REGISTRATION REPORT

Part B

Section 6

Mammalian Toxicology

Detailed summary of the risk assessment

Product code: AG-F8-250 CS

Chemical active substance:

Flurochloridone, 250 g/L

Central Zone

Member State: Poland

CORE ASSESSMENT

(authorization)

Applicant: Country organization / representative of ADAMA as specified in Part A

Submission date: January 2020

MS Finalisation date: October 2020 (initial Core Assessment)

March 2021 (final Core Assessment)

Version history

When	What
January 2020	dRR submitted by the Applicant
October 2020	Initial zRMS assessment The report in the dRR format has been prepared by the Applicant, therefore all comments, additional evaluations and conclusions of the zRMS are presented in grey commenting boxes. Minor changes are introduced directly in the text and highlighted in grey. Not agreed or not relevant information are ~~struck through and shaded for transparency~~.
March 2021	Final report (Core Assessment updated following the commenting period) Additional information/assessments included by the zRMS in the report in response to comments recieved from the cMS and the Applicant are highlighted in yellow. No comments after the commenting period.

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zRMS comments:

The report in the dRR format has been prepared by the Applicant, therefore all comments, additional evaluations and conclusions of the zRMS are presented in grey commenting boxes. Minor changes are introduced directly in the text and highlighted in grey. Not agreed or not relevant information ~~is struck through~~ and shaded for transparency.

Reviewer comments:

This dossier has been prepared to support first approval of AG-F8-250 CS, a capsule suspension containing 250 g/L flurochloridone for use in potato, in Central Zone according to article 33 of the Regulation 1107/2009. AG-F8-250 CS/Racer 250 CS was not a representative formulation reviewed during the Annex I inclusion/Active substance renewal of flurochloridone

For the purposes of the current product registration, APPL provided an assessment of the toxicological potential based on *in vivo* tests. ZRMS PL points out that since there are *in vivo* tests already exist the information gained on animal studies are more than just a classification. Existing animal studies allow to identify of effects following a single exposure to the plant protection product can be established. The data is sufficient to indicate the time course and characteristics of the effect with full details of behavioral changes and possible gross pathological findings at post-mortem. ZRMS PL is aware of some EU-countries are known for no longer accepting *in vivo* studies however, since acceptability of vertebrate studies conducted or initiated after 14 June 2011 is subject to intense current discussion on European level, any decision at this time should be done on Member State level.

Considering toxicity potential assessments based on *in vivo* tests AG-F8-250 CS/Racer 250 CS has a low toxicity in respect to acute oral and dermal toxicity. Inhalation are not provided, for justification see Appendix 2 point A 2.4. The product is no irritant to the skin and eyes. Based on *in vivo* study product is skin sensitizer.

The main concern of the reviewer relates to the classification of the product.

Repr. 1B H360Df hazard classification of flurochloridone has been agreed by the ECHA/RAC committee. This proposal is available in the RAC Opinion CLH-O-0000001412-86-242/F adopted 30 November 2018 by consensus. This opinion takes into account data submitted in the CLH dossier (DS Spain) and comments provided by MSCAs.

RAC opinion also supports proposal agreed by the EFSA experts to classify flurochloridone as R61 according 67/548/EU see EFSA Journal 2010;8(12):1869 (translation between classification in accordance with Directive 67/548/EEC and current 1272/2008: Repr. Cat 1 R61 = Repr. 1B H360Df).

In cases when RAC opinion has been adopted, reviewer consider this opinion as the latest reliable scientific evidence even if the procedure for formal inclusion of the substance into Annex VI to the CLP Regulation is still on-going.

Thus, RAC opinion for flurochloridone classification should be taken into account when labeling the product.

All exposure calculations (OPEX) used for estimation of operator, workers and B&R exposure to the **flurochloridone** considering all tasks according to the critical use(s) identify safe use of the product AG-F8-250 CS/Racer 250 CS.

6 Mammalian Toxicology (KCP 7)

6.1 Summary

Table 6.1-1: Information on AG-F8-250 CS*

Product name and code	Racer 25 CS/AG-F8-250 CS
Formulation type	Capsule suspension [Code: CS]
Active substance(s) (incl. content)	Flurochloridone; 250 g/L
Function	Herbicide
Product already evaluated as the 'representative formulation' during the approval of the active substance(s)	Yes
Product previously evaluated in another MS according to Uniform Principles	No

* Information on the detailed composition of AG-F8-250 CS can be found in the confidential dRR Part C.

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 AG-F8-250 CS according to Regulation (EC) No 1272/2008

Hazard class(es), categories	Skin Sens. 1, Repr. ~~2~~ **1B**
Hazard pictograms or Code(s) for hazard pictogram(s)	GHS07, GHS08
Signal word	Warning
Hazard statement(s)	H317, ~~H361d,~~ **H360Df**
Precautionary statement(s)	P261, P272, P280, P302+P352, P333+P313, P321, P362+364, P501 P201, P202, P308+P313, P405
Additional labelling phrases	To avoid risks to man and the environment, comply with the instructions for use. [EUH401]

Table 6.1-3: Summary of risk assessment for operators, workers, residents and bystanders for AG-F8-250 CS

	Result	PPE / Risk mitigation measures
Operators	Acceptable	~~No specific PPE (work wear)~~ Certified protective garment **NOTE !:** **However, OPEX exposure assessment according to the AOEM Model (EFSA calculator) identified safe aplication of the product and does not indicate the need for the operator to use protective clothing (calculated exposure is below the reference value AOEL 0.04 mg/kg bw/d) taking into account the classification of the active substance flurochloridone as toxic to reproduction Repr. Cat 1B H360 Df*, operators must wear a certified protective garment (protective gloves, protective coverall and waterproof boots) during handling concentrat, mixing and loading spray dilution and during aplication.**
Workers	Acceptable	No specific PPE (work wear)
Residents	Acceptable	None
Bystanders	Acceptable	None

*** This proposal is available in the ECHA/RAC Opinion CLH-O-0000001412-86-242/F adopted 30 November 2018 by consensus.**

No unacceptable risk for operators, workers, 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 the following table.

