

FINAL REGISTRATION REPORT

Part B

Section 6

Mammalian Toxicology

Detailed summary of the risk assessment

Product code: **FLUDIO 025 GF**

Product names: **FLUDIO ŽEL 025 FS /**

FUNABEN[®] ŽEL 025 FS

Chemical active substance:

Fludioxonil, 25 g/L

Central Zone

Zonal Rapporteur Member State: **Poland**

CORE ASSESSMENT

(authorization)

Applicant: **Synthos Agro Sp z o.o.**

Submission date: **01/2023**

MS Finalisation date: **06/2023; 10/2023**

Version history

When	What
01/2023	Initial dRR
04/2023	Updated calculation for exposure assessment
06/2023	Initial zRMS assessment
10/2023	Final Registration Report

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6 Mammalian Toxicology (KCP 7)

6.1 Summary

Table 6.1-1: Information on FLUDIO 025 GF *

Product name	FLUDIO ŽEL 025 FS/ FUNABEN® ŽEL 025 FS
Product code	FLUDIO 025 GF
Formulation type	Flowable concentrate for seed treatment [Code: FS]
Active substance(s) (incl. content)	fludioxonil; 25 g/L
Function	Fungicide
Product already evaluated as the 'representative formulation' during the approval of the active substance(s)	No
Product previously evaluated in another MS according to Uniform Principles	No

* Information on the detailed composition of FLUDIO 025 GF can be found in the confidential dRR Part C.

Justification regarding the difference in the formulation type between the product code name - FLUDIO 025 GF and the product trade names - FLUDIO ŽEL 025 FS, FUNABEN® ŽEL 025 FS is presented in Part C.

The product code name FLUDIO 025 GF is used in all draft Registration Report.

Justified proposals for classification and labelling

According to the criteria given in Regulation (EC) No 1272/2008 of the European Parliament and of the Council of 16 December 2008, the following classification and labelling with regard to toxicological data is proposed for the preparation:

Table 6.1-2: Justified proposals for classification and labelling for FLUDIO 025 GF according to Regulation (EC) No 1272/2008

Hazard class(es), categories	None
Hazard pictograms or Code(s) for hazard pictogram(s)	None
Signal word	None
Hazard statement(s)	None
Precautionary statement(s)	<p>WARNING SECTION OF THE LABEL (first page): None</p> <p>Other section of the label: P270 – Do not eat, drink or smoke when using this product.</p> <p>And P280 as follows: Operator: „Stosować odzież roboczą (kombinezon) oraz rękawice ochronne w trakcie przygotowywania cieczy roboczej, zaprawiania, pakowania zaprawionych ziaren oraz czyszczenia sprzętu.” “Wear work wear (coverall) nad protective gloves during mixing/loading, seed treatment, seed packing and cleaning.”</p> <p>Worker: „Stosować odzież roboczą (kombinezon) oraz rękawice ochronne w czasie kontaktu z zaprawionym ziarnem” “Wear work wear (coverall) nad protective gloves during during contact with treated seeds”.</p> <p>Section “First aid”: P101: If medical advice is needed, have product container or label at hand.</p>
Additional labelling phrases	To avoid man and the environment, comply with the instructions for use. [EUH401] Contains 1,2-benzisothiazol-3(2H)-one. May produce an allergic reaction. [EUH208]

Table 6.1-3: Summary of risk assessment for operators, workers, residents and bystanders for FLUDIO 025 GF

	Result	PPE / Risk mitigation measures
Operators	Acceptable	There is no risk for operator health based on the exposure estimation. However, due to the model limitations and the possibility of underestimation it is recommended to: “Wear work wear (coverall) nad protective gloves during mixing/loading, seed treatment, seed packing and cleaning.”
Workers	Acceptable	There is no risk for operator health based on the exposure estimation. However, due to the model limitations and the possibility of underestimation it is recommended t:o “Wear work wear (coverall) nad protective gloves during during contact with treated seeds.”
Residents	Acceptable	None
Bystanders	Acceptable	None

No unacceptable risk for operators, workers was identified when the product is used as intended and provided that the PPE/ risk mitigation measures stated in Table 6.1-3 are applied.

No unacceptable risk for residents and bystanders was identified when the product is used as intended. No specific PPE is necessary.

A summary of the critical uses and the overall conclusion regarding exposure for operators, workers and residents/bystanders is presented in Table 6.1-4.

Data gaps

Data gaps should be listed in the summary to give an overview (especially for cMS).

Noticed data gaps are:

No critical areas of concern were identified in the mammalian toxicology section.

(EFSA Scientific Report (2007) 110)

Table 6.1-4 Critical uses and overall conclusion of exposure assessment

1	2	3	4	5	6	7	8	9	10			
Use-No.*	Crops and situation (e.g. growth stage of crop)	F, Fn, Fpn, G, Gn, Gpn or I**	Application		Application rate		PHI (d)	Remarks: (e.g. safener/synergist (L/ha)) critical gap for operator, worker, resident or bystander exposure based on SeedTropex.	Acceptability of exposure assessment			
			Method / Kind (incl. application technique ***)	Max. number (min. interval between applications) a) per use b) per crop/ season	Max. application rate kg as/ha a) a.s. 1 b) a.s. 2	Water L/ha min / max			Operator	Worker	Residents	Bystander
1	Winter rye (BBCH 00)	F	Seed treatment	1	Fludioxonil 5 – 10 g	-	-	200 mL/100 kg seeds Sowing rate: 100 – 200 kg seeds/ha				
2	Winter wheat (BBCH 00)	F	Seed treatment	1	Fludioxonil: 7,5-12,5g	-	-	200 ml/100 kg seeds Sowing rate: 150-250 kg seeds/ha				
3	Winter barley (BBCH 00)	F	Seed treatment	1	Fludioxonil: 6-10g	-	-	200 ml/100 kg seeds Sowing rate: 120-200 kg seeds/ha				
4	Winter triticale (BBCH 00)	F	Seed treatment	1	Fludioxonil 5 – 10 g	-	-	200 ml/100 kg seeds Sowing rate: 100-200 kg seeds/ha				
5	Spring wheat (BBCH 00)	F	Seed treatment	1	Fludioxonil: 7,5-12,5g	-	-	200 ml/100 kg seeds Sowing rate: 150-250 kg seeds/ha				
6	Spring barley (BBCH 00)	F	Seed treatment	1	Fludioxonil: 6-10g	-	-	200 ml/100 kg seeds Sowing rate: 120-200 kg seeds/ha				

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

** 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

*** e.g. LC: low crops, HC: high crop, TM: tractor-mounted, HH: hand-held

Explanation for column 10 “Acceptability of exposure assessment”

A	Exposure acceptable without PPE / risk mitigation measures
R	Further refinement and/or risk mitigation measures required
N	Exposure not acceptable/ Evaluation not possible

6.2 Toxicological Information on Active Substance(s)

Information regarding classification of the active substances and on EU endpoints and critical areas of concern identified during the EU review are given in Table 6.2-1.

