of the feeding study. It can therefore not be ascertained that residues in edible matrices of ruminants will be below the enforcement LOQ and tentative MRLs for these commodities were calculated, based on extrapolation from the highest available dosing level. EFSA notes that a feeding study including a higher dosing level was submitted to the RMS. However, the data gap still remains as the study was not yet evaluated by the RMS.
MRLs for poultry products are not required because poultry is not expected to be exposed to significant levels of fludioxonil residues.

New Dietary Burden calculations were performed, taking into account STMR and HR values from the recent EFSA evaluation on the confirmatory data following the Art. 12 MRL review were used and used Animal model 2017 (see point 7.2.4). The calculated dietary burdens for all relevant groups exceed the trigger value of 0.004 mg/kg bw/d. The dietary burdens, however, are not exceeding those calculated in the previous EFSA assessment (EFSA Journal 2019;17(8):5812); therefore, further investigation of residues in animal commodities is not required.
Additionally, as a refinement, dietary burdens have been further re-calculated considering only the intended uses for the current application. Finally it was concluded that there is no risk for animal MRL to be exceeded.
Data and explanation presented by Applicant in point 7.2.4.1 have been accepted and are sufficient to support the proposed uses.

Succeeding crops
The crops under consideration can be grown in rotation.
According to the EFSA Journal 2011;9(8):2335: *The potential incorporation of soil residues into succeeding and rotational crops was investigated in lettuce, winter and spring wheat, sugar beets, corn, mustard, turnips and radishes. These studies showed a comparable metabolism to the primary crops and significant residues in rotational crops are not expected, provided that fludioxonil is applied according to the GAPs supported in the framework of this review.*
The metabolic pathway of Fludioxonil in rotational crops is similar to that in primary crops and no formation of new metabolites was observed. Hence the same residue definition of as for primary crops applies to the rotational crops.
According to the EFSA Scientific Report (2007) 110, 1-85: *Plant-back restrictions and MRLs for rotational crops do not need to be established.*
No waiting periods beyond normal agricultural practice are proposed for succeeding crops to be planted.
No additional data are required to support the uses of GLOB182F / Surrender.

Consumer risk assessment
The TDMI calculation presented by Applicant in Appendix 3 is based on the MRLs value for all the crops for which an MRL has been set for fludioxonil under EU Regulation No. 2020/856. ~~Reg. 2021/1098~~ Reg. 2021/1807 is currently in force, so new calculation result is presented in point 7.2.8 and in Appendix 3. For the assessment, an ADI of 0.37 mg/kg bw/day was used. Chronic exposure calculation for fludioxonil residues in all crops was

performed using PRIMo Model rev. 3.1 and using MRLs values according to the current ~~Reg. 2021/1098~~ Reg. 2021/1807 in Tier I. A conversion factor of 2.8 was applied for root and tuber vegetables. Chronic intakes for all consumer groups are below the ADI. With the current EFSA model the highest chronic risk assessment was calculated for NL toddler with ~~52~~ 63% of ADI. For this diet, the highest contributor is ~~apples~~ potatoes with ~~15~~ 16% of ADI. Therefore the intended uses will not result in a consumer chronic exposure exceeding the ADI.
Acute exposure calculations were not carried out because an ARfD was not deemed necessary for this active substance.
The proposed uses of fludioxonil in the product GLOB182F / Surrender do not represent unacceptable chronic and acute risks for the consumer.

OVERALL CONCLUSION:
There are sufficient data to support the uses of GLOB182F / Surrender on maize, sweet corn and sunflower at the intended GAP.

7.1.1 Critical GAP(s) and overall conclusion

Selection of critical uses and justification
The critical GAPs with respect to consumer intake and risk assessment for the preparation GLOB182F / Surrender are presented in Table 7.1-1. They have been selected from the individual GAPs in the EU for maize, sweet corn and sunflower. A list of all intended uses within the EU 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 fludioxonil as laid down in Reg. (EU) 396/2005 is not expected.
The chronic and the short-term intakes of fludioxonil residues are unlikely to present a public health concern.
As far as consumer health protection is concerned, izRMS agrees with the authorization of the intended use(s).

According to available data, no specific mitigation measures should apply.

Data gaps
Noticed data gaps are: none.

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 ****	**Member state(s)**	**Product code**	**F, Fn, Fpn G, Gn, Gpn or I*****	**Pests or Group of pests controlled** **(additionally: developmental stages of the pest or pest group)**	**Formulation**		**Application**				**Application rate**					**PHI (days)**	**Remarks:** Min-Max. TGW (thousand grain weight, g/1000 seeds) Min-Max. Sowing density per ha (seeds/ha)	**Conclusion**
						Type	**Conc.** of as	Method / Kind	Timing / Growth stage of crop & season	Max. number a) per use b) per crop/ season	Min. interval between applications (days)	L/ton seeds a) max. rate per appl. b) max. total rate per crop/season	Kg a.s./ton seeds a) max. rate per appl. b) max. total rate per crop/season	g a.s./ha a) max. rate per appl. b) max. total rate per crop/season	Sowing rate (kg seeds/ha) min/ max	Water L/ton seeds min/ max			

1	Maize (forage) (ZEAMX)	zRMS + all cMS*	GLOB182F	I (treatment seeds) F (sowing)	*Fusarium* sp. (FUSASP) Pythium sp. (PYTHSP)	FS	100 g/L	Seed treatment	BBCH 00	a) 1 b) 1	/	a) 0.5 b) 0.5	a) 0.050 b) 0.050	a) 1.2-2.375 b) 1.2-2.375	24-47.5	4-8L (incl. product)	N/A	TGW: 240-380 Sowing density: 100,000-125,000 12-23.75 mL product/ha	A
2	Maize (grain) (ZEAMX)	zRMS + all cMS*	GLOB182F	I (treatment seeds) F (sowing)	*Fusarium* sp. (FUSASP) Pythium sp. (PYTHSP)	FS	100 g/L	Seed treatment	BBCH 00	a) 1 b) 1	/	a) 0.5 b) 0.5	a) 0.050 b) 0.050	a) 0.96-1.71 b) 0.96-1.71	19.2-34.2	4-8L (incl. product)	N/A	TGW: 240-380 Sowing density: 80,000-90,000 9.6-17.1 mL product/ha	A
3	Sweet corn (ZEAMS)	zRMS + all cMS*	GLOB182F	I (treatment seeds) F (sowing)	*Fusarium* sp. (FUSASP) Pythium sp. (PYTHSP)	FS	100 g/L	Seed treatment	BBCH 00	a) 1 b) 1	/	a) 0.5 b) 0.5	a) 0.050 b) 0.050	a) 0.2925-0.825 b) 0.2925-0.825	5.9-16.5	4-8L (incl. product)	N/A	TGW: 90-220 Sowing density: 65,000-75,000 2.93-8.25 mL product/ha	A
4	Sunflower (HELAN)	PL, AT, FR, IT, LV, ES	GLOB182F	I (treatment seeds) F (sowing)	*Botrytis cinerea* (BOTRCI) Downy mildew (PLASHA) *Fusarium* sp. (FUSASP)	FS	100 g/L	Seed treatment	BBCH 00	a) 1 b) 1	/	a) 1.5 b) 1.5	a) 0.150 b) 0.150	a) 0.525-1.6875 b) 0.525-1.6875	3.5-11.3	4-8L (incl. product)	N/A	TGW: 20-50 Sowing density: 175,000-225,000 5.25-16.88 mL product/ha	A