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 [Exposure model]**	**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**	**Water L/ha** **min / max**			**Operator**	**Worker**	**Residents**	**Bystander**
1	Potato (SOLTU)	F	Spraying, LCTM	1 ; 1	0.5	200 - 300	n.a.	Guidance on the assessment of exposure of operators, workers, residents and bystanders in risk assessment for plant protection products; EFSA Journal 2014;12(10):3874	R#	A	A	A

* 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

 # detailed explanation see table Table 6.1-5

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

Data gaps

Noticed data gaps are:

- None

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)

	Flurochloridone
Common Name	Flurochloridone
CAS-No.	61213-25-0
Classification and proposed labelling	
With regard to toxicological endpoints (according to the criteria in Reg. 1272/2008, as amended)	No harmonised classification Classification according to Regulation (EC) No. 1272/2008: Acute Tox. 4 (H302) Skin Sens.1 (H317) ~~Repr.2 (H361d)~~ **Repr. 1B H360Df May damage the unborn child. Suspected of damaging fertility** **Mentioned above hazard classyfication has been agreed by the ECHA/RAC committee.** **This proposal is available in the RAC Opinion CLH-O-0000001412-86-242/F adopted 30 November 2018 by consensus.** **This opnion takes into account data submitted in the CLH dossier (DS Spain) and comments provided by MSCAs.** **This opinion also supports proposal agreed by the EFSA experts see EFSA Journal 2010;8(12):1869.**
Additional C&L proposal	No harmonised classification
Agreed EU endpoints	
AOEL systemic	0.04 mg/kg bw/d
Reference	SANCO/10098/2011 final – 09/03/2011 EFSA Journal 2010;8(12):1869
Conditions to take into account/critical areas of concern with regard to toxicology	
According to Review Report/EFSA Conclusion for flurochloridone	EFSA classification proposal: • **Acute Tox. 4** (H302) • **Skin Sens.1** (H317) • **Repr.1B** (H360Df): R62 “Possible risk of impaired fertility” (repr. Cat. 3) + R61 “May cause harm to the unborn child” (repr. Cat. 2) CLH proposal was submitted on 28.04.17. Legal deadline for opinion adoption: 31.03.19.

6.3 Toxicological Evaluation of Plant Protection Product

A summary of the toxicological evaluation for AG-F8-250 CS 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.

Table 6.3-1: Summary of evaluation of the studies on acute toxicity including irritancy and skin sensitisation for AG-F8-250 CS

Type of test, species, model system (Guideline)	Result	Acceptability	Classification (acc. to the criteria in Reg. 1272/2008)	Reference
LD_{50} oral, rat (OECD 401)	> 5000 mg/kg bw	Yes	None	XXX 1986a
LD_{50} dermal, rat (OECD 402)	> 2000 mg/kg bw	Yes	None	XXX 1986b
LC_{50} inhalation, rat	Not submitted, not necessary. Justification presented in Appendix 2			
Skin irritation, rabbit (OECD 404)	Non-irritant	Yes	None	XXX 1986a
Eye irritation, rabbit (OECD 405)	Slight irritant	Yes	None	XXX 1986b
Skin sensitisation, guinea pig (OECD 406)	Sensitising	Yes	H317	XXX 2006
Supplementary studies for combinations of plant protection products	No data – not required			

Table 6.3-2: Additional toxicological information relevant for classification/labelling of AG-F8-250 CS

	Substance (concentration in product, % w/w)	Classification of the substance (acc. to the criteria in Reg. 1272/2008)	Reference	Classification of product (acc. to the criteria in Reg. 1272/2008)
Toxicological properties of active substance(s) (relevant for classification of product)	Flurochloridone (25 % (w/w))	No harmonised classification Classification according to Regulation (EC) No. 1272/2008: Acute Tox. 4 (H302) Skin Sens.1 (H317) ~~Repr.2 (H361d)~~ **Repr. 1B H360Df****	Reg. 1272/2008 / MSDS* ****Hazard classification has been agreed by the ECHA/RAC committee.** **This proposal is available in the RAC Opinion CLH-O-0000001412-86-242/F adoptet 30 November 2018 by consensus. This opnion takes into account data submitted in the CLH dossier (DS Spain) and comments provided by MSCAs. This opinion also supports proposal agreed by the EFSA experts see EFSA Journal 2010;8(12):1869.**	~~Not relevant~~ **H360Df Category 1B reproductive toxicant** **Based on the content of Flurochloridone.** **Generic concentration limits of ingredients of a mixture classified as reproduction toxicants or for effects on or via lactation that trigger classification of the mixture:** **≥ 0.3%** Classification of product is based on relevant studies that were performed and not by calculation according to the criteria in Reg. 1272/2008

	Substance (concentration in product, % w/w)	Classification of the substance (acc. to the criteria in Reg. 1272/2008)	Reference	Classification of product (acc. to the criteria in Reg. 1272/2008)
Toxicological properties of non-active substance(s) (relevant for classification of product)	1,2-benzisothia-zoline-3-one (CAS No. 2634-33-5, < 0.05%) Lignosulfonic acid, sodium salt, sulfomethylated (CAS No. 68512-34-5, < 1%) Sodium hydroxyde (CAS No. 1310-73-2, < 0.2%)	H302, H315, H318, H317 H319 H314	MSDS*	Not relevant Classification of product is based on relevant studies that were performed and not by calculation according to the criteria in Reg. 1272/2008
	C12 aromatic solvent (≥ 20 - < 25%)	H304	MSDS*	According to CLP Regulation (EC) 1272/2008, a mixture which contains a total of 10 % or more of a substance or substances classified in Category 1, and has a kinematic viscosity of 20,5 mm^2/s or less, measured at 40°C, shall be classified in Category 1. Kinematic viscosity of the product is above this threshold. Therefore, no classifcation is required for this endpoint.
Further toxicological information	No data – not required			

* Material safety data sheet by the applicant

6.4 Toxicological Evaluation of Groundwater Metabolites

There is no harmonised classification for flurochloridone yet.

However, based on the EFSA classification proposal as R61 and R62 for flurochloridone, the metabolite R42819, which may be found in groundwater at levels above the threshold value of 0.1 µg/L, is considered as relevant, leading to a critical area of concern.

The models of PEC_{GW} for application to potatoes for metabolite R42819 do not predict an exceeding of the 0.1 µg/L threshold at Tier 2 assessment level (see dRR Part B8).

Thus, no unacceptable risk is expected with this groundwater metabolite and no further toxicological evaluation was conducted.

ZRMS remarks:

No toxicological information is available on the metabolite R42819 that may be found in groundwater at levels

above the threshold value of 0.1 µg/L (Tier 1: 0.611 µg/L (PEARL, Okehampton)) according to environmental models; based on the classification proposal as **H360Df for the parent**, this metabolite can be considered as relevant according to the Guidance document on assessment of the relevance of metabolites in groundwater (European Commission, 2003) and a critical area of concern can be identified.
The Reviewer points out that the **H360Df classification has been accepted by the ECHA/RAC committee** (**opinion CLH-O-0000001412-86-242/F adopted 30 November 2018**), although there is no formal EC decision regarding the harmonized classification of the parent substance yet, however, due to the teratogenic potential of Flurochloridone, one should bear in mind the risk resulting from potential leaching of the above-mentioned metabolite to groundwater.

6.5 Dermal Absorption (KCP 7.3)

A summary of the dermal absorption rates for the active substances in AG-F8-250 CS are presented in the following table.