Table 6.2-1: Information on active substance(s)) regarding toxicology

	Fludioxonil
Common Name	Fludioxonil
CAS-No.	131341-86-1
Classification and proposed labelling	
With regard to toxicological endpoints (according to the criteria in Reg. 1272/2008, as amended)	Hazard classes, categories: None Code(s) for hazard pictogram: None Signal word: Warning None Hazard statements: None Precautionary statements: None
Additional C&L proposal	No additional C&L are proposed.
Agreed EU endpoints	
AOEL systemic	0.59 mg/kg bw/d
Reference	EFSA Scientific Report (2007) 110
Conditions to take into account/critical areas of concern with regard to toxicology	
According to Review Report/EFSA Conclusion for active substance	None

6.3 Toxicological Evaluation of Plant Protection Product

A summary of the toxicological evaluation for FLUDIO 025 GF is given in the following tables. Full summaries of studies on the product that have not been previously considered within an EU peer review process are described in detail in Appendix 2.

According to Regulation (EC) No 1107/2009 “The use of non-animal test methods and other risk assessment strategies should be promoted”. Animal testing for the purposes of registration procedure should be minimized and tests on vertebrates should be undertaken as a last resort.

To avoid animal testing, skin corrosion/irritation and eye irritation or serious eye damage tests were performed based on alternative *in vitro* methods.

Table 6.3-1: Summary of evaluation of the studies on acute toxicity including irritancy and skin sensitisation for FLUDIO 025 GF

Type of test, species, model system (Guideline)	Result	Acceptability	Classification (acc. to the criteria in Reg. 1272/2008)	Reference
LD ₅₀ oral, rat (calculation method)	-	Yes	None	Additivity formula (calculation method)
	Justification presented in Appendix 2			
LD ₅₀ dermal, rat (calculation method)	-	Yes	None	Additivity formula (calculation method)
	Justification presented in Appendix 2			
LC ₅₀ inhalation, rat (calculation method)	-	Yes	None	-
	Not submitted, not necessary. Justification presented in Appendix 2)			
FLUDIO 025 GF: <i>In Vitro</i> Skin Corrosion: Reconstructed Human Epidermis Test Method (OECD 431)	Non-Corrosive	Yes	None	Krakowian D., 2022
FLUDIO 025 GF. Reconstructed human Cornea-like Epithelium (RhCE) test method for identifying chemicals not requiring classification and labelling for eye irritation or serious eye damage (OECD 492)	Not-Irritant	Yes	None	Krakowian D., 2019
Skin sensitisation (calculation method)	Not sensitizer	Yes	None	Additivity formula (calculation method)
	Justification presented in Appendix 2			
Supplementary studies for combinations of plant protection products	No data – not required	Yes / No / Supplementary		

Formulation does not contain any substances classified as:

- acute dermal toxicity,
- acute inhalation toxicity,
- respiratory sensitizer,
- germ cell mutagenic,
- cancerogenic,
- toxic on reproduction,
- toxic on specific target organs (single exposure, repeat exposure),
- aspiration hazard.

Thus according to points 3.4, 3.5, 3.6, 3.7, 3.8, 3.9., 3.10 of Regulation (EC) 1272/2008 product FLUDIO 025 GF does not need to be classified in above mentioned categories.

6.4 Toxicological Evaluation of FLUDIO 025 GF

All metabolite concentrations are predicted to stay below 0.1 µg/L – no groundwater assessment is required.

6.5 Dermal Absorption (KCP 7.3)

A summary of the dermal absorption rates for the active substances in FLUDIO 025 GF are presented in the following table.

Table 6.5-1: Dermal absorption rates for active substances in FLUDIO 025 GF

Fludioxonil		
	Value	Reference
Concentrate	40 50% (default)	Guidance on dermal absorption. <i>EFSA Journal</i> 2017;15(6);4873.
Dilution	50% (default)	SANTE/2018/10591 (rev.1 24 October 2018)

6.5.1 Justification for proposed values - fludioxonil

No data on dermal absorption for fludioxonil in FLUDIO 025 GF is available. Justifications for default values according to Guidance on Dermal Absorption (*EFSA Journal* 2017; 15(6):4873) are presented in the following table.

Default values of dermal absorption for FLUDIO 025 GF according to Guidance on Dermal Absorption (*EFSA Journal* 2017;15(6):4873) and SANTE/2018/10591 (rev.1 24 October 2018) are 40 50% for concentrate and 50% for dilution. FLUDIO 025 GF is water based formulation (FS).

Regarding to Guidance on Dermal Absorption (2017), a default dermal absorption value of:

- 10% may be applied for concentrated products that are water based formulation;
- 50% may be applied for (in use) dilutions of water based formulation.

Regarding to SANTE/2018/10591 (rev.1 24 October 2018) a plant protection product is considered a "dilution" when the active substance is present in the plant protection product at a concentration lower than or equal to 50 g/L (or 50 g/kg or 5%).

Based on above, Applicant has proposed for FLUDIO 025 GF a default dermal absorption value of 40 50% for the concentrate and 50% for the spray solution.

Table 6.5-2: Default dermal absorption rates for fludioxonil

	Value	Justification for value	Acceptability of justification
Concentrate	40 50 %	In the absence of any supporting dermal absorption data for FLUDIO 025 GF, it is proposed a dermal absorption value of 40 50% for the concentrate and 50 % in-use dilution, based on Guidance on dermal absorption. <i>EFSA Journal</i> 2017; 15(6);4873 and SANTE/2018/10591 (rev.1 24 October 2018).	accepted
Dilution	50 %		accepted

6.6 Exposure Assessment of Plant Protection Product (KCP 7.2)

Table 6.6-1: Product information and toxicological reference values used for exposure assessment

Product name	FLUDIO 025 GF/ FUNABEN® ŻEL 025 GF
Product code	FLUDIO 025 GF
Formulation type	FS
Category	Fungicide
Active substance (incl. content)	Fludioxonil 25 g/L
AOEL systemic	0.59 mg/kg bw/d
Inhalation absorption	100%
Oral absorption	100%
Dermal absorption	Concentrate: 40 50 % Dilution: 50 % (Default)

6.6.1 Selection of critical use(s) and justification

The critical GAP used for the exposure assessment of the plant protection product is shown in Table 6.1-4. A list of all intended uses within the zone is given in Part B, Section 0.

6.6.2 Operator exposure (KCP 7.2.1)

Comments of zRMS:	<p>The estimations of operator exposure to fludioxonil contained in FLUDIO 025 GF (based on SeedTROPEX model) performed by the Applicant are accepted.</p> <p><u>Conclusions:</u> According to the results of estimations, the use of FLUDIO 025 GF containing fludioxonil (25 g/L) using mechanical seed treatment machines of continuous movement with closed mixing chamber, causes acceptable health risk for unprotected operator wearing work wear (with long sleeved and long trousers). The exposure to fludioxonil amounts to the value lower than the AOEL set for this substance. However, due to the model limitations and the possibility of underestimation, evaluator suggests to equip the operator with protective gloves.</p> <p>Thus, the following sentence regarding the use of PPE is recommended by the evaluator to be placed in the label:</p> <p>„Stosować odzież roboczą (kombinezon) oraz rękawice ochronne w trakcie przygotowywania cieczy roboczej, zaprawiania, pakowania zaprawionych ziaren oraz czyszczenia sprzętu.”</p> <p>“Wear work wear (coverall) nad protective gloves during mixing/loading, seed treatment, seed packing and cleaning.”</p>
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6.6.2.1 Estimation of operator exposure

A summary of the exposure models used for estimation of operator exposure to the active substances during application of FLUDIO 025 GF according to the critical use is presented in Table 6.6-2. The outcome of the estimation is presented in Table 6.6-4. (Detailed calculations are in Appendix 3).