5	Sunflower (HELAN)	HU, RO, SI	GLOB182F	I (treatment seeds) F (sowing)	*Botrytis cinerea* (BOTRCI) Downy mildew (PLASHA) *Fusarium* sp. (FUSASP)	FS	100 g/L	Seed treatment	BBCH 00	a) 1 b) 1	/	a) 1.25-1.5 b) 1.25-1.5	a) 0.125-0.150 b) 0.125-0.150	a) 0.4375-1.6875 b) 0.4375-1.6875	3.5-11.3	4-8L (incl. product)	N/A	TGW: 20-50 Sowing density: 175,000-225,000 4.375-16.88 mL product/ha	A
6	Sunflower (HELAN)	DE	GLOB182F	I (treatment seeds) F (sowing)	*Botrytis cinerea* (BOTRCI) Downy mildew (PLASHA) *Fusarium* sp. (FUSASP)	FS	100 g/L	Seed treatment	BBCH 00	a) 1 b) 1	/	a) 1.5 b) 1.5	a) 0.150 b) 0.150	a) 1.15 b) 1.15	4.5- 7.7	4-8L (incl. product)	N/A	TGW: 60-90 Sowing density: 75,000-85,000 seeds/ha 6.75-11.48 mL product/ha	A

* 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 17 “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 GLOB182F /Surrender is composed of fludioxonil.

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

Reference value	Source	Year	Value	Study relied upon	Safety factor
Fludioxonil					
ADI	EFSA Scientific Report (2007) 110, 1-85	2007	0.37 mg/kg bw/day	Rat, 2 years	100
ARfD	EFSA Scientific Report (2007) 110, 1-85	2007	Not allocated - not necessary	N/A	N/A

7.1.2.1 Summary for fludioxonil

Table 7.1-3: Summary for fludioxonil

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, 2	Maize (grain)	Yes	Yes (~~7~~ 10 trials)	Yes	Yes	Yes	No	NR
3	Sweet corn	Yes	Yes (3 trials)	Yes	Yes	Yes		NR
4, 5, 6	Sunflower	Yes	Yes (7 trials)	Yes	Yes	Yes		NR

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

Fludioxonil is a non-systemic compound and when applied to seeds, no residues should normally be found in plants or plant products and therefore normally no residue trials are necessary. Residue trials are provided and all residues are below LOQ. Therefore, it can be concluded that no residues above the MRLs are expected in the requested crops.

As residues of fludioxonil do not exceed the trigger values defined in Reg (EU) No 283/2013, 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.

No chronic risk for the consumer is identified.
Since no ARfD is set for fludioxonil, no acute risk assessment is required.

7.1.2.2 Summary for GLOB182F/ Surrender

Table 7.1-4: Information on GLOB182F / Surrender (KCA 6.8)

Crop	PHI for GLOB182F / Surrender proposed by applicant	PHI/ Withholding period* sufficiently supported for	PHI for GLOB182F / Surrender proposed by zRMS	zRMS Comments (if different PHI proposed)
		Fludioxonil		
Maize	N/A	NR	N/A	-
Sweet corn	N/A	NR	N/A	-
Sunflower	N/A	NR	N/A	-

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).

Table 7.1-5: Waiting periods before planting succeeding crops

Waiting period before planting succeeding crops		Overall waiting period proposed by zRMS for product code
Crop group	Led by fludioxonil	
Leafy vegetables	NR	NR
Root vegetables	NR	NR
Other crops	NR	NR

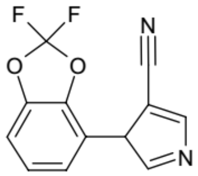
NR: not relevant

Assessment

7.2 Fludioxonil

General data on Fludioxonil are summarized in the table below.

Table 7.2-1: General information on Fludioxonil

Active substance (ISO Common Name)	Fludioxonil
IUPAC	4-(2,2-difluoro-1,3-benzodioxol-4-yl)-1*H*-pyrrole-3-carbonitrile
Chemical structure	
Molecular formula	$C_{12}H_6F_2N_2O_2$
Molar mass	248.2
Chemical group	Phenylpyrrole
Mode of action (if available)	- Inhibits transport-associated phosphorylation of glucose, reducing mycelial growth. - Inhibition of a MAP-kinase in signal transduction of osmo-regulation (glycerol synthesis).
Systemic	No
Company (ies)	Syngenta
Rapporteur Member State (RMS)	DK Renewal ongoing RMS – France Co-RMS - Spain
Approval status	Approved 01/11/2008 COMISSION DIRECTIVE 2007/76/EC REGULATION (EU) No 540/2011
Restriction	Only uses as fungicide may be authorised.
Review Report	SANCO/2818/07 – rev. 2 10/09/2007
Current MRL regulation	~~Regulation (EC) No 2020/856 Reg. (EU) 2021/1098~~ Reg. (EU) 2021/1807
Peer review of MRLs according to Article 12 of Reg No 396/2005 EC performed	Yes
EFSA Journal: Conclusion on the peer review	Yes EFSA Scientific Report (2007) 110, 1-85.
EFSA Journal: conclusion on article 12	Yes EFSA Journal 2011; 9(8): 2335. EFSA Journal 2019;17(8):5812 - *Evaluation of confirmatory data following the Article 12 MRL review for fludioxonil*
Current MRL applications on intended uses	Maize, sunflower Reasoned opinion available (EFSA Journal 2011; 9(8): 2335)

7.2.1 Stability of Residues (KCA 6.1)

7.2.1.1 Stability of residues during storage of samples

Available data

No new data submitted in the framework of this application. Stability of Fludioxonil residues when stored deep frozen was assessed in several crop and animal matrices during the EU Review of Fludioxonil. As these data are out of protection, they can be used by the applicant and they showed Fludioxonil residues to be stable up to two years.