Table 6.5-1: Dermal absorption rates for active substances in AG-F8-250 CS

	Flurochloridone	
	Value	**Reference**
Concentrate	0.3%*	Kane T.J., 2007 EFSA Journal 2010;8(12):1869
Dilution	10%*	Kane T.J., 2007 EFSA Journal 2010;8(12):1869

* Based on a pro rata adaptation of dermal absorption and rounding of values according to EFSA guidance on dermal absorption (2017)

6.5.1 Justification for proposed values - Flurochloridone

Proposed dermal absorption rates for flurochloridone are based on a dermal absorption study on a formulation identical to AG-F8-250 CS (Racer 25 CS) which is described in details in the Addendum I to the DAR. In conclusion, dermal penetration of flurochloridone formulated as Racer 25 CS through human dermatomed skin was low. The absorbed dose was < 0.26% and < 4.21% at the high (concentrate, 250 g/L) and low dose level (spray dilution 3.75 g/L), respectively.

The absorption value cited for the concentrate (rounded to 0.3 %) is appropriate to use in for the risk assessment evaluation of AG-F8-250 CS, as the concentration is the same.

However, the low dose used in that study (3.75 g/L) was higher than the intended for use of AG-F8-250 CS, as is defined in the GAP (dilutions 200L – 300L water resulting in concentrations of 2.5 to 1.667 g/L). Therefore, according to the EFSA guidance on dermal absorption (2017), a pro rata adaptation was performed (4.21 % x 3.75 / 1.667), resulting in a (rounded) value of 10 %. Thus for exposure calculations values of 0.3 % for the concentrate and of 10 % for the spray dilution were used.

Table 6.5-2: Summary of the results of submitted dermal absorption studies for flurochloridone

Test	Concentrate	Spray dilution	Formulation in study	Acceptability of study	Justification provided on representativity of study formulation for current product	Acceptability of justification	Reference*
In vitro (human)	0.26%	4.21%	AG-F8-250 CS	Yes, Endpoint can be used for current product, pro rata corection has been accepted	Yes (see Appendix A 2.10)	Justification accepted.	Kane T.J., 2007

* indicates that a study was reviewed at EU level

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 and code	AG-F8-250 CS
Formulation type	Capsule Suspension [code: CS]
Category	Herbicide
Active substance(s) (incl. content)	Flurochloridone 250 g/L
AOEL systemic	0.04 mg/kg bw/d
Inhalation absorption	100%
Oral absorption	100%
Dermal absorption	Concentrate: 0.3% Dilution: 10% (Based on product (formulation))

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)

6.6.2.1 Estimation of operator exposure

A summary of the exposure model used for estimation of operator exposure to the active substances during application of AG-F8-250 CS according to the critical use is presented in Table 6.6-2. The outcome of the estimation is presented in Table 6.6-3. Detailed calculations are in Appendix 3.

As long as no harmonised approach on the setting of acute reference values for non-dietary human exposure is available, no acute exposure calculations are necessary.

Table 6.6-2: Exposure models for intended uses

Critical use(s)	Potato (max. 2 L product/ha, 0.5 kg flurochloridone/ha)
Model(s)	Guidance on the assessment of exposure of operators, workers, residents and bystanders in risk assessment for plant protection products; EFSA Journal 2014;12(10):3874 calculator version: 30/03/2015

Table 6.6-3: Estimated operator exposure

		Flurochloridone	
Model data	**Level of PPE**	**Total absorbed dose (mg/kg/day)**	**% of systemic AOEL**
Tractor mounted boom spray application outdoors to low crops			
Application rate		0.5 kg a.s./ha	
Spray application (AOEM**;** 75th percentile) Body weight: 60 kg	Work wear (arms, body and legs covered) M/L and A	0.0096651	24.2

Results:

The potential total systemic exposure of the operator, who is dressed with work wear that covers the body, arms and legs, corresponds to 24% of the AOEL for flurochloridone for potato.

Thus the use with AG-F8-250 CS is at an acceptable risk for the operator, according to the EFSA-OPEX model.

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), a study to provide measurements of operator exposure was not necessary and was therefore not performed.

6.6.3 Worker exposure (KCP 7.2.3)

6.6.3.1 Estimation of worker exposure

The product is used in pre-emergence of both crops and weeds. Thus, workers are not exposed to flurochloridone via foliage contaminated with the product. No inspection or maintenance is routinely performed and moreover, harvest is done fully automatically. Concluding, there should be no re-entry with direct contact to the foliage for workers and consequently no exposure.
Therefore, an estimation of the worker exposure is not considered necessary. It was performed nevertheless to demonstrate the acceptable risk for the worker.

Table 6.6-3 shows the exposure model used for estimation of worker exposure after entry into a previously treated area or handling a crop treated with AG-F8-250 CS according to the critical use. Outcome of the estimation is presented in Table 6.6-6. Detailed calculations are in Appendix 3.

Table 6.6-3: Exposure models for intended uses

Critical use(s)	Potato (max. 2 L product/ha, 0.5 kg flurochloridone/ha)
Model	Guidance on the assessment of exposure of operators, workers, residents and bystanders in risk assessment for plant protection products; EFSA Journal 2014;12(10):3874 calculator version: 30/03/2015

Table 6.6-6: Estimated worker exposure

		Flurochloridone	
Model data	**Level of PPE**	**Total absorbed dose (mg/kg bw/day)**	**% of systemic AOEL**
Inspection, irrigation - Outdoor Work rate: 2 hours/day, DT_{50}: 30 days DFR: 3 µg/cm^2/kg a.s./ha Interval between treatments: 365 days			
Number of applications and application rate		1 x 0.5 kg a.s./ha	
Body weight: 60 kg	Potential exposure TC: 12500 cm^2/person/h	0.0625000	156.3
	Work wear (arms, body and legs covered) TC: 1400 cm^2/person/h	0.0070000	17.5
	Work wear (arms, body and legs covered) and gloves TC: not available	NA	NA

Results:

The potential total systemic exposure of the worker, who is dressed with work wear that covers the body, arms and legs, corresponds to 18% of the AOEL for flurochloridone for potato.

Thus the use with AG-F8-250 CS is at an acceptable risk for the worker, according to the EFSA-OPEX model.

6.6.3.2 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.

6.6.4 Resident and bystander exposure (KCP 7.2.2)

6.6.4.1 Estimation of resident and bystander exposure

The estimation of resident exposure was performed according to the EFSA guidance on "the assessment of exposure of operators, workers, residents and bystanders in risk assessment for plant protection products" (EFSA Journal 2014;12(10):3874). According to this guidance, a bystander risk assessment is required for plant protection products that have significant acute toxicity or the potential to exert toxic effects after a single exposure, based on the 95th percentile data values.
However, the guidance does not define how an acute AOEL or the RVAAS shall be appropriately derived. Consequently, it was decided by the EFSA working group to remove the concept from the final version of the guidance.
Therefore the risk assessment for bystanders was performed with the German model (Martin *et al*., 2008) in order to however provide exposure estimates for bystanders for comparison with the AOEL.

Table 6.6-4 shows the exposure models used for estimation of resident and bystander exposure to flurochloridone. The outcome of the estimation is presented in
Table 6.6-69 (longer term resident exposure) and
Table 6.6-510 (acute bystander exposure). Detailed calculations are in Appendix 3.