Table 6.6-2: Exposure models for intended uses

Critical use	Seed treatment of cereals (wheat, barley, rye, triticale) (max. 2 L product/ton) (Worst case: Winter wheat; 200 ml/ 100 kg seeds; sowing rate: 250 kg seeds/ha)
Model	Operator exposure is estimated using the “Seed-Treatment Operator EXposure” data (Seed-TROPEX). Seed-TROPEX is an exposure data base submitted to UK-PSD in 1996 for national registrations, contains results from studies performed in the UK and France. The Seed-TROPEX data base submitted in 1996 consists of two parts: Exposure values for operators involved in seed treatment activities and exposure values for operators loading and sowing treated seed.

The generic exposure values used for the estimation of the operator exposure for the critical use of FLUDIO 025 GF on cereals are derived from the SeedTROPEX studies and UK HSE data. They are presented in Table 6.6-3.

The total potential dermal exposure values given in the Seed-TROPEX data base represent the sum of residues detected on outer clothing (long-sleeved work jacket, long trousers, Tyvek coverall where worn), inner clothing (long underwear representing the operators’ skin), cap (representing the unprotected face) or face/neck wipes, hands and gloves of the operators. The total potential dermal exposure is therefore the total amount of active ingredient the skin of an operator would potentially be exposed to if no clothing at all was worn. Given the nature of the task and the potential for exposure during seed treatment operations, operators are assumed to wear suitable protective clothing and in addition protective gloves for activities such as opening and/or connecting product containers, calibrating or cleaning machinery.

FLUDIO 025 GF is packed in 0.2 L, 0.25 L, 0.4 L, 0.5 L, 0.8 L, 1 L, 5 L, 10 L, 20 L, 200 L or 1000 L HDPE packaging. The model was run for the 5 L packaging which is considered as a worst case scenario since it requires the biggest number of mixing-loading operations. A medium sized industrial cereal treatment facility treating 3-8 tons of cereal per h. During 9 h of work, throughput is equal 75 tons per day. Amount product needed to treating 75 tons is equal 150 L. Based on this, frequency of operation per day is equal 30 (150 L PPP per day/5L packaging).

The high performance of the pickling machine treating 3-8 tons of cereal per h and is designed for medium and large farms.

Table 6.6-3 Task-related generic exposures of seed treatment plant operatives as used in Seed-TROPEX (geometric mean values)

Task	Total potential dermal exposure (mL/operation)*	Estimated actual dermal exposure (mL/operation)*	Potential inhalation exposure (mL/operation)*
Calibration	0.033	0.014	0.001**
Mixing/loading	Fast-couple	0.0052	0.005
	Pre-mix	0.0047	0.001
Bagging (mg as/h)	Good LEV	1.84	0.698
	Poor LEV	1.84	0.698
Cleaning	0.872	0.083	0.016**
* Exposure during bagging in mg/h.			
** In the original SeedTROPEX model, these values were incorrect (under estimated).			

*** These values are based on a combination of SeedTROPEX data and HSE data.

Table 6.6-4: Estimated operator exposure

		fludioxonil	
Model data	Level of PPE	Total absorbed dose* (mg/kg/day)	% of systemic AOEL
Application equipment: Continuous flow seed treaters with closed mixing chamber			
Application rate		0.05 kg a.s./ton	
Undiluted			
SEEDTROPEX Model – 10 hours/day (1 operation of calibration and 1 operation for cleaning per day and 8 hours for seed bagging); – Treatment capacity: 75 tons per day; – Amount of product used: 150 L/day; – Packaging: 5 L; – 60 kg operator.	No PPE**	0.0687 0.344	11.7% 58.3 %
	PPE***	0.0351 0.113	6% 19.2 %
Dilution: 1:10			
SEEDTROPEX Model – 10 hours/day (1 operation of calibration and 1 operation for cleaning per day and 8 hours for seed bagging); – Treatment capacity: 75 tons per day; – Amount of product used: 150 L/day; – Packaging: 5 L; – 60 kg operator.	No PPE	0.1740	29.5 %
	PPE	0.090	15.1 %

*- sum of calibration, mixing/loading, bagging under poorly ventilated conditions and cleaning.

** - Operator wearing long sleeved jacket and long trousers but no gloves.

*** - Operator wearing long sleeved jacket, long trousers and gloves.

The Seed-TROPEX model does not contain data for the assessment of exposure of operators treating seeds on mobile equipment. For the following reasons exposure to operators treating seed on mobile equipment is considered to be in the same range or less than the exposure to operators working in static plants. Treatment on mobile equipment is usually done outside. This will most likely lead to lower levels of dust in the vicinity of the operators compared to working in a closed environment.

6.6.2.2 Measurement of operator exposure

Since the operator exposure estimations carried out indicated that the acceptable operator exposure level (AOEL) will not be exceeded under conditions of intended uses and consideration of the above mentioned personal protective equipment (PPE: long sleeved work jacket and long trousers are worn with the addition of chemical resistant gloves during the handling of product or treated seeds), a study to provide measurements of operator exposure was not necessary and was therefore not performed.

According to the model calculations, it can be concluded that the risk for the operator using undiluted FLUDIO 025 GF on cereals at up to 2 L/ton is acceptable without the use of personal protective equipment. The % AOEL for FLUDIO 025 GF is equal to **11.7-58.3%**. In the case of use diluted product on cereals, the risk is acceptable without the use of personal protective equipment. The % AOEL for FLUDIO 025 GF is equal to 29.5 % for an operator working with the concentrated formulation and using no

PPE. When PPE is used, the % AOEL for an operator performing all tasks during a working shift and when handling the diluted formulation decreases to 15.1 %.

According to the model calculation, it is concluded that the risk for the operator using undiluted FLUDIO 025 GF at 2 L/ton seeds for the cereal seed treatment is acceptable without of the use of personal protective equipment. Nevertheless, suitable protective clothing (coveralls, gloves) should be worn when handling the product or treated seed.

6.6.3 Worker exposure (KCP 7.2.3)

Comments of zRMS:	<p>Dermal absorption and inhalation are the main routes of exposure during sowing: dermal via contact with treated seeds and equipment; inhalation exposure as a result of the drift from particles abraded from seeds. According to the results of estimations, the exposure to fludioxonil (25 g/L) contained in the product FLUDIO 025 GF during sowing of treated seeds, causes acceptable health risk for unprotected worker wearing work wear (with long sleeved and long trousers). The exposure to fludioxonil amounts to the value lower than the AOEL set for this substance. However, the protective gloves are strongly recommended for worker during sowing activities (opening sacks, filling the tanks of a sowing machine).</p> <p>The recommendation of using PPE by the worker should be placed on the label of the product. The evaluator suggests the following sentence regarding the use of PPE to be placed in the label:</p> <p>„Stosować odzież roboczą (kombinezon) oraz rękawice ochronne w czasie kontaktu z zaprawionym ziarnem”</p> <p>“Wear work wear (coverall) nad protective gloves during during contact with treated seeds”.</p>
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6.6.3.1 Estimation of worker exposure

Table 6.6-5 shows the exposure model used for estimation of worker exposure after entry into a previously treated area or handling a crop treated with FLUDIO 025 GF according to the critical use. Outcome of the estimation is presented in Table 6.6-7. Detailed calculations are in Appendix 3.