Table 7.2-2: Summary of stability data achieved at ≤ - 18°C (unless stated otherwise)

Matrix	Characteristics of the matrix	Acceptable Maximum Storage duration	Reference
Data relied on in EU			
Plant products			
Tomato, apples, peas	High water content	24 months	DK, 2006 EFSA, 2007
Rape seed	High oil content	24 months	DK, 2006 EFSA, 2007
Grain, straw	High starch content	24 months	DK, 2006 EFSA, 2007
Corn, sorghum, potato	High starch content	24 - 27 months	DK, 2006 EFSA, 2007
Grapes	High acid content	28 months	DK, 2006 EFSA, 2007
Animal Products			
Cattle	Muscle	12 months	DK, 2006 EFSA, 2007
	Liver	19 months	DK, 2006 EFSA, 2007
	Milk	19 months	DK, 2006 EFSA, 2007
Poultry	Eggs	19 months	DK, 2006 EFSA, 2007

Conclusion on stability of residues during storage

Storage stability studies of Fludioxonil assessed in this section cover the requested use on maize and sunflower belonging to high starch and high oil content commodities for GLOB182F.

7.2.1.2 Stability of residues in sample extracts (KCA 6.1)

Extracts of untreated control samples of each crop matrix were fortified with Fludioxonil and stored along with the treated samples discussed in Annex point 7.2.1.1. The results show that residues of Fludioxonil in sample extracts are stable.

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 are submitted in the framework of this application. Reference is made to data evaluated during the EU Review of Fludioxonil which are out of protection.

During the EU Review of Fludioxonil, the metabolism of Fludioxonil was investigated after foliar application in grapes, lettuce, tomatoes, peach and green onions as well as after seed treatment in potatoes, wheat, rice, cotton and soybean. Metabolic patterns in the different studies were shown to be similar and the relevant residue for enforcement in all crops was proposed as the parent Fludioxonil. For risk assessment, the residue was defined as the sum of Fludioxonil and its metabolites oxidized to metabolite 2,2-difluoro-benzo[1,3]dioxole-4-carboxylic acid, expressed as Fludioxonil.

Furthermore, the metabolism studies performed after seed treatment in potatoes, wheat, rice, cotton and soybean demonstrated that there was no translocation of Fludioxonil residues from the treated seed to the final agricultural commodity.

Therefore, the intended use of GLOB182F as a seed treatment on maize and sunflower seeds is covered by the available metabolism studies evaluated during the EU Review of Fludioxonil.

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	Grape	Pyrrole-4-^{14}C	foliar treatment, F	500 g as/ha	3	Day of the 1st appl. & 26 days later; day of the 3rd appl. & 14 & 35 (at maturity) days later	/	DK, 2006 EFSA, 2007
	Tomato	Pyrrole-4-^{14}C	foliar treatment, G	750 g as/ha	3	At the 1st & 3rd appl.; at maturity (40 DAT)	/	DK, 2006 EFSA, 2007
	Peach	Phenyl-U-^{14}C	foliar treatment, F	280 g as/ha 2800 g as/ha	3	28 DAT	/	DK, 2006 EFSA, 2007
				4200 g as/ha	2	30 & 114 DAT	/	
Leafy vegetables	Lettuce	Pyrrole-4-^{14}C	foliar treatment, F	200 g as/ha	3	0, 6 & 13 days after 3rd appl.	/	DK, 2006 EFSA, 2007
				600 g as/ha	3	0, 6 & 13 days after 3rd appl.	/	
Root and tuber vegetables	Green onion	Phenyl-U-^{14}C	foliar treatment, F	124 g as/ha 6169 g as/ha	2	0, 7, 14 & 28 DAT	/	DK, 2006 EFSA, 2007
	Potato	Pyrrole-4-^{14}C	Seed treatment, F	2.5 g as/100 kg seed	1	0, 40, 71 & 95 DAT	/	DK, 2006 EFSA, 2007
Pulses and oilseeds	Cotton	Pyrrole-4-^{14}C	Seed treatment, G	2.5 g as/100 kg seed 5.0 g as/100 kg seed	1	186 DAT	/	DK, 2006 EFSA, 2007
	Soybean	Pyrrole-4-^{14}C	Seed treatment, G	5.0 g as/100 kg seed	1	28, 38 & 133 DAT	/	DK, 2006 EFSA, 2007
Cereals	Rice	Pyrrole-4-^{14}C	Seed treatment, F	6.5 g as/100 kg seed	1	38, 76 & 152 DAT	/	DK, 2006 EFSA, 2007
	Wheat	Pyrrole-4-^{14}C	Seed treatment, G	6.4 g as/100 kg seed	1	11, 18, 25, 32, 39, 46 & 53 DAT	2 stem injection experiments were performed to aid to identify metabolites.	DK, 2006 EFSA, 2007

Summary of plant metabolism studies reported in the EU

Metabolism in crops following foliar application with ^{14}C-fludioxonil

Following the foliar application of ^{14}C-fludioxonil to 5 different crops, the major component of the residues present was parent fludioxonil, accounting for from 22% of the TRR in peach to 73.2% of the

TRR in tomatoes.

The metabolic pathway was characterized by a large number of metabolites. In the case of grapes, up to 16 individual components were formed in addition to fludioxonil, none of which accounted for > 2.4% of the TRR, and where 70.3% of the TRR was parent fludioxonil.

The metabolic pathway was similar in all crop groups and proceeded mainly through oxidation with subsequent conjugation of metabolites with sugar. Cleavage of the pyrrole ring, probably via the formation of succinamic acid derivatives, resulted in the formation of 2,2-difluoro-benzo[1,3]dioxole metabolites.

The structure of the metabolites indicated that the cleavage of the bond between the benzene and the pyrrole ring did not occur. This fact has shown the suitability of both pyrrole and phenyl labelled ^{14}C-fludioxonil for metabolism studies.

Metabolism in crops following seed treatment with ^{14}C-fludioxonil

Metabolism studies following seed treatment with [pyrrole-4-^{14}C]-fludioxonil were performed in 5 different crops.

Uptake and translocation of fludioxonil from the treated seed was low. This was expected for a non-systemic chemical and was confirmed by the low TRR in the plant sample.

In food items, TRR ranged from < 0.002 mg/kg in rice grain to 0.015 mg/kg in dry soybeans. No individual component occurred at > 0.01 mg/kg. Therefore, no significant residues in food items following seed treatment at the investigated rates are expected. Although TRR levels were low, characterization of metabolites observed in potato and soybean studies indicated that the metabolism was similar to those identified in foliar treated crops.

A wheat study, performed by injecting ^{14}C-labelled-fludioxonil in the stem, provided additional identification of plant metabolites. This study confirmed that the metabolism of fludioxonil in wheat was the same as that seen in the foliar treated crops. Most of the injected radioactivity (78.5%) remained at the injection point, providing further evidence of the lack of translocation of fludioxonil.

The metabolism of fludioxonil, similar in all crops, was characterized by the generation of a large number of metabolites and proceeds mainly through oxidation. Cleavage of the pyrrole ring, probably via the formation of succinamic acid derivatives, resulted in the formation of 2,2-difluoro-benzo[1,3]dioxole metabolites.