Table 6.6-4: Exposure models for intended uses

Critical use(s)	Potato (max. 2 L product/ha, 0.5 kg flurochloridone/ha)
Model	For residents the following model was applied: Guidance on the assessment of exposure of operators, workers, residents and bystanders in risk assessment for plant protection products; EFSA Journal 2014;12(10):3874 calculator version: 30/03/2015 For bystanders the following model was applied: Martin S. *et al*. (2008) [Guidance for Exposure and Risk Evaluation for Bystanders and Residents Exposed to Plant Protection Products During and After Application; J. Verbr. Lebensm. 3 (2008): 272-281 Birkhäuser Verlag Basel] and Bundesanzeiger (BAnz), 06 January 2012, Issue No. 4, pp. 75-76.

Table 6.6-5: Estimated resident exposure

		Flurochloridone	
Model data		**Total absorbed dose (mg/kg bw/day)**	**% of systemic AOEL**
Tractor mounted boom spray application outdoors to low crops Buffer zone: 2-3 (m) Drift reduction technology: no DT_{50}: 30 days DFR: 3 µg/cm^2/kg a.s./ha Interval between treatments: 365 days			
Number of applications and application rate		1 x 0.5 kg a.s./ha	
Resident child Body weight: 10 kg	Drift (75th perc.)	0.0067585	16.9
	Vapour (75th perc.)	0.0010700	2.68
	Deposits (75th perc.)	0.0011340	2.84
	Re-entry (75th perc.)	0.0084375	21.1
	Sum (mean)	**0.0123603**	**30.9**
Resident adult Body weight: 60 kg	Drift (75th perc.)	0.0016100	4.03
	Vapour (75th perc.)	0.0002300	0.58
	Deposits (75th perc.)	0.0003407	0.85
	Re-entry (75th perc.)	0.0046875	11.7
	Sum (mean)	**0.0049832**	**12.5**

Table 6.6-6: Estimated bystander exposure

	Flurochloridone	
Model data	**Total absorbed dose (mg/kg bw/day)**	**% of systemic AOEL**
Tractor mounted boom spray application outdoors to low crops Buffer zone: 1 (m) Drift reduction technology: no DFR: 3 µg/cm^2/kg a.s./ha		
Application rate	0.5 kg a.s./ha	
Bystander child Drift rate: 2.77 % (1 m) Body weight: 16.15 kg	0.0018059	4.51
Bystander adult Drift rate: 2.77 % (1 m) Body weight: 60 kg	0.0023106	5.78

Conclusion

The calculated total systemic exposure values are below the AOEL. Therefore, it is concluded that there is no undue risk to any bystander after accidental short-term exposure to AG-F8-250 SC. There is also no undue risk to residents. This has no labelling implications.

The risk assessment complies with the Uniform Principles.

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 flurochloridone 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

List of data submitted by the applicant and relied on

None.

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
KCP 7.1.1/01	XXX	1986a	Single oral toxicity study in the rat – Racer ME Agan Report no. 818607 GLP Unpublished	Y	ADM
KCP 7.1.2/01	XXX	1986b	Acute dermal toxicity study in the rat – Racer ME Agan Report no. 828607 GLP Unpublished	Y	ADM
KCP 7.1.4/01	XXX	1986a	Acute dermal irritation/corrosion – Racer ME Agan Report no. 808607 GLP Unpublished	Y	ADM
KCP 7.1.5/01	XXX	1986b	Acute eye irritation/corrosion study – Racer ME Agan Report no. 798607 GLP Unpublished	Y	ADM
KCP 7.1.6/01	XXX	2006	Racer 25 CS: Contact hypersensitivity in albino Guinea pigs, maximisation test Agan Report no. A46607 GLP Unpublished	Y	ADM
KCP 7.3/03	Kane T. J	2007	Flurochloridone, *in vitro* Dermal Penetration Study Using Human Skin Huntington Life Sciences Ltd., Report No. AGM0265 Agan Report No. 90009461 GLP	N	ADM

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
			Unpublished		

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

Not relevant.

Comments of zRMS:	Unless specifically indicated, all reports in this section are submitted to address mandatory data requirements for the approval of AG-F8-250 CS/Racer 250 CS

A 2.2 Acute oral toxicity (KCP 7.1.1)

Comments of zRMS:	Study considered valid according to OECD GD. Agreed endpoint can be used for current product. According to Regulation (EC) No 1272/2008 classification is not warranted.

Reference	KIIIA 7.1.1/01
Report	Single oral toxicity study in the rat – Racer ME XXX, 1986a Report study no. 818607
Guideline(s)	Yes, OECD TG 401
Deviations	No
GLP	Yes
Acceptability	Yes
Duplication (if vertebrate study)	No

This acute oral toxicity study was submitted and reviewed as part of the EU inclusion process for AG-F8-250 CS. The full study details are not summarised as they were evaluated during the EU review and end-points were fixed.

Conclusion/endpoint: During the EU review, the oral LD50 of Racer ME (=AG-F8-250 CS) in rats was determined to be > 5000 mg/kg bw. In accordance with CLP Regulation (EC) 1272/2008, AG-F8-250 CS does not require classification.

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

Comments of zRMS:	Study considered valid according to OECD GD. Agreed endpoint can be used for current product. According to Regulation (EC) No 1272/2008 classification is not warranted.

Reference	KIIIA 7.1.2/01
Report	Acute dermal toxicity study in the rat – Racer ME XXX, 1986b Report study no. 828607
Guideline(s)	Yes, OECD TG 402
Deviations	No
GLP	Yes

Acceptability	Yes
Duplication (if vertebrate study)	No

This acute dermal toxicity study was submitted and reviewed as part of the EU inclusion process for AG-F8-250 CS. The full study details are not summarised as they were evaluated during the EU review and endpoints were fixed.

Conclusion/endpoint: During the EU review, the dermal LD50 of Racer ME (=AG-F8-250 CS) in rats was determined to be greater than 2000 mg/kg bw. In accordance with CLP Regulation (EC) 1272/2008, AG-F8-250 CS does not require classification.

A 2.4 Acute inhalation toxicity (KCP 7.1.3)

No inhalation toxicity study is required according to Commission Regulation (EU) 284/2013 since the active ingredient flurochloridone has a vapour pressure of 4.4 x 10^{-4} Pa at 25 °C (DAR), which is well below the trigger value of 1x10^{-2} Pa at 25°C and the generation of inhalable droplets (< 50 µm) of the liquid formulation is considered to be non-relevant under normal use condition.