Table 6.6-5: Exposure models for intended uses

Critical use	Seed treatment of Cereals (max. 2 L product/ton) (Worst case: Winter wheat; 200 ml/ 100 kg seeds; sowing rate: 250 kg seeds/ha)
Model	Worker exposure is estimated using the “Seed-Treatment Operator EXposure” data (Seed-TROPEX) for Operator. Seed-TROPEX is an exposure data base submitted to UK-PSD in 1996 for national registrations, contains results from studies performed in the UK and France. The Seed-TROPEX data base submitted in 1996 consists of two parts: Exposure values for operators involved in seed treatment activities and exposure values for operators loading and sowing treated seed.

Workers other than operators may be exposed only while sowing the treated seeds, when opening sacks containing the treated seeds and when filling the tanks of a sowing machine.

As for bagging, for loading and sowing activities dust is likely to be the main source of exposure, whereby it is reasonable to conclude that the contents of active ingredient in the dust is related to the loading of active ingredient on the seed.

The SeedTROPEX modelling is based on generic exposure figures for dermal and inhalation exposure covering exposure during loading and sowing of treated seed. These generic exposure figures were de-

terminated based on studies performed with active substances applied at 370 or 500 g a.s./ton seed. They are expressed in mg a.s./hour and do not take into account the amount of active substance applied to seed. The estimation is based on 10 hours of work for an operator weighing 70 kg. The generic Seed-TROPEX exposure values for loading and sowing treated seeds are given in Table 6.6-6. Exposure by inhalation of operators loading and sowing of treated seed was based on an average ventilation rate of 29 L/min.(Seed-TROPEX studies).

Table 6.6-6: Generic exposure values for dermal and inhalation exposure during loading and sowing of treated seeds

Exposition	Possible dermal Absorption (mg/person per day) without personal protective equipment	Actual dermal exposure (mg/person per day) with personal protective equipment	Inhalation exposure (mg/person per day) without respiratory protection
Preparation and sowing of seeds – standard values (mg/hour)	1.48	0.73	0.02
10-hour work	14.8	7.3	0.2

Table 6.6-7: Estimated worker exposure during loading and sowing of treated seeds

fludioxonil		
Level of PPE	Total absorbed dose (mg/kg bw/day)	% of systemic AOEL
Sowing of treated seeds Work rate: 10 hours/day Body weight: 70 kg		
Application rate	0.05 kg a.s./ton	
No PPE	0.024 0.109	4.1 % 18.4 %
PPE	0.0133 0.055	2.3 % 9.32 %

** gloves and protective clothes during all operations

6.6.3.2 Refinement of generic DFR value (KCP 7.2)

Not required.

6.6.3.3 Measurement of worker exposure

Since the worker exposure estimations carried out indicated that the acceptable operator exposure level (AOEL) will not be exceeded under conditions of intended uses and considering above mention PPE, a study to provide measurements of worker exposure was not necessary and was therefore not performed.

Based on the calculation of worker exposure with the SeedTROPEX model, it is concluded that there is no unacceptable risk anticipated for workers wearing adequate work clothing (but no PPE) when loading and sowing seeds treated with 2 L FLUDIO 025 GF /ton.

6.6.4 Resident and bystander exposure (KCP 7.2.2)

Comments of zRMS:	<p>The AAOEL value for the fludioxonil is not allocated. Consequently, it is assumed that the estimation of bystander exposure is covered by the calculation of resident exposure towards the active substance.</p> <p>Due to the method of application of product (treatment on mobile equipment, usually done outside) the bystander/resident exposure to the active substance is possible. Hence, the estimation of exposure for this group of people is justified. However, it is not expected that exposure value of bystander/resident will exceed those of operators and workers.</p> <p>According to the results of estimations provided by the Applicant, the exposure to fludioxonil contained in the FLUDIO 025 GF according to the list of intended uses presented in GAP Table, causes acceptable health risk for bystander and resident (adult and child) based on SeedTROPEX model.</p>
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6.6.4.1 Estimation of resident and bystander exposure

The exposure assessment for bystanders covers the exposure that a resident could reasonably be expected to incur in a single day. Therefore, there is no need for a separate acute risk assessment for residents. No bystander risk assessment is required for PPPs that do not have significant acute toxicity or the potential to exert toxic effects after a single exposure. Exposure in this case will be determined by average exposure over a longer duration, and higher exposures on one day will tend to be offset by lower exposures on other days. Therefore, exposure assessment for residents also covers bystander exposure.

Table 6.6-88 shows the exposure model used for estimation of resident and bystander exposure to fludioxonil. The outcome of the estimation is presented in Table 6.6-10. Detailed calculations are in Appendix 3.

Table 6.6-8: Exposure models for intended uses

Critical use	Seed treatment of cereals (max. 2 L product/ton) (Worst case: Winter wheat; 200 ml/ 100 kg seeds; sowing rate: 250 kg seeds/ha)
Model	“Seed-Treatment OPERator EXposure” data (Seed-TROPEX).

Fludioxonil (3.9×10^{-7} Pa at 25 °C) have low vapour pressures, it is unlikely that bystanders will be exposed to significant levels of vapour during seed treatment operations.

Bystander exposure with seed treatment operations is usually limited to co-workers involved in such tasks as driving fork-lift trucks. Seed-TROPEX contains data for three fork lift truck drivers operating in cereal seed treatment plants. The geometric mean levels of potential dermal exposure and potential inhalation exposure for these individuals are given in Table 6.6-9.

Table 6.6-9: Generic exposure values

Potential dermal exposure	Potential inhalation exposure
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[ml formulation/h]	
0.000756	0.00000865

Table 6.6-10: Estimated bystander and resident exposure

fludioxonil		
Level of PPE	Total absorbed dose (mg/kg bw/day)	% of systemic AOEL
Assuming a duration of exposure: 8 hours/day Body weight: 60 kg No protection provided by normal work wear		
Application rate	0.05 kg a.s./ton	
No PPE	0.00280 0.00129	0.05 % 0.22

6.6.4.2 Measurement of resident and/or bystander exposure

Since the resident and/or bystander exposure estimations carried out indicated that the acceptable operator exposure level (AOEL) for fludioxonil will not be exceeded under conditions of intended uses and considering above mentioned risk mitigation measures, a study to provide measurements of resident/bystander exposure was not necessary and was therefore not performed.

6.6.5 Combined exposure

Not relevant. The product contains only one active substance.