Overall conclusion for plant metabolism

Metabolism studies following foliar application and seed treatment with [^{14}C]-fludioxonil were performed in ten different crops.

The metabolic pathway was characterized by the generation of a large number of metabolites. The major component of the residue was parent fludioxonil. In all the crop samples examined and among all the detected and/or identified components of the TRR, only parent fludioxonil was present at > 0.05 mg/kg or exceeded 13% of the TRR.

The metabolic pathway was similar in all crop groups and proceeded mainly through oxidation, followed by conjugation of the oxidised metabolites with sugars.

The structure of the metabolites indicated that the cleavage of the bond between the benzene and the pyrrole ring did not occur. This fact has shown the suitability of both pyrrole and phenyl labelled ^{14}C-fludioxonil for metabolism studies.

Uptake and translocation of fludioxonil from the treated seed were very low. This was expected for a non-systemic chemical.

Conclusion on metabolism in primary crops

As European data are out of protection, the results of the metabolism studies in cereals can be used by the applicant and are sufficient to support the intended use of GLOB182F as seed treatment in maize and sunflower.

7.2.2.2 Nature of residue in rotational crops (KCA 6.6.1)

Available data

No new data are submitted in the framework of this application. The data evaluated during the EU Review of Fludioxonil are out of protection and are sufficient to describe the behaviour of the formulated product, so no further studies are required.

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

Crop group	Crop	Label position	Application and sampling details					Reference
			Method, F or G *	Rate (kg a.s./ha)	Sowing intervals (DAT)	Harvest Intervals (DAT)	Remarks	
EU data								
Leafy vegetables	Lettuce	Pyrrole-4-^{14}C	Soil spraying, F	0.750	90	50% and 100% maturity	/	DK, 2006 EFSA, 2011
Root and tuber vegetables	Sugar beets	Pyrrole-4-^{14}C	Soil spraying, F	0.750	140, 320, 345	25%, 50% and 100% maturity	/	DK, 2006 EFSA, 2011
	Turnips	Pyrrole-4-^{14}C	Soil spraying, F	0.124	33, 90	100% maturity	/	DK, 2006 EFSA, 2011
	Radishes	Pyrrole-4-^{14}C	Soil spraying, F	0.062	32, 90	100% maturity	/	DK, 2006 EFSA, 2011
		Phenyl-U-^{14}C	Soil spraying, F	1.117	30, 90, 210	100% maturity	/	DK, 2006 EFSA, 2011
Pulses and oilseeds	Mustard	Pyrrole-4-^{14}C	Soil spraying, F	0.124	33, 90	100% maturity	/	DK, 2006 EFSA, 2011
		Pyrrole-4-^{14}C	Soil spraying, F	0.062	32, 90	100% maturity	/	DK, 2006 EFSA, 2011
		Phenyl-U-^{14}C	Soil spraying, F	1.117	30, 90, 210	100% maturity	/	DK, 2006 EFSA, 2011
Cereals	Winter wheat	Pyrrole-4-^{14}C	Soil spraying, F	0.750	140, 320, 345	25%, 50% and 100% maturity	/	DK, 2006 EFSA, 2011
	Spring wheat	Pyrrole-4-^{14}C	Soil spraying, F	0.124	33, 90	25% and 100% maturity	/	DK, 2006 EFSA, 2011
		Pyrrole-4-^{14}C	Soil spraying, F	0.062	32, 90	25%, 50% and 100% maturity	/	DK, 2006 EFSA, 2011
		Phenyl-U-^{14}C	Soil spraying, F	1.117	30, 90, 210	25%, 50% and 100% maturity	/	DK, 2006 EFSA, 2011

	Corn	Pyrrole-4-^{14}C	Soil spraying, F	0.750	140, 320, 345	25%, 50% and 100% maturity	/	DK, 2006 EFSA, 2011

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

Summary of plant metabolism studies reported in the EU

Four metabolism studies in rotational crops were submitted on lettuce, winter and spring wheat, sugar beets, corn, mustard, turnips, radishes.

Significant TRR levels were only identified in radish samples (30 DAT, 1.117 kg a.s./ha) and in wheat samples (30 DAT, 0.124 and 1.117 kg a.s./ha); in all other crops TRR levels never exceeded 0.01 mg/kg. The highest TRR levels were observed in wheat straw (0.355 mg/kg) and radish tuber (0.135 mg/kg). Parent Fludioxonil accounted for 0.016 mg/kg in radish tubers and CGA 192155 accounted for 0.015 mg/kg in wheat straw. Other metabolites were tentatively identified as CGA 265378, CGA 308103, CGA 340351, CGA 227731 and CGA 260766, none of which accounted for more than 0.05 mg/kg each.

The metabolic pathway of Fludioxonil in rotational crops is similar to that in primary crops and no formation of new metabolites was observed. Hence the same residue definition of as for primary crops applies to the rotational crops.

Conclusion on metabolism in rotational crops

As European data are out of protection, the results of the above metabolism studies can be used by the applicant and are sufficient to support the intended use of GLOB182F as seed treatment in maize and sunflower.

7.2.2.3 Nature of residues in processed commodities (KCA 6.5.1)

Available data

No new data are submitted in the framework of this application. The data evaluated during the EU Review of Fludioxonil are out of protection and are sufficient to describe the behaviour of the formulated product, so no further studies are required.

The effect of hydrolysis on the nature of the residue of Fludioxonil under conditions typical of those found in industrial and household processes such as pasteurisation, boiling and sterilisation was investigated.

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

Conditions (Duration, Temperature, pH)	Identified compound(s) (%)	Reference
EU data		
Pasteurisation (20 minutes, 90°C, pH 4)	Fludioxonil (100%)	DK, 2006 EFSA, 2007
Baking, boiling, brewing (60 minutes, 100°C, pH 5)	Fludioxonil (100%)	DK, 2006 EFSA, 2007
Sterilisation (20 minutes, 120°C, pH 6)	Fludioxonil (100%)	DK, 2006 EFSA, 2007

This study showed that Fludioxonil is stable with respect to hydrolysis and that no breakdown or reaction products were formed during hydrolysis of Fludioxonil under representative processing conditions. Thus, it was concluded that for processed crop commodities the same residue definition is applicable.

Conclusion on nature of residues in processed commodities

As European data are out of protection, the results of the above metabolism studies can be used by the applicant and are sufficient to support the intended use of GLOB182F as seed treatment in maize and sunflower.