In addition, as AG-F8-250 CS is a capsule suspension formulation and

- not a gas or liquefied gas
- not a smoke generation formulation or fumigant
- not used with fogging/misting equipment
- not a vapour releasing formulation
- not supplied in an aerosol dispenser
- not a powder or granules containing a significant proportion of particles of diameter < 50 µm (> 1 % on a weight basis)
- not to be applied from aircraft in cases where inhalation exposure is relevant,
- does not contain an active substance with a vapour pressure > 1 × 10^{-2} Pa and is not to be used in enclosed spaces such as warehouses or glasshouses,
- is not to be applied in a manner which generates a significant proportion of particles or droplets of diameter < 50 µm (> 1 % on a weight basis),

an acute inhalation toxicity study is not required according to Commission Regulation (EU) 284/2013.

Comments of zRMS:	Justification waiving inhalation study accepted. No further action required.

A 2.5 Skin irritation (KCP 7.1.4)

Comments of zRMS:	Study considered valid according to OECD GD. Agreed endpoint can be used for current product. According to Regulation (EC) No 1272/2008 classification is not warranted.

Reference	KIIIA 7.1.4/01
Report	Acute dermal irritation/corrosion – Racer ME XXX 1986a Report study no. 808607
Guideline(s)	Yes, OECD TG 404
Deviations	No

GLP	Yes
Acceptability	Yes
Duplication (if vertebrate study)	No

This skin irritation study was submitted and reviewed as part of the EU inclusion process for AG-F8-250 CS. The full study details are not summarised as they were evaluated during the EU review and end-points were fixed.

Conclusion/Endpoints: During the EU review, Racer ME (=AG-F8-250 CS) caused very slight reversible irritation when applied topically to rabbits at dose level of 0.5 mL. In accordance with CLP Regulation (EC) 1272/2008, AG-F8-250 CS does not require classification.

A 2.6 Eye irritation (KCP 7.1.5)

Comments of zRMS:	Study considered valid according to OECD GD. Agreed endpoint can be used for current product. According to Regulation (EC) No 1272/2008 classification is not warranted.

Reference	KIIIA 7.1.5/01
Report	Acute eye irritation/corrosion study – Racer ME XXX 1986b Report study no. 798607
Guideline(s)	Yes, OECD TG 405
Deviations	No
GLP	Yes
Acceptability	Yes
Duplication (if vertebrate study)	No

This eye irritation study was submitted and reviewed as part of the EU inclusion process for AG-F8-250 CS. The full study details are not summarised as they were evaluated during the EU review and end-points were fixed.

Conclusion: During the EU review, Racer ME (=AG-F8-250 CS) caused slight transient eye irritation in rabbits. According to CLP Regulation (EC) 1272/2008, AG-F8-250 CS does not require classification.

A 2.7 Skin sensitisation (KCP 7.1.6)

Comments of zRMS:	Study considered valid according to OECD GD. Agreed endpoint can be used for current product. According to Regulation (EC) No 1272/2008 classification is warranted as a skin sensitizing (category 1), H317 (may cause an allergic skin reaction).

Reference	KIIIA 7.1.6/01
Report	Racer 25 CS: Contact hypersensitivity in albino Guinea pigs, maximisation test XXX, 2006 Report study no. A46607
Guideline(s)	Yes, OECD TG 406
Deviations	No
GLP	Yes
Acceptability	Yes
Duplication (if vertebrate study)	No

This skin sensitisation study was submitted and reviewed as part of the EU inclusion process for AG-F8-250 CS. The full study details are not summarised as they were evaluated during the EU review and end-points were fixed.

Conclusion: During the EU review, challenge with 1% Racer 25 CS (=AG-F8-250 CS) elicited a sensitisation response in a 56% of previously induced Guinea pigs (above the threshold for classification of 30%). According to CLP Regulation 1272/2008/EC, classification as skin sensitising (category 1), H317 (may cause an allergic skin reaction) is required and the signal word “Warning” is indicated.

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

No supplementary studies are to be considered.

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)

In the *in vitro* dermal absorption study, the lowest concentration tested was greater than the lowest concentration recommended on the label of AG-F8-250 CS.
Therefore, pro-rata correction was used to derive dermal absorption values for other dilutions with concentrations of the same formulation lower than the highest dilution (c.f. Table 6.5-1).

Comparative dermal absorption, in vitro using human skin

Comments of zRMS:	This study was conducted according to OECD Guideline 428 and in compliance with GLP. All the recoveries where between the recovery boundaries mentioned in the dermal absorption guidance (EFSA Guidance on Dermal Absorption (EFSA Journal 2017;15(6):4873 [60 pp.]. doi: 10.2903/j.efsa.2017.4873) see Remarks. To support calculations for dermal absorption from in vitro studies excel spreadsheet (provided by BfR) has been used (available on request). Representative absorption (as a percentage of the total) vs time profiles showed in all cells and dose groups absorption to be completed. The study is considered to be acceptable and the dermal absorption for AG-F8-250 CS is covered by this study.

Reference	IIIA, 7.3/03
Report	Flurochloridone, *in vitro* Dermal Penetration Study Using Human Skin Kane T., 2007 Huntington Life Sciences Ltd., Report No. AGM0265 Agan Report No. 90009461
Guideline(s)	Yes, OECD TG 428
Deviations	Yes, the test was performed with non-radiolabelled test compound due to difficulty in preparing a radiolabelled capsule suspension formulation
GLP	Yes
Acceptability	Yes
Duplication (if vertebrate study)	No

Materials and methods

Test material: RACER 25 CS (= Flurochloridone 25 CS) containing 247 g/L flurochloridone; Lot number D-GC2802 and Flurochloridone, Lot number FLCLDN(4)-848(V1), purity 99.5% as reference material.

Dose levels: The formulated test substance was applied at two dose levels: a low dose reflecting a typical concentration recommended for application in the field (3:200 dilution with water, 375 g/L flurochloridone) and a high dose representing the undiluted formulation. Application volume was 10 µL/cm^{-2}.

Dose level	**Cell number**	**Human donor number**	**Applied dose**
High nominal 2500 µg/cm^2	1 2 3 4 5 6 7	H1 H1 H1 H2 H2 H3 H3	2554 µg/cm^2
Low nominal 37.5 µg/cm^2	8 9 10 11 12 13 14	H1 H1 H1 H2 H2 H3 H3	34.4 µg/cm^2

H1 (73 year old female, abdominal skin),
H2 (47 year old female, skin from the back),
H3 (64 year old female, abdominal skin).

Skin preparation: After thawing human skin (cadaver skin from three female donors, age 47-73 years, from the abdomen or back) was dermatomed to slices that contained the epidermis and some dermis with a thickness of 200-400 µm. Pieces of dermatomed skin (exposure are approximately 0.95 cm^2) were cut and placed in the diffusion cells onto the receptor chamber. The integrity of the skin was checked by applying 3 mL distilled water (+ 250 µL ^3H_2O) to the surface of the skin and kept occluded for 1 hour. Tritiated water was then removed and replenished with 3 mL distilled water. The penetration was then determined after 3 hours. The permeability coefficient (K_p) of each skin sample was calculated for the time period of 1-4 hours. Skin with $K_p \leq 3.5 \cdot 10^{-3}$ cm·h^{-1} was considered acceptable. In case total absorption and absorption profiles of the test substance on skin samples with a $K_p > 3.5 \cdot 10^{-3}$ cm·h^{-1} were similar to the data from skin with a $K_p \leq 3.5 \cdot 10^{-3}$ cm·h^{-1}, they were also considered to be acceptable.