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
KCP 7.1.4	Krakowian D.	2022	FLUDIO 025 GF. Reconstructed human Cornea-like Epithelium (RhCE) test method for identifying chemicals not requiring classification and labelling for eye irritation or serious eye damage Krakowian D., 2022. Study code: EIT-06-21 Łukasiewicz Research Network – Institute of Industrial Organic Chemistry, Branch Pszczyna GLP Unpublished	N	SynthosAgro Sp. z o.o.
KCP 7.1.4	Krakowian D.	2022	FLUDIO 025 GF: <i>In vitro</i> Skin Corrosion: Reconstructed Human Epidermis Test Method. Krakowian D., 2022. Study code: SCT-03-21. Łukasiewicz Research Network – Institute of Industrial Organic Chemistry, Branch Pszczyna GLP Unpublished	N	SynthosAgro Sp. z o.o.

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

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

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

Appendix 2 Detailed evaluation of the studies relied upon

A 2.1 Statement on bridging possibilities

Comments of zRMS:	Comment on statement; acceptable or not
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The bridging was not necessary.

A 2.2 Acute oral toxicity (KCP 7.1.1)

Comments of zRMS:	Taking into account the composition of the product and the provisions of the Regulation EC No. 1272/2008, the formulation FLUDIO 025 GF does not require classification in regards to oral acute toxicity.
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FLUDIO 025 GF contains one component (1,2-benzizotiazol-3(2H)-on) which is classified as Acute Tox. 4 with hazard statement H302. 1,2-benzizotiazol-3(2H)-on concentration in the product is equal to 0.018 %.

Acute oral toxicity value (ATE_{mix}) for FLUDIO 025 GF can be estimated according to principles of Regulation (EC) 1272/2008, formula in section 3.1.3.6.1 (additivity formula) as follows:

$$\frac{100}{ATE_{mix}} = \sum_n \frac{C_i}{ATE_i}$$

Where:

- C_i - concentration of ingredient i (% w/w or % v/v)
- i - the individual ingredient from 1 to n
- n - the number of ingredients
- ATE_i - Acute Toxicity Estimate of ingredient i.

Therefore, ATE_{mix} value is equal to:

$$ATE_{mix} = \frac{100}{\frac{0.018}{500}} = 2\,777\,778$$

The estimated value ATE_{mix} of acute oral toxicity for FLUDIO 025 GF is higher than 2000 mg/kg bw. No classification is required according to Regulation (EC) No. 1272/2008.

A 2.3 Acute percutaneous (dermal) toxicity (KCP 7.1.2)

Comments of zRMS:	Taking into account the composition of the product and the provisions of the Regulation EC No. 1272/2008, the formulation FLUDIO 025 GF does not require classification in regards to dermal acute toxicity.
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FLUDIO 025 GF does not contain any component which is classified as acute dermal toxicity, therefore the product will not be classified as acute dermal toxicity.

Therefore, no classification is required.

A 2.4 Acute inhalation toxicity (KCP 7.1.3)

Comments of zRMS:	Taking into account the composition of the product and the provisions of the Regulation EC No. 1272/2008, the formulation FLUDIO 025 GF does not require classification in regards to inhalation acute toxicity.
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No data on acute inhalation toxicity for fludioxonil in FLUDIO 025 GF is available.

FLUDIO 025 GF contains active substance with a vapour pressure below 1×10^{-2} Pa (vapour pressure fludioxonil: 3×10^{-7} Pa at 25 °C). Thus, according to the Commission Regulations (EU) No 284/2013, the study of acute inhalation toxicity for FLUDIO 025 GF is not required.

FLUDIO 025 GF does not contain any component which is classified as acute inhalation, therefore the product will not be classified as acute inhalation toxicity.
Therefore, no classification is required.

A 2.5 Skin irritation (KCP 7.1.4)

Comments of zRMS:	<p>The study presented by the Applicant (Krakowian D., 2022, Study code: SCT-03-21) is accepted without reservation. The obtained results show that product FLUDIO 025 GF is considered to be non-corrosive to skin. Thus it cannot be classified as category 1 acc. to Regulation EC 1272/2008. This result does not exclude the irritation potential of tested formulation. Further <i>in vitro</i> test was not carried out, thus the additive formula (calculation method) was used to finalize the assessment.</p> <p>Calculation method: Two ingredients contained in the formulation FLUDIO 025 GF were taken into account for the purpose of product classification:</p> <ul style="list-style-type: none">- 0.018%, Skin Irrit., H315- 0.14%, Skin Irrit., H315 <p>The sum of the concentration values of the relevant ingredient is below generic concentration limit that triggers classification of the mixture in regards to the skin irritation.</p> <p>Conclusion: Taking into account the composition of the product, the formulation FLUDIO 025 GF does not require classification in regards to skin irritation.</p>
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A 2.5.1 Study 1

Reference	KCP 7.1.4
Report	FLUDIO 025 GF: <i>In vitro</i> Skin Corrosion: Reconstructed Human Epidermis Test Method. Krakowian D., 2022. Study code: SCT-03-21
Guideline(s)	OECD 431 (2019)/EU Methods B.40
Deviations	No
GLP	Yes
Acceptability	Yes
Duplication (if vertebrate study)	No

Materials and methods

Test material (Lot/Batch No.)	FLUDIO 025 GF (Batch No. SNS-F-06-22)
Test sytem	EpiDerm™ tissues (human reconstructed epidermis model)
No. of inserts	2 inserts with tissues of the human skin model EpiDerm
Initial test using one animal	No
Exposure	Topical exposure; 50.0 µL test item are applied without preparation on two tissues.
Exposure time	3 min., 60 min.
Negative control	sterile deionized water
Positive control	8 N potassium hydroxide
Viability Test	MTT Viability Test
Vehicle/Dilution	None
Remarks	None

Results and discussions

Table A 1: Tissue viability [%] – 1-hour exposure

	Negative control	Positive control	FLUDIO 025 GF
Tissue no. 1 viability	104.3	1.3	104.9
Tissue no. 2 viability	95.7	1.4	101.4
Mean Tissue viability	100.0	1.3	103.2
SD (±)	4.3	0.1	1.7

Table A 2: Tissue viability [%] – 3-minute exposure

	Negative control	Positive control	FLUDIO 025 GF
Tissue no. 1 viability	89.8	1.7	70.2
Tissue no. 2 viability	110.2	1.8	98.6
Mean Tissue viability	100.0	1.8	84.4
SD (±)	10.2	0.0	14.2

Conclusion

After the 3-minute exposure to the test item, the mean value of relative tissue viability was equal to 84.4 %. After the 1-hour exposure to the test item, the mean value of relative tissue viability was equal to 103.2 %. These values are above the threshold of non-corrosive effects on the skin (viability ≥ 50 % after 3-minutes exposure and ≥ 15 % after 60-minutes exposure).

The test item, FLUDIO 025 GF, is considered to be **non-corrosive to skin** in the Reconstructed human Epidermis (RhE) Test Method. It can not be classified as category 1 in the UN GHS classification.

No classification is required according to Regulation (EC) No. 1272/2008.