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

Endpoints	
Plant groups covered	Fruits and fruiting vegetables (grape, tomato, peach) Leafy vegetables (lettuce) Root and tuber vegetables (onions, potatoes) Pulses and oilseeds (cotton, soybean) Cereals (wheat, rice)
Rotational crops covered	Leafy vegetables (lettuce) Root and tuber vegetables (sugar beets, turnips, radishes) Pulses and oilseeds (mustard) Cereals (wheat, corn)
Metabolism in rotational crops similar to metabolism in primary crops?	Yes
Processed commodities	a.s. is stable under standard hydrolysis conditions
Residue pattern in processed commodities similar to pattern in raw commodities?	Yes
Plant residue definition for monitoring	Fludioxonil (EFSA, 2007) Reg. (EU) ~~2021/1098~~ 2021/1807
Plant residue definition for risk assessment	Sum of Fludioxonil and its metabolites, which can be oxidised to metabolite CGA 192155 (2,2-difluro-benzo[1,3]dioxole-4-carboxylic acid) (EFSA, 2007)
Conversion factor from enforcement to RA	1 for cereals after seed treatment, fruits and leafy vegetables (EFSA, 2007)

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. The data evaluated during the EU Review of Fludioxonil are out of protection and are sufficient to describe the behaviour of the formulated product, so no further studies are required.

Two metabolism studies with [pyrrole-4-^{14}C]-fludioxonil were carried out in goats and hens.

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	Pyrrole-4-^{14}C	2	3.5	4	Milk	Daily	DK, 2006 EFSA, 2007
						Urine and faeces	Daily	
						Tissues	After sacrifice	
Laying poultry	Hens	Pyrrole-4-^{14}C	5	6.3	8	Eggs	Daily	DK, 2006 EFSA, 2007
						Excreta	Daily	
						Tissues	After sacrifice	

Summary of animal metabolism studies reported in the EU

Lactating goats were dosed with 3.5 mg/kg bw/d of ^{14}C-fludioxonil. The parent compound was identified as the major component of the TRR in liver (13.9 %) and fat (82.6 %). In kidneys the major components were identified as the glucuronide conjugate of mono-hydroxylated fludioxonil (37.7 % of the TRR). Since metabolism in rats and ruminants was demonstrated to be similar, the findings in ruminants can also be extrapolated to pigs.

Laying hens were dosed with 6.3 mg/kg bw/d of ^{14}C-fludioxonil. The sulphate conjugate of the N-hydroxylated fludioxonil was the major component of the residue in egg yolks and thigh muscle. In egg whites and liver, the major metabolites resulted from the opening of the oxidised pyrrole ring. Parent compound was major in breast muscle.

Identification of metabolites indicated that the major metabolic pathways were similar in both species; this pathway proceeds through the hydroxylation of the pyrrole and benzodioxol rings followed by conjugation reactions. In hens, further reactions involve the opening of the pyrrole ring. Hence the relevant residue for enforcement and risk assessment in commodities of animal origin is defined as the sum of fludioxonil and its metabolites oxidized to metabolite 2,2-difluoro-benzo[1,3]dioxole-4 carboxylic acid (CGA 192155), expressed as fludioxonil.

Conclusion on metabolism in livestock

As European data are out of protection, the results of the above metabolism studies can be used by the applicant and are sufficient to support the intended use of GLOB182F as seed treatment in maize and sunflower.

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	14 days in milk
	5 days in eggs
Animal residue definition for monitoring	Not required (In case of uses other than cereals and grapes, sum of Fludioxonil and its metabolites, which can be oxidised to metabolite CGA192155 (2,2-difluoro-benzo[1,3]dioxole-4 carboxylic acid)) (EFSA 2007) Sum of fludioxonil and its metabolites oxidized to metabolite 2,2-difluoro-benzo[1,3]dioxole-4 carboxylic acid (CGA 192155), expressed as fludioxonil (EFSA 2011, Reg. (EU) 2021/1807)
Animal residue definition for risk assessment	Not required (In case of uses other than cereals and grapes, sum of Fludioxonil and its metabolites, which can be oxidised to metabolite CGA192155 (2,2-difluoro-benzo[1,3]dioxole-4 carboxylic acid)) (EFSA 2007) Sum of fludioxonil and its metabolites oxidized to metabolite 2,2-difluoro-benzo[1,3]dioxole-4 carboxylic acid (CGA 192155), expressed as fludioxonil (EFSA 2011, Reg. (EU) 2021/1807)
Conversion factor	None
Metabolism in rat and ruminant similar	Yes
Fat soluble residue	Not assessed (EFSA Scientific Report (2007) 110, 1-85) Yes (EFSA Journal 2011;9(8):2335)

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. According to SANTE/2019/12752, when a non-systemic active substance is applied to seeds, no quantifiable residues are expected in plants or plant products (zero residue situation). However, special consideration should be given to the occurrence of toxicological relevant soil metabolites that are taken up by the plant and to root and tuber vegetables for which a contamination from the treated seed could occur.

The lack of Fludioxonil translocation in plants is supported by a number of radio-labelled seed treatment metabolism studies that have been conducted in rice, wheat, soybean, cotton and potatoes (see Annex point 7.2.2.1). Each of these studies demonstrated that there was no translocation of Fludioxonil residues from the treated seed to the final agricultural commodity. Following the review of these studies, EFSA (2007) also concluded: "After seed treatment uptake, translocation of Fludioxonil from the treated seed is low. In wheat grain, TRR are 0.003 mg/kg after seed application of radiolabelled Fludioxonil at a rate exceeding by 50% the proposed representative use rate. In straw, TRR are below 0.02 mg/kg. Therefore, no significant residue in cereal food and feed items resulting from seed treatment is expected."

Additionally, no relevant metabolites in soil have to be considered for Fludioxonil since, following the use of Fludioxonil as a seed treatment, only the degradation in the dark has to be taken into account as the treated seeds are incorporated into the soil. As the metabolites of Fludioxonil are only formed in the light by photolysis, they are not relevant for the use of Fludioxonil as seed treatment product. In consequence, a zero-residue situation can be postulated based on the non-systemic properties of the active substance.

Residue trials in sweet corn, maize and rape seed (extrapolation to sunflower seeds possible according to SANTE/2019/12752) for seed dressing with Fludioxonil in Northern and Southern EU countries were evaluated and accepted during the EU review of the maximum residue levels (MRLs) for Fludioxonil according to Article 12 of regulation (EC) No 396/2005. A suitable number of trails for both Northern and Southern EU according to the GAP were evaluated. Fludioxonil residues were always found to be below 0.02 mg/kg. A summary of the data evaluated during the EU review of the maximum residue levels (MRLs) for Fludioxonil according to Article 12 of regulation (EC) No 396/2005 is provided in table 7.2-9 below. These trials can we referred for GLOB182F since they have been used to support the intended uses of the reference products (Fludioxonil 025 FS and Maxim ML 035 FS) in the zRMS and all CMs for more than 10 years and are therefore out of protection.

Fludioxonil is also registered for foliar use in a lot of vegetables, these applications represent the critical use of Fludioxonil and are used to determine the MRL's.