Exposure: An amount of 9.5 µL (10 µL/cm^2) was applied to each skin sample. The receptor fluid was 5% w/v bovine serum albumin in 0.01 M phosphate buffered saline at pH 7.4 (selected in a pre-test for sufficient solubility of flurochloridone, at least 131 µg/mL). The receptor fluid was retained and exchanged to fresh receptor fluid at 1, 2, 6 and 24 hours after application. Each skin sample was swabbed with three cotton wool buds at 6 hours after application using 1% Tween 80 in distilled water and another dry bud to remove residual cleaning solution. At 24 h after application, the skin samples were tape stripped. The collected strips corresponding to the upper and lower *stratum corneum* and the remaining skin were collected. Receptor and donor chambers were cleaned from potentially remaining flurochloridone and the cleaning solution was retained for analysis. The flurochloridone content in the collected samples (receptor fluids, cotton wool swabs, tape strips and remaining skin, cleaning solutions) were analysed using a validated analytical method by gas chromatography with electron capture detection.

Findings

Permeability: The permeability check of the membranes revealed unacceptable Kp values for skin samples from donor H2 (cells 4, 5, 11, 12). In addition results from cell 12 were excluded due to its very low recovery value (<80%). The remaining cells had acceptable Kp and recovery values.

Penetration: Flurochloridone formulated as RACER 25 CS was absorbed through human dermatomed skin at only very low amounts (see Table 6.12.1.1-2). Only 0.1% and 0.45% of applied dose were found in the receptor fluid at the low and high dose level, respectively. Most of flurochloridone (85-90% of the applied dose) could be removed at the skin swab (at 6 hours) and the surface tape strip (at 24 hours). In the treated skin markedly decreasing amounts were detected moving from the upper (2.4-4.5% of applied dose) to the lower *stratum corneum* (<0.04-<1.15%) and to the remaining skin (<0.01-<0.10%).
According to Notifier, the latter reveals that it is very unlikely that the amount remaining to be associated with the *stratum corneum* is available for systemic absorption as *in vivo*, it would be expected that it is lost by processes of proliferation, differentiation and desquamation. However RMS opinion is that the

amount in the remaining skin plus *stratum corneum* should be considered as potentially absorbable since a dermal in vivo study (Jeffcoat, 1988; see DAR) demonstrated that the amount detected in the application site after washing should be included in the amount absorbed.

Therefore the total absorbed dose was considered to be <0.26% and <4.21% of the applied dose for the high and low dose level corresponding to the undiluted product and a typical field dilution (3:200), respectively.

Table A 1 Penetration of flurochloridone through human skin.

Concentration	high, 250 g/L		low, 3.75 g/L	
	[% of dose]	[µg]	[% of dose]	[µg]
Receptor fluid	0.01	0.31	0.45	0.15
Remaining skin	<0.01	<0.10	<0.10	<0.03
Receptor chamber	<0.01	<0.05	<0.15	<0.05
Upper stratum corneum	0.19	4.52	2.37	0.78
Lower stratum corneum	<0.04	<0.95	<1.15	<0.38
Total absorbed°	**<0.26**	**<5.93**	**<4.21**	**<0.76**
Skin surface (swabs + skin surface strip)	89.86	2180	85.44	27.94
Donor chamber	0.40	9.79	0.63	0.21
Total non-absorbed°°	**<90.26**	**<2189.79**	**<86.07**	**<28.15**
Total recovery	**<90.53 (90.46)°°°**	**<2196 (2195)°°°**	**<90.28 (88.89)°°°**	**<29.52 (29.08)°°°**
Absorption rate [µg/(cm^2·h)]	0.016		0.023	

° considered to be systemically available;
°° considered to be not systemically available
°°° minimum value considering all values <x as 0

The steady state absorption rate was 0.016 and 0.023 µg/(cm^2·h) for the high and low dose level, respectively.

Conclusion/endpoint:

Dermal penetration of flurochloridone formulated as RACER 25 CS through human dermatomed skin was low. The total absorbed dose was <0.26% and <4.21% at the high and low dose level, respectively. This includes the amount of flurochloridone associated with the remaining skin, plus the amount associated with the *stratum corneum*.

A 2.11 Other/Special Studies

Not relevant.

Appendix 3 Exposure calculations

A 3.1 Operator exposure calculations (KCP 7.2.1.1)

A 3.1.1 Calculations for flurochloridone

Table A 2: Input parameters considered for the estimation of operator exposure

Substance name	flurochloridone	
Product name	AG-F8-250 CS	
Reference value non acutely toxic active substance (RVNAS)	0.04	mg/kg bw/day
Reference value acutely toxic active substance (RVAAS)		mg/kg bw/day
Crop type	Root and tuber vegetables	
Substance properties		
Formulation type	Soluble concentrates, emulsifiable concentrate, etc.	
Miniumum volume water for application (liquids)	200	L/ha
Maximum application rate of active substance	0.5	kg a.s. /ha
50% Dissipation Time DT50	30	days
Initial Dislodgeable Foliar Residue	3	µg/cm2 of foliage/kg a.s. applied/ha
Dermal absorption of product	0.30%	
Dermal absorption of in-use dilution	10.00%	
Oral absorption of active substance	100.00%	
Inhalation absorption of active substance	100.00%	
Vapour pressure of active substance	low volatile substances having a vapour pressure of <5*10-3Pa	
Scenario		
Indoor or Outdoor application	Outdoor	
Application method	Downward spraying	
Application equipment	Vehicle-mounted	
Buffer strip	2-3	m
Number of applications	1	
Interval between multiple applications	365	days
Season (upward spraying orchards only)	not relevant	

Table A 33: Estimation of longer term operator exposure towards flurochloridone according to EFSA guidance

1. Total

	Without RPE/PPE	With RPE/PPE	
Longer term			
Total systemic exposure from mixing, loading and application (mg a.s./day)	0.8831427	0.5799084	
Total systemic exposure from mixing, loading and application per kg body weight (mg/kg bw/day)	0.0147190	0.0096651	
% of RVNAS	36.80%	24.16%	