A 2.6 Eye irritation (KCP 7.1.5)

Comments of zRMS:	The study presented by the Applicant (Krakowian D., 2022, Study code: EIT-06-21) is accepted without reservation. The obtained results show that product FLUDIO 025 GF is considered to be non-irritant to eye, thus does not require classification acc. to Regulation EC 1272/2008.
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	<p>The results of the calculation method (additivity formula) confirmed test results. Four ingredients contained in the formulation FLUDIO 025 GF were taken into account for the purpose of product classification:</p> <ul style="list-style-type: none"> - 0.018%, Eye Dam.1., H3118 - 0.009%, Skin Corr.1, H314 - 0.14%, Eye Irrit., H319 - 1.89%, Eye Irrit., H319 <p>$10 \times (0.018 + 0.009) + 0.14 + 1.89 = 2.3\%$</p> <p>The sum of concentration values of the relevant ingredients is below the generic concentration limit that triggers classification of the mixture in regards to the eye irritation.</p> <p><u>Conclusion:</u> The formulation FLUDIO 025 GF does not requires classification in regards to eye irritation.</p>
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A 2.6.1 Study 1

Reference	KCP 7.1.5
Report	FLUDIO 025 GF: Reconstructed human Cornea-like Epithelium (RhCE) test method for identifying chemicals not requiring classifications and labelling for eye irritation or serious eye damage. D. Krakowian, 2022, Study code: EIT-06-21.
Guidelines	OECD Guideline No 492 (2019)/ EU Method B.69. Council Regulation (EC) No. 440/2008
Deviations	No
GLP	Yes
Acceptability	Yes
Duplication (if vertebrate study)	No

Materials and methods

Test material (Lot/Batch No.)	FLUDIO 025 GF (Batch No. SNS-F-06-22)
Test system	The EpiOcular™ tissue construct is a nonkeratinized epithelium prepared from normal human keratinocytes.
No. of inserts	2 tissues
Initial test using one animal	No
Exposure	Topical exposure; 50.0 µL test item are applied without preparation on two tissues.
Exposure time	30 min.
Negative control	sterile deionized water
Positive control	methyl acetate
Viability Test	MTT Viability Test
Vehicle/Dilution	None
Remarks	None

Results and discussions

Table A 3: Relative Tissue viability [%]

	Negative control	Positive control	FLUDIO 025 GF
Tissue no. 1 viability	105.2	44.3	97.7
Tissue no. 2 viability	94.8	30.7	94.0
Mean Tissue viability	100.0	37.5	95.8
SD (±)	5.2	18	1.9

Conclusion

After treatment with the test item, the mean value of relative tissue viability was equal to 95.8%. This value is above the threshold for non-irritants (viability >60%). FLUDIO 025 GF is considered to be non-irritating to eye in the Reconstructed human Cornea-like Epithelium (RhCE) test method. No further testing is needed to classify the test item, as it does not require classification for eye irritation or serious eye damage (no category).

Under the experimental conditions, FLUDIO 025 GF is **not an eye irritant**. Thus, no classification is required according to Regulation (EC) No. 1272/2008. The other additional researches (*in vivo* or *in vitro*) are not necessary for classification of FLUDIO 025 GF.

A 2.7 Skin sensitisation (KCP 7.1.6)

Comments of zRMS:	Two ingredients contained in the formulation FLUDIO 025 GF were taken into account for the purpose of product classification regarding skin sensitization: - 0.018%, Skin Sens.1., H317 - 0.0094%, Skin Sens 1A., H317 The sum of concentration values of the relevant ingredients is below the generic concentration limit that triggers classification of the mixture in regards to the skin sensitization. <u>Conclusion:</u> Taking into account the composition of the product, the formulation FLUDIO 025 GF does not requires classification in regards to skin sensitization.
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Calculation method (Regulation (EC) No 1272/2008)

FLUDIO 025 GF does not contain any component which is classified as respiratory sensitizer with hazard statement H334, therefore the product will not be classified as respiratory sensitizer with hazard statement H334.

FLUDIO 025 GF contains two components which are classified as Skin Sens. 1 with hazard statement H317:

- the concentration of the first component in FLUDIO 025 GF is equal to 0.018%. This concentration is below concentration limit for this substance (0.05%) presented in Table 3.1 of Annex VI to of Regulation 1272/2008.
- the concentration of the second component in FLUDIO 025 GF is equal to 0.01%.

The total amount of substances which are classified as Skin Sens.1 in FLUDIO 025 GF is equal 0.0274%. This concentration is below concentration limit (1%) stated in Table 3.4.5 of Regulation 1272/2008.

Thus, no classification is required according to Regulation (EC) No. 1272/2008.

A 2.8 Supplementary studies for combinations of plant protection products (KCP 7.1.7)

A 2.9 Data on co-formulants (KCP 7.4)

A 2.9.1 Material safety data sheet for each co-formulant

Information regarding material safety data sheets of the co-formulants can be found in the confidential dossier of this submission (Registration Report - Part C).

A 2.9.2 Available toxicological data for each co-formulant

Available toxicological data for each co-formulant can be found in the confidential dossier of this submission (Registration Report - Part C).

A 2.10 Studies on dermal absorption (KCP 7.3)

According requirements from Reg. No. 284/2013/WE the study shall be conducted when dermal exposure is a significant exposure route and no acceptable risk is estimated using default absorption value.

In order to make assessment of exposure, Applicant for FLUDIO 025 GF has proposed a default dermal absorption value of 40 50% for the concentrate and 50 % for the spray solution, based on Guidance on Dermal Absorption (*EFSA Journal* 2017;15(6)4873) and SANTE/2018/10591 (rev.1 24 October 2018).

Use of plant protection product FLUDIO 025 GF is safe for operator, taking into account proposed dose of product, type of usage, type of personal protective equipment (gloves, protective garment and sturdy footwear). Maintain general rules of safety and hygiene of working with plant protection products and comply with requirements enclosed in label, risk during employ FLUDIO 025 GF is acceptable, absorbed dose of fludioxonil have safe value, below AOEL for this active ingredient.

According to above there isn't necessity to do tests of dermal absorption for FLUDIO 025 GF.

A 2.11 Other/Special Studies

Appendix 3 Exposure calculations

A 3.1 Operator exposure calculations (KCP 7.2.1.1)

Table A 4: Task-related generic exposures of seed treatment plant operatives as used in SeedTROPEX (geometric mean values)

Task		Total potential dermal exposure (mL/operation)*	Estimated actual dermal exposure (mL/operation)*	Potential inhalation exposure (mL/operation)*
Calibration		0.033	0.014	0.001**
Mixing/loading	Fast-couple	0.0052	0.005	0.0001
	Pre-mix	0.0047	0.001	0.0001
Bagging (mg as/h)	Good LEV	1.84	0.698	0.0054***
	Poor LEV	1.84	0.698	0.054***
Cleaning		0.872	0.083	0.016**
* Exposure during bagging in mg/h.				
** In the original SeedTROPEX model, these values were incorrect (under estimated).				
*** These values are based on a combination of SeedTROPEX data and HSE data.				