The data submitted show that when Fludioxonil is applied to seeds, no residues will be found in plants or plant products and no exceedance of the MRL will occur.

Table 7.2-9: Summary of EU reported and new data supporting the intended uses of GLOB182F 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
Sweet corn (residue data on inmature maize)	SANTE/2019/12752	N-EU (3)	**Trials GAP: 3 x GAP compliant (5.0 g a.s./100 kg seed)** 3 x <0.02	<0.01	<0.01	0.01*	0.01*	Y
		S-EU (3)	**Trials GAP: 2 x GAP compliant (5.0 g a.s./100 kg seed)** 3 x <0.02	<0.01	<0.01	0.01*	0.01*	Y
Sunflower seeds (extrapolation from rape seed)	SANTE/2019/12752	N-EU (7)	**Trials GAP: 7 x GAP compliant (15.00 g a.s./100 kg seed)** 7 x <0.02	<0.01	<0.01	0.01*	0.01*	Y
		S-EU (5)	**Trials GAP: 5 x GAP compliant (15.00 g a.s./100 kg seed)** 5 x <0.02	<0.01	<0.01	0.01*	0.01*	Y
Maize grain	SANTE/2019/12752	N-EU (10)	**Trials GAP: 10 x GAP compliant (5.0 g a.s./100 kg seed)** ~~7~~ 10 x <0.02	<0.01	<0.01	0.01*	0.01*	Y
		S-EU (4)	**Trials GAP: 5 x GAP compliant (5.0 g a.s./100 kg seed)** ~~5~~ 4 x <0.02	<0.01	<0.01	0.01*	0.01*	Y

* Reg. (EU) ~~2021/1098~~ 2021/1807

7.2.3.2 Conclusion on the magnitude of residues in plants

According to the available data, the intended use on maize and sunflower seeds is considered acceptable for outdoor use.

The data submitted show that no exceedance of the MRL will occur.

The uses are considered acceptable.

7.2.4 Magnitude of residues in livestock

7.2.4.1 Dietary burden calculation

Since Fludioxonil is a non-systemic active substance that is applied to maize and sunflower seeds, no residues should normally be found in plants or plant products that will be fed to livestock and therefore no dietary burden calculations are necessary.

A dietary burden calculation has been made by EFSA in the framework of the Art. 12 evaluation of Fludioxonil (EFSA Journal 2011;9(8):2335). For the current application, however, the Animal model 2017 is applicable; the dietary burdens have been therefore re-calculated. As input, the values from the recent EFSA evaluation on the confirmatory data following the Art. 12 MRL review were used (EFSA Journal 2019;17(8):5812) updated for the uses under consideration. The input values are summarised in Table 7.2-10 and the results of the dietary burden calculations are reported in Table 7.2 13.

Table 7.2-10: Input values for the dietary burden calculation (considering the uses from EFSA Journal 2019;17(8):5812)

Feed Commodity	**Median dietary burden**		**Maximum dietary burden**	
	Input value (mg/kg)	**Comment**	**Input value (mg/kg)**	**Comment**
Risk assessment residue definition: sum of Fludioxonil and its metabolites oxidized to metabolite 2,2-difluoro-benzo[1,3]dioxole-4 carboxylic acid (CGA 192155), expressed as Fludioxonil				
Citrus, pomace	39.96	Median residue (5.30) x PF (7.5)	39.96	Median residue (5.30) x PF (7.5)
Apple, pomace	12.19	Median residue (2.3) x PF (5.3)	12.19	Median residue (0.295) x PF (5.3)
Carrots	1.13	Median residue (0.41) x PF (2.8)	1.51	Highest residue (0.54) x PF (2.8)
Wheat, rye grain	0.01	Median residue	0.01	Median residue
Barley, oat grain	0.01	Median residue	0.01	Median residue
Maize grain	0.01	Median residue	0.01	Median residue
Wheat, rye bran	0.01	Median residue	0.01	Median residue
Wheat, rye straw	0.04	Median residue	0.05	Highest residue
Barley, oat straw	0.04	Median residue	0.05	Highest residue
Peas, beans, lupins (dry)	0.02	Median residue	0.02	Median residue
Potatoes	0.02	Median residue	0.04	Highest residue
Rape seed Cotton seed Sunflower seed Soya bean	0.01	Median residue	0.01	Median residue
Rape seed meal Cotton seed meal Sunflower seed meal	0.01	Median residue	0.01	Median residue

Feed Commodity	Median dietary burden		Maximum dietary burden	
	Input value (mg/kg)	Comment	Input value (mg/kg)	Comment
Soya bean meal				

Table 7.2-11: Results of the dietary burden calculation

Relevant groups	Dietary burden				Most critical diet (a)	Most critical commodity (b)		Trigger (0.004 mg/kg bw/d) exceeded	Previous assessment (EFSA, 2019) max. burden (mg/kg bw/d)
	mg/kg bw/d		mg/kg DM						
	Med.	Max.	Med.	Max.					
Cattle (all diets)	0.394	0.411	10.24	10.69	Dairy cattle	Citrus	dried pulp	Yes	0.411
Cattle (dairy only)	0.394	0.411	10.24	10.69	Dairy cattle	Citrus	dried pulp	Yes	0.411
Sheep (all diets)	0.212	0.238	4.99	5.60	Lamb	Apple	pomace, wet	Yes	0.238
Sheep (ewe only)	0.166	0.187	4.99	5.60	Ram/Ewe	Apple	pomace, wet	Yes	0.187
Swine (all diets)	0.207	0.224	8.91	9.74	Swine (breeding)	Citrus	dried pulp	Yes	0.225
Poultry (all diets)	0.080	0.102	1.14	1.44	Poultry broiler	Carrot	culls	Yes	0.102
Poultry (layer only)	0.075	0.096	1.10	1.40	Poultry layer	Carrot	culls	Yes	0.096

(a): When several diets are relevant (e.g. cattle, sheep and poultry "all diets"), the most critical diet is identified from the maximum dietary burdens expressed as "mg/kg bw per day"
(b): The most critical commodity is the major contributor identified from the maximum dietary burden expressed as "mg/kg bw per day".

The calculated dietary burdens for all relevant groups exceed the trigger value of 0.004 mg/kg bw/d. The dietary burdens, however, are not exceeding those calculated in the previous EFSA assessment (EFSA Journal 2019;17(8):5812); therefore, further investigation of residues in animal commodities is not required.

Additionally, as a refinement, dietary burdens have been further re-calculated considering only the intended uses for the current application. The input values are summarised in Table 7.2-10 and the results of the dietary burden calculations are reported in Table 7.2 13.