2. Longer term exposure

2.1 Mixing and loading

	Systemic exposure [µg a.s. /day]	Systemic exposure [µg a.s./kg bw/day]	Formula
Without RPE/PPE			
Hands	173.6430524	2.8940509	*D15*'i_AbsorpProduct*
Body	102.8265406	1.7137757	*D16*'i_AbsorpProduct*
Head	3.8912691	0.0648545	*D17*'i_AbsorpProduct*
Inhalation	9.6477701	0.1607962	*D21*'i_AbsorpInhalation*
Sum	290.0086322	4.8334772	
With RPE/PPE (as selected above)			
Hands	173.6430524	2.8940509	*D18*'i_AbsorpProduct*
Body	1.2365262	0.0206088	*D19*'i_AbsorpProduct or D15*'i_AbsorpProduct*'F24*
Head	3.8912691	0.0648545	*D20*'i_AbsorpProduct or D17*'i_AbsorpProduct*'F25*
Inhalation	9.6477701	0.1607962	*D21*'i_AbsorpInhalation*'G25*
Sum	188.4186179	3.1403103	
Water soluble	188.4186179	3.1403103	*C70*'F26*

2.2 Application

	Systemic exposure [µg a.s. /day]	Systemic exposure [µg a.s./kg bw/day]	Formula
Without RPE/PPE			
Hands	370.8084497	6.1801408	*D30*'i_AbsorpInuse*
Body	207.3316784	3.4555280	*D31*'i_AbsorpInuse*
Head	9.7992054	0.1633201	*D32*'i_AbsorpInuse*
Inhalation	5.1946863	0.0865781	*D35*'i_AbsorpInhalation*
Sum	593.1340199	9.8855670	
With RPE/PPE (as selected above)			
Hands	370.8084497	6.1801408	*D33*'i_AbsorpInuse*
Body	5.6874578	0.0947910	*D34*'i_AbsorpInuse or D31*'i_AbsorpInuse*'F38*
Head	9.7992054	0.1633201	*D32*'i_AbsorpInuse*'F39*
Inhalation	5.1946863	0.0865781	*D35*'i_AbsorpInuse*'G39*
Sum	391.4897993	6.5248300	

A 3.2 Worker exposure calculations (KCP 7.2.3.1)

A 3.2.1 Calculations for flurochloridone

Table A 44: Input parameters considered for the estimation of worker exposure

Worker exposure from residues on foliage for AG-F8-250 CS

Crop type	Root and tuber vegetables		
Indoor or outdoor	Outdoor		
Application method	Downward spraying		
Application equipment	Vehicle-mounted		
Worker's task	Inspection, irrigation		
Main body parts in contact with foliage	Hand and body		
Application rate of active substance	0.5	kg a.s./ha	*i_AppRate*
Number of applications	1		*i_AppNo*
Interval between multiple applications	365	days	*i_AppInt*
Half-life of active substance	30	days	*d_HalflifeAS*
Multiple application factor	1.0		*d_MAF*
Dermal absorption of the product	0.30%		*i_AbsorpProduct*
Dermal absorption of the in-use dilution	10.00%		*i_AbsorpInuse*
Dislodgeable foliar residue (i_AppRate*i_DFR)	1.5	µg a.s./cm^2	*d_DFR*
Working hours	2	hr	*d_WorkHr*
Dermal transfer coefficient - Total potential exposure	12500	cm^2/hr	*d_DermTcUCV*
Dermal transfer coefficient - arms, body and legs covered	1400	cm^2/hr	*d_DermTcCV1*
Dermal transfer coefficient - hands, arms, body and legs covered	no TC available for this assessment	cm^2/hr	*d_DermTcCV2*
Inhalation transfer coefficient for automated applications	NA	ha/hr*10^(-3)	*d_InhalTcAut*
Inhalation transfer coefficient for cutting ornamentals	NA	ha/hr*10^(-3)	*d_InhalTcCut*
Inhalation transfer coefficient for sorting / bundling ornamentals	NA	ha/hr*10^(-3)	*d_InhalTcSort*

Table A 55: Estimation of worker exposure towards flurochloridone according to EFSA guidance

1. Total

	Potential exposure	Work wear - arms, body and legs covered	Working wear and gloves	Comments
Total systemic exposure (mg a.s./day)	3.7500000	0.4200000	no TC available for this assessment	
Total systemic exposure per kg body weight (mg/kg bw/day)	0.0625000	0.0070000		
% of RVNAS	156.25%	17.50%		

2. Details

	Systemic exposure [mg a.s. /day]	Systemic exposure [mg a.s./kg bw/day]	Formula	Comments
Dermal - Potential	3.7500000	0.0625000	*d_DermTcUCV*d_WorkHr*i_DFR*i_MAF/1000*i_AbsorpInuse*	
Dermal - Work wear - arms, body and legs covered	0.4200000	0.0070000	*d_DermTcCV1*d_WorkHr*d_DFR*d_MAF/1000*i_AbsorpInuse*	
Dermal - Working wear and gloves	no TC available for this assessment		*d_DermTcCV2*d_WorkHr*d_DFR*d_MAF/1000*i_AbsorpInuse*	
Inhalation				Na for outdoor activities

A 3.3 Resident and bystander exposure calculations (KCP 7.2.2.1)

A 3.3.1 Calculations for flurochloridone

Table A 66: Input parameters considered for the estimation of resident exposure

Resident exposure for AG-F8-250 CS

Croptype	Root and tuber vegetables		
Application method	Downward spraying		
Application equipment	Vehicle-mounted		*i_AppEquip*
Formulation type	Soluble concentrates, emulsifiable concentrate, etc.		*i_FormVal*
Buffer strip	2-3	m	*i_Buffer*
Application rate of the product	0.5	kg a.s./ha	*i_AppRate*
Concentration of active substance (in-use dilution for liquid applications)	2.5	g a.s./l	*d_ConcAS*
Dermal absorption of product	0.30%		*i_AbsorpProduct*
Dermal absorption of in-use dilution	10.00%		*i_AbsorpInuse*
Oral absorption	100.00%		*i_AbsorpOralInuse*
Dislodgeable foliar residue (i_AppRate*i_DFR)	1.5	µg a.s./cm^2	*d_DFR*
Vapour pressure of in-use dilution	low volatile substances having a vapour pressure of <5*10-3Pa	Pa	*i_Volat*
Concentration in air	0.001	mg/m^3	*d_AirCon*
Resident dermal spray drift exposure 75th percentile - adult	0.47	ml spray dilution/person	
Resident dermal spray drift exposure 75th percentile - child	0.327	ml spray dilution/person	
Resident inhal. spray drift exposure 75th percentile - adult	0.00010	ml spray dilution/person	
Resident inhal. spray drift exposure 75th percentile - child	0.00022	ml spray dilution/person	
Resident dermal spray drift exposure mean - adult	0.22318	ml spray dilution/person	
Resident dermal spray drift exposure mean - child	0.18	ml spray dilution/person	
Resident inhal. spray drift exposure mean - adult	0.00009	ml spray dilution/person	
Resident inhal. spray drift exposure mean - child	0.00017	ml spray dilution/person	
Exposure duration dermal	2	hours	*d_ReExpDur*
Exposure duration inhalation	24	hours	*d_ReExpDurInhal*
Exposure duration entry into treated crops	0.25	hours	*d_ExpDurTreatCrop*
Light clothing adjustment factor	18.0%		*d_ClothAF*
Breathing rate adult	0.23	m^3/day/kg	*d_BreathRAd*
Breathing rate child (1-3 year old)	1.07	m^3/day/kg	*d_BreathRCh*
Drift percentage on surface (75th percentile)	5.60%		
Drift percentage on surface (mean)	4.10%		
Turf transferable residues percentage	5.00%		*d_Turf*
Transfer coeff. of surface deposits-adult	7300	cm^2/hour	*d_ReTCAd*
Transfer coeff. of surface deposits-child (1-3 year old)	2600	cm^2/hour	*d_ReTCCh*
Saliva extraction percentage	50.00%		*d_SalExt*
Surface area of hands mouthed	20	cm^2	*d_AreaHM*
Frequency of hand to mouth activity	9.5	events/hour	*d_ReFreqHM*
Ingestion rate for mouthing of grass per day	25	cm^2	*d_MouthGrass*
Dislodgeable residues percentage transferability for object to mouth	20.00%		*d_DRP*
Transfer coefficient for entry into treated crops (75th percentil	7500	cm^2/h	*d_TcEntryAd*
Transfer coefficient for entry into treated crops (75th percentil	2250	cm^2/h	*d_TcEntryCh*
Transfer coefficient for entry into treated crops (mean) - adult	5980	cm^2/h	*d_TcEntryAd*
Transfer coefficient for entry into treated crops (mean) - child	1794	cm^2/h	*d_TcEntryCh*