A 3.1.1 Calculations for fludioxonil

Table A 5: Input parameters considered for the estimation of operator exposure

Formulation type	FS		Crop type	Cereals (worst case: winter wheat)
Application rate	0.05 kg/ha		Application rate (L/ton)	2
Dermal absorption (DA)	100	% (concentr.)	Pack size (L)	5
	50	% (dilution)	Operation number	30
Inhalation absorption (IA)	100	%	Throughput (tons/day)	75
Body weight (BW)	60	kg/person	Amount product handled (L/day)	150
AOEL	0.59	mg/kg bw/d		

Calculation method:

(1)	Total Potetial Dermal Exposure	=	Generic exposure value (Table A.6)	x	Ca.i.
	Estimeted Acute Dermal Exposure				
	Inhalation Exposure				
(2)	Total Potetial Dermal Exposure (2)	=	Total Potetial Dermal Exposure (1)	x	Frequency of operation
	Estimeted Acute Dermal Exposure (2)				
	Inhalation Exposure (2)				
(3)	Total Potetial Dermal Exposure (3)	=	Total Potetial Dermal Exposure (2)	x	DA
	Estimeted Acute Dermal Exposure (3)				
(4)	Inhalation Exposure (4)	=	Inhalation Exposure (3)	x	IA
(5)	Total Potetial Dermal Exposure (5)	=	Total Potetial Dermal Exposure (4)	/	BW
	Estimeted Acute Dermal Exposure (5)				
	Inhalation Exposure (5)				
(6)	Sum of AOELs for a single operator performing: calibration, fast couple mixing/loading, bagging and cleaning (worst case).				

Table A 6: Estimation of acute operator exposure towards fludioxonil according to Seed TROPEX model – undiluted

FLUDIOXONIL							
OPERATOR EXPOSURE (Geometric mean value)							
TASK	Total Potential Dermal Exposure (1)	Estimated Acute Dermal Exposure (1)	Inhalation Exposure (1)	Frequency of operation per day *	Total Potential Dermal Exposure (2)	Estimated Acute Dermal Exposure (2)	Inhalation Exposure (2)
	[mg/person per operation]	[mg/person per operation]			[mg/person per day]		
Calibration (1)	0,825	0,35	0,025	1	0,825	0,35	0,025
mixing/ loading (pre-mix) (1)	0,1175	0,025	0,0025	30	3,525	0,75	0,075
mixing/ loading (fast-coupling) worst case (1)	0,13	0,125	0,0025	30	3,9	3,75	0,075
Bagging (good LEV)	1,84	0,698	0,0054	8	14,72	5,584	0,0432
Bagging (poor LEV) worst case	1,84	0,698	0,054	8	14,72	5,584	0,432
Cleaning (1)	21,8	2,075	0,4	1	21,8	2,075	0,4
SYSTEMIC EXPOSURE							
Task	Total Potential Dermal Exposure (3)	Estimated Acute Dermal Exposure (3)	Inhalation Exposure (4)	X	Total Potential Dermal Exposure (5)	Estimated Acute Dermal Exposure (5)	Inhalation Exposure (5)
	[mg/person per day]				[mg/kg bw/day]		
Calibration	0,0825	0,035	0,025		0,001375	0,000583333	0,000416667
mixing/ loading (pre-mix)	0,3525	0,075	0,075		0,005875	0,00125	0,00125
mixing/ loading (fast-coupling) worst case	0,39	0,375	0,075		0,0065	0,00625	0,00125
Bagging (good LEV)	1,472	0,5584	0,0432		0,024533333	0,009306667	0,00072
Bagging (poor LEV) worst case	1,472	0,5584	0,432		0,024533333	0,009306667	0,0072
Cleaning	2,18	0,2075	0,4		0,036333333	0,003458333	0,006666667
SYSTEMIC EXPOSURE as percentage of AOEL (0.16 mg/kg bw/day)							
Task	Total Potential Systemic Dermal Exposure	Total Acute Systemic Exposure	X	% AOEL (no PPE)	% AOEL (PPE)		
	[mg/kg bw/day]			%			
Calibration	0,001375	0,001		0,233050847	0,169491525		
mixing/ loading (pre-mix)	0,005875	0,0025		0,995762712	0,423728814		
mixing/ loading (fast-coupling) worst case	0,0065	0,0075		1,101694915	1,271186441		
Bagging (good LEV)	0,024533333	0,010026667		4,15819209	1,699435028		
Bagging (poor LEV) worst case	0,024533333	0,016506667		4,15819209	2,797740113		
Cleaning	0,036333333	0,010125		6,15819209	1,716101695		
Multiple Activity task (6)	0,068741667	0,035131667	11,65112994	5,954519774			

FLUDIOXONIL							
OPERATOR EXPOSURE (Geometric mean value)							
TASK	Total Potential Dermal Exposure (1)	Estimated Acute Dermal Exposure (1)	Inhalation Exposure (1)	Frequency of operation per day *	Total Potential Dermal Exposure (2)	Estimated Acute Dermal Exposure (2)	Inhalation Exposure (2)
	[mg/person per operation]	[mg/person per operation]			[mg/person per day]		
Calibration (1)	0,825	0,35	0,025	1	0,825	0,35	0,025
mixing/ loading (pre-mix) (1)	0,1175	0,025	0,0025	30	3,525	0,75	0,075
mixing/ loading (fast-coupling) worst case (1)	0,13	0,125	0,0025	30	3,9	3,75	0,075
Bagging (good LEV)	1,84	0,698	0,0054	8	14,72	5,584	0,0432
Bagging (poor LEV) worst case	1,84	0,698	0,054	8	14,72	5,584	0,432
Cleaning (1)	21,8	2,075	0,4	1	21,8	2,075	0,4
SYSTEMIC EXPOSURE							
Task	Total Potential Dermal Exposure (3)	Estimated Acute Dermal Exposure (3)	Inhalation Exposure (4)	X	Total Potential Dermal Exposure (5)	Estimated Acute Dermal Exposure (5)	Inhalation Exposure (5)
	[mg/person per day]				[mg/kg bw/day]		
Calibration	0,4125	0,175	0,025		0,006875	0,002916667	0,000416667
mixing/ loading (pre-mix)	1,7625	0,375	0,075		0,029375	0,00625	0,00125
mixing/ loading (fast-coupling) worst case	1,95	1,875	0,075		0,0325	0,03125	0,00125
Bagging (good LEV)	7,36	2,792	0,0432		0,122666667	0,046533333	0,00072
Bagging (poor LEV) worst case	7,36	2,792	0,432		0,122666667	0,046533333	0,0072
Cleaning	10,9	1,0375	0,4		0,181666667	0,017291667	0,006666667
SYSTEMIC EXPOSURE as percentage of AOEL (0.16 mg/kg bw/day)							
Task	Total Potential Systemic Dermal Exposure	Total Acute Systemic Exposure	X	% AOEL (no PPE)	% AOEL (PPE)		
	[mg/kg bw/day]			%			
Calibration	0,006875	0,003333333		1,165254237	0,564971751		
mixing/ loading (pre-mix)	0,029375	0,0075		4,978813559	1,271186441		
mixing/ loading (fast-coupling) worst case	0,0325	0,0325		5,508474576	5,508474576		
Bagging (good LEV)	0,122666667	0,047253333		20,79096045	8,009039548		
Bagging (poor LEV) worst case	0,122666667	0,053733333		20,79096045	9,107344633		
Cleaning	0,181666667	0,023958333		30,79096045	4,060734463		
Multiple Activity task (6)	0,343708333	0,113525	58,25564972	19,24152542			

* - Bagging [h]

Table A 7: Estimation of acute operator exposure towards fludioxonil according to Seed TROPEX model – diluted 1:10