Table 7.2-12: Input values for the dietary burden calculation (considering only the intended uses)

Feed Commodity	Median dietary burden		Maximum dietary burden	
	Input value (mg/kg)	Comment	Input value (mg/kg)	Comment
Risk assessment residue definition: sum of Fludioxonil and its metabolites oxidized to metabolite 2,2-difluoro-benzo[1,3]dioxole-4 carboxylic acid (CGA 192155), expressed as Fludioxonil				
Corn, field (forage/silage)	0.01	Median residue	0.01	Median residue
Corn, field (stover)	0.01	Median residue	0.01	Median residue
Corn, field (grain)	0.01	Median residue	0.01	Median residue
Corn pop (grain)	0.01	Median residue	0.01	Median residue
Sunflower (meal)	0.01	Median residue	0.01	Highest residue

Table 7.2-13: Results of the dietary burden calculation

Relevant groups	Dietary burden				Most critical diet (a)	Most critical commodity (b)		Trigger (0.004 mg/kg bw/d) exceeded	Previous assessment (EFSA, 2019) max. burden (mg/kg bw/d)
	mg/kg bw/d		mg/kg DM						
	Med.	Max.	Med.	Max.					
Cattle (all diets)	0.001	0.001	0.04	0.04	Dairy cattle	Corn, field	gluten feed	No	0.411
Cattle (dairy only)	0.001	0.001	0.03	0.03	Dairy cattle	Corn, field	gluten feed	No	0.411
Sheep (all diets)	0.001	0.001	0.02	0.02	Lamb	Corn, field	gluten feed	No	0.238
Sheep (ewe only)	0.001	0.001	0.02	0.02	Ram/Ewe	Corn, field	gluten feed	No	0.187
Swine (all diets)	0.001	0.001	0.02	0.02	Swine (breeding)	Corn, field	gluten feed	No	0.225
Poultry (all diets)	0.002	0.002	0.02	0.02	Poultry broiler	Corn, field	hominy meal	No	0.102
Poultry (layer only)	0.002	0.002	0.02	0.02	Poultry layer	Corn, field	hominy meal	No	0.096

(a): When several diets are relevant (e.g. cattle, sheep and poultry "all diets"), the most critical diet is identified from the maximum dietary burdens expressed as "mg/kg bw per day"
(b): The most critical commodity is the major contributor identified from the maximum dietary burden expressed as "mg/kg bw per day".

The calculated dietary burdens for all relevant groups do not exceed the trigger value of 0.004 mg/kg bw/d; therefore, further investigation of residues in animal commodities is not required.

Conclusion on feeding studies
European data are sufficient to support the intended uses of GLOB182F.

The requested uses do not modify the previously calculated daily intakes for animals. A risk for animal MRLs to be exceeded is not expected.

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

Data/information on processing studies were reviewed during the Annex I inclusion of Fludioxonil and were considered acceptable. No further studies have been performed.

The effect of processing on the nature of Fludioxonil was investigated in the framework of the peer review (see Annex point 7.2.2.3). This study showed that Fludioxonil is stable under these conditions and that no formation of toxicologically relevant metabolites occurs. Thus, for processed commodities the same enforcement residue definition as for raw agricultural commodities (RAC) is applicable. Also, for risk assessment, considering that all metabolites are oxidized to a common moiety, it is unlikely that new metabolites will occur.

Considering the results of available residue trials and metabolism studies on rotational crops, the presence of residues in vegetables following a seed treatment seems very unlikely and concentration of residues in processed commodities is therefore not expected. Therefore, processing studies on vegetables were not performed.

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. The data evaluated during the EU Review of Fludioxonil are out of protection and are sufficient to describe the behaviour of the formulated product, so no further studies are required.

Under the peer review, one rotational crop study with non-radiolabelled Fludioxonil was submitted. Fludioxonil was applied 4 times, with a seven-day interval, at an application rate of 0.282 kg as/ha on bare soil. Succeeding crops of lettuce, turnips and wheat were planted/sowed and analysed to determine residue levels of Fludioxonil. Planting or sowing was carried out 30, 90, 150 and 210 DAT.

No residues exceeding 0.01 mg/kg were found in any of the samples planted/sown at a 30d plant-back interval.

Table 7.2-14: 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					
Bare soil	4 x 0.282	Leafy vegetables	Lettuce	30 90 150 210	DK, 2006 EFSA, 2007
		Root and tuber vegetables	Turnips	30 90 150 210	DK, 2006 EFSA, 2007
		Cereals	Wheat	30 90 150 210	DK, 2006 EFSA, 2007

Conclusion on rotational crops studies

Considering the fact that Fludioxonil was applied to a bare soil which is a worst-case situation as no interception by plants is taken into account, it is expected that residues of Fludioxonil resulting from soil uptake will never exceed 0.01 mg/kg. Specific plant-back restrictions related to the use of Fludioxonil are therefore not required, provided that Fludioxonil is applied in compliance with the GAPs evaluated in the framework of the EU peer review.

As European data are out of protection, the results of the above rotational crop study can be used by the applicant and are sufficient to support the intended use of GLOB182F as seed treatment in vegetables.

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

The available data for the active substance sufficiently address aspects of the residue situation that might arise from the use of GLOB182F. Therefore, other special studies are not needed.

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

7.2.8.1 Input values for the consumer risk assessment

Consumer risk assessment calculations were performed taking into account all the crops for which an MRL has been set for Fludioxonil under EU Regulation No. ~~2020/856 2021/1098~~ 2021/1807. Where the MRL for a particular crop is below the LOQ, calculations have been made with the LOQ for that crop.

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

Commodity	Chronic risk assessment	
	Input value (mg/kg)	Comment
Risk assessment residue definition: sum of Fludioxonil and its metabolites oxidized to metabolite 2,2-difluoro-benzo[1,3]dioxole-4 carboxylic acid (CGA 192155), expressed as Fludioxonil		
Maize/corn	0.01*	EU MRL (Reg. (EU) No ~~2020/856 2021/1098~~ 2021/1807)
Sunflower seeds	0.01*	EU MRL (Reg. (EU) No ~~2020/856 2021/1098~~ 2021/1807)
All other commodities without root and tuber vegetables	EU MRL	EU MRL (Reg. (EU) No ~~2020/856 2021/1098~~ 2021/1807)
Root and tuber vegetables	EU MRL x CF (2.8)	Reg. (EU) No 2021/1807)

* Indicates that MRL has been set at LOQ

7.2.8.2 Conclusion on consumer risk assessment

Chronic exposure calculations for all crops were performed using revision 3.1 of the EFSA Pesticide Residues Intake Model (PRIMo) (EFSA, 2017). Results are shown in table 7.4-12 below. Extensive calculation sheets are presented in Appendix 3.

Table 7.2-16: Consumer risk assessment

TMDI (% ADI) according to EFSA PRIMo	~~52.0~~ 63.0% (based on NL toddler)
IEDI (% ADI) according to EFSA PRIMo	No IEDI calculations were performed as the TMDI calculations using the MRLs were already acceptable. No refinement of the chronic risk assessment is required.
IESTI (% ARfD) according to EFSA PRIMo*	No IESTI calculations were performed as no ARfD was set.