Table A 77: Estimation of resident exposure towards flurochloridone according to EFSA guidance

1.1 1-3 year old child

	Spray drift (75th percentile)	Vapour (75th percentile)	Surface deposits (75th percentile)	Entry into treated crops (75th percentile)	All pathways (mean)
Total systemic exposure (mg a.s./day)	0.0675850	0.0107000	0.0113400	0.0843750	0.1236025
Total systemic exposure per kg body weight (mg/kg bw/day)	0.0067585	0.0010700	0.0011340	0.0084375	0.0123603
% of RVNAS	16.90%	2.68%	2.84%	21.09%	30.90%

1.2 Adult

	Spray drift	Vapour	Surface deposits	Entry into treated crops	All pathways (mean)
Total systemic exposure (mg a.s./day)	0.0966000	0.0138000	0.0204400	0.2812500	0.2989919
Total systemic exposure per kg body weight (mg/kg bw/day)	0.0016100	0.0002300	0.0003407	0.0046875	0.0049832
% of RVNAS	4.03%	0.58%	0.85%	11.72%	12.46%

Table A 18: Input parameters considered for the estimation of acute bystander exposure

Estimation of bystander and resident exposure (adults and children)

Active substance (a.s.)		flurochloridone
Product		AG-F8-250 SC
Intended uses	Potato	Field Crops, Tractor Mounted (FCTM)
Treated area per day (A)	20	ha/d
Application rate (AR)	0.5	kg a.s./ha
Number of applications (NA)	1	1)

1) Consideration of more than two applications are not necessary if degradation of the active substance on foliage of at least 50 % can be assumed between two applications (otherwise use multiple application factor).

Dermal absorption (DA)	10	% (worst case, e.g. during application)
Inhalation absorption (IA)	100	%
Oral absorption (OA)	100	%
Systemic AOEL	0.04	mg/kg bw/d
Body weight (BW)	60	kg/person (adults)
	16.15	kg/person (children)

Distance between application and bystander or resident:

FCTM:	1	m
High crops not selected		
		m
Home & garden not selected		
		m

Drift deposit (D) for 1 appl. based on appl. technique and distance: **2.77 % (FCTM, 1 m)**

Airborne vapour concentration (ACv) 0.001 mg/m^3 2)

2) 1 $\mu g/m^3$ for semivolatile substances, i.e. vapour pressure (20 °C): ≥ $1x10^{-5}$ - < $5x10^{-3}$ Pa; 15 $\mu g/m^3$ for volatile substances, i.e. vapour pressure (20 °C): ≥ $5x10^{-3}$ Pa

Table A 19: **Estimation of acute bystander exposure towards active substance according to Martin S. *et al.***

Estimation of bystander exposure during/after application in Field Crops, Tractor Mounted

Input parameters considered for the estimation of bystander exposure:

Intended use(s):	Potato		**Drift (D):**	2.77	% (FCTM, 1 m)
Application rate (AR):	0.5	kg a.s./ha	**Exposed Body Surface Area (BSA):**	1	m² (adults)
				0.21	m² (children)
Body weight (BW):	60	kg/person (adults)	**Specific Inhalation Exposure (I^*_A):**	0.001	mg/kg a.s. (6 hours, adults)
	16.15	kg/person (children)		0.00057	mg/kg a.s. (6 hours, children)
Dermal absorption (DA):	10.00	% ('worst case')	**Area Treated (A):**	20	ha/d (based on Field Crops, Tractor Mounted (FCTM))
Inhalation absorption (IA):	100	%	**Exposure duration (T):**	5	min
AOEL:	0.04	mg/kg bw/d			

Bystander exposure towards flurochloridone					
Adults			**Children**		
Bystander: Dermal exposure after application in Potato (via spray drift)					
SDE_B = (AR x D x BSA x DA) / BW			SDE_B = (AR x D x BSA x DA) / BW		
(50 x 2.77% x 1 x 10%) / 60			(50 x 2.77% x 0.21 x 10%) / 16.15		
External exposure	1.385	mg/person	External exposure	0.29085	mg/person
External exposure	0.02308333	mg/kg bw/d	External exposure	0.01800929	mg/kg bw/d
Absorbed dose:	**0.0023083**	**mg/kg bw/d**	**Absorbed dose:**	**0.0018009**	**mg/kg bw/d**
Bystander: Inhalation exposure after application in Potato					
SIE_B = (I^*_A x AR x A x T x IA) / BW			SIE_B = (I^*_A x AR x A x T x IA) / BW		
(0,000 / 360 x 0.5 x 20 x 5 x 100%) / 60			(0,000 / 360 x 0.5 x 20 x 5 x 100%) / 16.15		
External exposure	0.00013889	mg/person	External exposure	7.9821E-05	mg/person
External exposure	2.3148E-06	mg/kg bw/d	External exposure	4.9425E-06	mg/kg bw/d
Absorbed dose:	**0.0000023**	**mg/kg bw/d**	**Absorbed dose:**	**0.0000049**	**mg/kg bw/d**
Total systemic exposure: SE_B = SDE_B + SIE_B			Total systemic exposure: SE_B = SDE_B + SIE_B		
Total systemic exposure (absorbed dose)	0.13863889	mg/person	Total systemic exposure (absorbed dose)	0.02916482	mg/person
Total systemic exposure (absorbed dose)	**0.0023106**	**mg/kg bw/d**	**Total systemic exposure** (absorbed dose)	**0.0018059**	**mg/kg bw/d**
% of AOEL:	**5.78**	**%**	**% of AOEL:**	**4.51**	**%**

Appendix 4 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)

Not relevant.