FLUDIOXONIL							
OPERATOR EXPOSURE (Geometric mean value)							
TASK	Total Potential Dermal Exposure (1)	Estimated Acute Dermal Exposure (1)	Inhalation Exposure (1)	Frequency of operation per day *	Total Potential Dermal Exposure (2)	Estimated Acute Dermal Exposure (2)	Inhalation Exposure (2)
	[mg/person per operation]	[mg/person per operation]				[mg/person per day]	
Calibration (1)	0,0825	0,035	0,0025	1	0,0825	0,035	0,0025
mixing/ loading (pre-mix) (1)	0,1175	0,025	0,0025	30	3,525	0,75	0,075
mixing/ loading (fast-coupling) worst case (1)	0,13	0,125	0,0025	30	3,9	3,75	0,075
Bagging (good LEV)	1,84	0,698	0,0054	8	14,72	5,584	0,0432
Bagging (poor LEV) worst case	1,84	0,698	0,054	8	14,72	5,584	0,432
Cleaning (1)	2,18	0,2075	0,04	1	2,18	0,2075	0,04
SYSTEMIC EXPOSURE							
Task	Total Potential Dermal Exposure (3)	Estimated Acute Dermal Exposure (3)	Inhalation Exposure (4)	X	Total Potential Dermal Exposure (5)	Estimated Acute Dermal Exposure (5)	Inhalation Exposure (5)
	[mg/person per day]				[mg/kg bw/day]		
Calibration (1)	0,04125	0,0175	0,0025		0,0006875	0,000291667	4,16667E-05
mixing/ loading (pre-mix) (1)	1,7625	0,375	0,075		0,029375	0,00625	0,00125
mixing/ loading (fast-coupling) worst case (1)	1,95	1,875	0,075		0,0325	0,03125	0,00125
Bagging (good LEV)	7,36	2,792	0,0432		0,122666667	0,046533333	0,00072
Bagging (poor LEV) worst case	7,36	2,792	0,432		0,122666667	0,046533333	0,0072
Cleaning (1)	1,09	0,10375	0,04		0,018166667	0,001729167	0,000666667
SYSTEMIC EXPOSURE as percentage of AOEL (0.16 mg/kg bw/day)							
Task	Total Potential Systemic Dermal Exposure	Total Acute Systemic Exposure	X	% AOEL (no PPE)	% AOEL (PPE)		
	[mg/kg bw/day]			%			
Calibration	0,0006875	0,000333333		0,116525424	0,056497175		
mixing/ loading (pre-mix)	0,029375	0,0075		4,978813559	1,271186441		
mixing/ loading (fast-coupling) worst case	0,0325	0,0325		5,508474576	5,508474576		
Bagging (good LEV)	0,122666667	0,047253333		20,79096045	8,009039548		
Bagging (poor LEV) worst case	0,122666667	0,053733333		20,79096045	9,107344633		
Cleaning	0,018166667	0,002395833		3,079096045	0,406073446		
Multiple Activity task (6)	0,174020833	0,0889625	29,4950565	15,07838983			

* - Bagging [h]

A 3.2 Worker exposure calculations (KCP 7.2.3.1)

Table A 8 : Generic exposure values for dermal and inhalation exposure during loading and sowing of treated seeds

Exposition	Possible dermal Absorption (mg/person per day) without personal protective equipment	Actual dermal exposure (mg/person per day) with personal protective equipment	Inhalation exposure (mg/person per day) without respiratory protection
Preparation and sowing of seeds – standard values (mg/hour)	1.48	0.73	0.02
10-hour work	14.8	7.3	0.2

A 3.2.1 Calculations for fludioxonil

Table A 9: Input parameters considered for the estimation of worker exposure

Formulation type	FS	Crop type	Cereals (worst case: winter wheat)
Working time [h/day]	10	Working time [h/day]	10
Dermal absorption (DA)	40-50 % (concentr.)	Body weight (BW)	70 kg/person
	50 % (dilution)	AOEL	0.59 mg/kg bw/d
Inhalation absorption (IA)	100 %		

Calculation:

Route specific exposure = Route specific × Working time

Systemic exposure [mg/person/day]= Route specific exposure × Absorption

Systemic exposure [mg/kg bw/day]= Route specific exposure/ 60 kg

Table A 10: Estimation of acute worker exposure towards fludioxonil according to Seed-TROPEX model – with PPE

Route of exposure	Route specific	Working time	Route specific exposure	Absorption	Systemic exposure	Systemic exposure	% AOEL
	[mg/person/h]	[h/day]	[mg/person/day]	[%]	[mg/person/day]	[mg/kg bw/day]	
Estimated actual dermal exposure	0,73	10	7,3	40-50	0,73 3.65	0,010428571 0.052142857	
Inhalation	0,02	10	0,2	100	0,2	0,002857143	
Total systemic dose					0,93 3.85	0,013285714 0.055	2,25181598 9.3220339

Table A 11: Estimation of acute worker exposure towards fludioxonil according to Seed-TROPEX model – without PPE

Route of exposure	Route specific	Working time	Route specific exposure	Absorption	Systemic exposure	Systemic exposure	% AOEL
	[mg/person/h]	[h/day]	[mg/person/day]	[%]	[mg/person/day]	[mg/kg bw/day]	
Estimated actual dermal exposure	1,48	10	14,8	40-50	1,48	0,021142857 0.105714286	
Inhalation	0,02	10	0,2	100	0,2	0,002857143	
Total systemic dose					1,68	0,024 0.108571429	4,06779661 18.401937

A 3.3 Resident and bystander exposure calculations (KCP 7.2.2.1)

Table A 12: Generic exposure values – according to SeedTROPEX model

Potential Dermal Exposure (PDE)	Potential Inhalation Exposure (PIE)
[ml formulation/h]	
0.000756	0.00000865

A 3.3.1 Calculations for fludioxonil

Table A 13: Input parameters considered for the estimation of acute bystander and resident exposure

Formulation type	FS	Concentration active substance in PPP (C _{a.i.})	25 g/L
Inhalation absorption (IA)	100 %	Body weight (BW)	60 kg/person
Dermal absorption (DA)	10-50	% (concentr.)	AOEL
	50	% (dilution)	Duration of exposure (t) [h]
			8

Table A 14: Estimation of bystander and resident exposure towards fludioxonil according to SeedTROPEX model

Potential Dermal Exposure (PDE)	Potential Inhalation Exposure (PIE)	Potential Systemic Dermal Exposure PSDE	Potential Systemic Inhalation Exposure PSIE	Total Potential Systemic Exposure TPSE	%AOEL
[ml formulation/h]		[mg/kg bw/day]			
0,000756	0,00000865	0,000252 0.00126	2,88333E-05	0,000280833 0.001288833	0,047599 0.218446

Calculation:

$$PSDE = PDE \times C_{a.i} \times t \times DA_{(concent.)} / BW$$

$$PSID = PIE \times C_{a.i} \times t / BW$$

$$TPSE = PSDE + PSID$$

A 3.4 Combined exposure calculations

Not applicable.

Appendix 5 Detailed evaluation of exposure and/or DFR studies relied upon (KCP 7.2, KCP 7.2.1.1, KCP 7.2.2.1, KCP 7.2.3.1)