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

The proposed use of Fludioxonil in the formulation GLOB128F does not represent an unacceptable chronic risk for the consumer.

7.3 Combined exposure and risk assessment

Not relevant. The product contains only one active substance.

7.4 References

EC (European Commission), 2007. Review report for the active substance fludioxonil. Finalised in the Standing Committee on the Food Chain and Animal Health at its meeting on 9 October 2007 in view of the inclusion of fludioxonil in Annex I of Directive 91/414/EEC. SANCO/2818/07 – rev. 2, 10 September 2007.

EFSA (European Food Safety Authority), 2007. Conclusion regarding the peer review of the pesticide risk assessment of the active substance fludioxonil. EFSA Scientific Report (2007) 110, 1-85.

EFSA (European Food Safety Authority), 2011. Reasoned opinion on the review of the existing maximum residue levels (MRLs) for fludioxonil according to Article 12 of Regulation (EC) No 396/2005. EFSA Journal 2011;9(8):2335.
EFSA (European Food Safety Authority), 2019. Reasoned Opinion on the evaluation of confirmatory data following the Article 12 MRL review for fludioxonil. EFSA Journal 2019;17(8):5812.

Denmark, 2006. Draft assessment report on the active substance fludioxonil prepared by the rapporteur Member State Denmark in the framework of Council Directive 91/414/EEC, February 2006.

Denmark, 2007. Final addendum to the draft assessment report on the active substance fludioxonil prepared by the rapporteur Member State Denmark in the framework of Council Directive 91/414/EEC, June 2007.

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
-	-	-	No data submitted by Applicant	-	-

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
-	-	-	No data submitted by Applicant	-	-

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
-	-	-	-	-	-

List of data relied on and 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
-	-	-	-	-	-

Appendix 2 Detailed evaluation of the additional studies relied upon

No studies submitted.

Appendix 3 Pesticide Residue Intake Model (PRIMo)

A 3.1 TMDI calculations - updated

European Food Safety Authority

EFSA PRIMo revision 3.1; 2019/03/19

Fludioxonil

LOQs (mg/kg) range from: to:

Toxicological reference values

ADI (mg/kg bw/day):	**0,37**	ARfD (mg/kg bw):	**not necessary**
Source of ADI:	**EFSA**	Source of ARfD:	**EFSA**
Year of evaluation:	**2007**	Year of evaluation:	**2007**

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 : ---

TMDI/NEDI/IEDI calculation (based on average food consumption)

Calculated exposure (% of ADI)	MS Diet	Expsoure (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	Exposure resulting from MRLs set at the LOQ (in % of ADI)	Exposure resulting from commodities not under assessment (in % of ADI)
63%	NL toddler	234,17	16%	Potatoes	15%	Apples	6%	Oranges		
52%	DE child	194,23	17%	Apples	11%	Oranges	10%	Potatoes		
52%	IE adult	193,32	27%	Sweet potatoes	9%	Potatoes	3%	Oranges		
38%	NL child	141,63	13%	Potatoes	8%	Apples	4%	Oranges		
31%	PT general	116,26	20%	Potatoes	3%	Wine grapes	2%	Oranges		
31%	SE general	115,54	16%	Potatoes	4%	Lettuces	2%	Oranges		
30%	GEMS/Food G11	111,84	15%	Potatoes	2%	Apples	2%	Oranges		
30%	GEMS/Food G07	111,37	14%	Potatoes	4%	Oranges	3%	Lettuces		
28%	GEMS/Food G08	104,57	15%	Potatoes	2%	Lettuces	2%	Apples		
27%	GEMS/Food G10	101,70	11%	Potatoes	4%	Lettuces	3%	Oranges		
26%	UK toddler	94,43	13%	Potatoes	5%	Oranges	2%	Apples		
26%	FI 3 yr	94,37	18%	Potatoes	1%	Apples	1%	Mandarins		
25%	GEMS/Food G15	92,81	13%	Potatoes	2%	Oranges	1%	Apples		
24%	FR child 3 15 yr	88,74	9%	Oranges	6%	Potatoes	2%	Apples		
24%	ES child	87,43	7%	Potatoes	6%	Oranges	5%	Lettuces		
24%	RO general	87,24	14%	Potatoes	2%	Apples	2%	Wine grapes		
23%	GEMS/Food G06	86,58	8%	Potatoes	3%	Tomatoes	3%	Oranges		
23%	FR toddler 2 3 yr	85,23	7%	Potatoes	4%	Apples	4%	Oranges		
22%	UK infant	80,41	12%	Potatoes	4%	Oranges	2%	Apples		
21%	FI 6 yr	79,20	15%	Potatoes	0,9%	Lettuces	0,9%	Mandarins		
20%	NL general	75,67	9%	Potatoes	3%	Oranges	2%	Apples		
20%	DE women 14-50 yr	74,08	5%	Oranges	4%	Potatoes	3%	Apples		
19%	PL general	71,48	13%	Potatoes	3%	Apples	0,7%	Tomatoes		
19%	DK child	70,30	9%	Potatoes	3%	Apples	2%	Lettuces		
19%	ES adult	69,33	6%	Lettuces	4%	Potatoes	3%	Oranges		
19%	DE general	69,10	5%	Potatoes	4%	Oranges	3%	Apples		
17%	LT adult	62,67	12%	Potatoes	3%	Apples	0,7%	Lettuces		
15%	IT toddler	56,74	3%	Potatoes	3%	Lettuces	1%	Oranges		
15%	FR infant	56,46	7%	Potatoes	2%	Apples	2%	Spinaches		
15%	IT adult	55,31	4%	Lettuces	2%	Potatoes	1%	Apples		
13%	UK vegetarian	49,25	5%	Potatoes	2%	Oranges	2%	Lettuces		
12%	FR adult	43,73	3%	Potatoes	3%	Wine grapes	2%	Oranges		
12%	UK adult	43,03	5%	Potatoes	2%	Oranges	1%	Lettuces		
11%	DK adult	41,73	5%	Potatoes	1%	Apples	1%	Wine grapes		
11%	FI adult	38,96	4%	Potatoes	2%	Lettuces	1%	Oranges		
4%	IE child	13,78	2%	Potatoes	0,4%	Apples	0,2%	Oranges		

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

A 3.2 IEDI calculations

No IEDI calculations were performed for Fludioxonil as the TMDI calculations using the MRLs do not exceed the ADI.

A 3.3 IESTI calculations - Raw commodities

No IESTI calculations were performed for Fludioxonil as no ARfD was set.

A 3.4 IESTI calculations - Processed commodities

No IESTI calculations were performed for Fludioxonil as no ARfD was set.