REGISTRATION REPORT

Part B

Section 7

Metabolism and Residues

Detailed summary of the risk assessment

Product code: 102000007779

Product name: FFA SC 508.8 G

Chemical active substance(s):

Flufenacet 508.8 g/L

Central Zone

Zonal Rapporteur Member State: POLAND

CORE ASSESSMENT

Applicant: Bayer Crop Science Division

Submission date: 30 June 2021

MS Finalisation date: February 2023 (initial Core Assessment)

June 2023 (final Core Assessment)

Version history

When	What
June 2021	Original Bayer Crop Science Division submission
February 2023	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~~.
June 2023	Final report (Core Assessment updated following the commenting period) No additional information or assessments after the commenting period.

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7.1 Summary and zRMS Conclusion

7.1.1 Critical GAP(s) and overall conclusion

Selection of critical uses and justification
The critical GAPs with respect to consumer intake and risk assessment for the preparation Flufenacet SC 508.8 G are presented in Table 7.1-1. A list of all intended uses on cereals in the countries of Central Zone (Poland, Slovakia, Ireland and Belgium) is given in Part B, Section 0.
Justification for the selection of the critical GAP.

Overall conclusion
The data available are considered sufficient for risk assessment. An exceedance of the current MRL of 0.1 mg/kg for wheat and barley and 0.05 mg/kg for rye for flufenacet as laid down in Reg. (EU) 1127/2014 is not expected.

The chronic and the short-term intakes of flufenacet residues are unlikely to present a public health concern.

As far as consumer health protection is concerned, zRMS agrees with the authorization of the intended use(s).

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

Data gaps
Noticed data gaps are:
- None.

Table 7.1-1: Acceptability of critical GAPs (and respective fall-back GAPs, if applicable)

1	2	3	4	5	6	7		8				9			10	11
GAP number (see part B.0)*	**Crop and/ or situation ****	**Zone**	**Product code**	**F, Fn, Fpn G, Gn, Gpn or I*****	**Pests or Group of pests controlled**	**Formulation**		**Application**				**Application rate per treatment**			**PHI (days)**	**Conclusion**
						Type	**Conc. of as**	**method kind**	**growth stage & season**	**number min max**	**interval between applications (min)**	**kg as/hL min max**	**water L/ha min - max**	**kg as/ha min - max**		
29, 53, 65, 77, 33, 57, 69, 81, 37, 61, 73, 85, 89, 97, 105, 113, 93, 101, 109, 117, 129, 133, 137, 141	Wheat, winter (TRZAW) (0500090), Triticale winter (TTLWI), (0500090), Barley winter (HORVW) (0500010), Rye (SECCW) (0500070), Durum wheat (TRZDW) (0500090), Spelt (TRZSP) (0500090)	Central	102000007779	F	ALOMY, POAAN, APESV, LOLSS, BBBBB, TTTDS	SC	Flufenacet 508.8 g/L	Spraying (broadcast, overall)	BBCH 00-09 (Autumn use)	a) 1 b) 1	-	0.061-0.244	100 - 400	0.244	As per growth stage	A
30, 54, 66, 78, 34, 58, 70, 82, 38, 62, 74, 86, 90, 98, 106, 114, 94, 102, 110, 118, 130, 134, 138, 142	Wheat, winter (TRZAW) (0500090), Triticale winter (TTLWI), (0500090), Barley winter (HORVW) (0500010), Rye (SECCW) (0500070), Durum wheat (TRZDW) (0500090), Spelt (TRZSP) (0500090)	Central	102000007779	F	ALOMY, POAAN, APESV, LOLSS, BBBBB, TTTDS	SC	Flufenacet 508.8 g/L	Spraying (broadcast, overall)	BBCH 10-13 (Autumn use)	a) 1 b) 1	-	0.061-0.244	100 - 400	0.244	As per growth stage	A
31, 55, 67, 79, 35, 59, 71, 83, 39, 63, 75, 87,	Wheat, winter (TRZAW) (0500090), Triticale winter (TTLWI),	Central	102000007779	F	ALOMY, POAAN, APESV, LOLSS,	SC	Flufenacet 508.8 g/L	Spraying (broadcast, overall)	BBCH 00-09 (Autumn use)	a) 1 b) 1	-	0.0305-0.122	100 - 400	0.122	As per growth stage	A

91, 99, 107, 115, 95, 103, 111, 119, 131, 135, 139, 143	(0500090), Barley winter (HORVW) (0500010), Rye (SECCW) (0500070), Durum wheat (TRZDW) (0500090), Spelt (TRZSP) (0500090)				BBBBB, TTTDS											
32, 56, 68, 80, 36, 60, 72, 84, 40, 64, 76, 88, 92, 100, 108, 116, 96, 104, 112, 120, 132, 136, 140, 144	Wheat, winter (TRZAW) (0500090), Triticale winter (TTLWI), (0500090), Barley winter (HORVW) (0500010), Rye (SECCW) (0500070), Durum wheat (TRZDW) (0500090), Spelt (TRZSP) (0500090)	Central	102000007779	F	ALOMY, POAAN, APESV, LOLSS, BBBBB, TTTDS	SC	Flufenacet 508.8 g/L	Spraying (broadcast, overall)	BBCH 10-13 (Autumn use)	a) 1 b) 1	-	0.0305-0.122	100 - 400	0.122	As per growth stage	A

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

** Use also code numbers according to Annex I of Regulation (EU) No 396/2005

*** F: professional field use, Fn: non-professional field use, Fpn: professional and non-professional field use, G: professional greenhouse use, Gn: non-professional greenhouse use, Gpn: professional and non-professional greenhouse use, I: indoor application

**** For more detailed information regarding the pests to be controlled within the different GAPs please see the list of all intended GAPs in Part B, Section 0

Explanation for Column 14 “Conclusion”

A	Exposure acceptable without risk mitigation measures, safe use
R	Further refinement and/or risk mitigation measures required
N	Exposure not acceptable, no safe use

7.1.2 Summary of the evaluation

The preparation FFA SC 508.8 G is composed of flufenacet.

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

Reference value	Source	Year	Value	Study relied upon	Safety factor
ADI	Review Report 7469/VI/98-Final	2003	0.005 mg/kg bw/day	2 year rat study	250
ARfD	Review Report 7469/VI/98-Final	2003	0.017 mg/kg bw/day	90 day, 1 year dog study	100

7.1.2.1 Summary for flufenacet

Table 7.1-3: Summary for flufenacet

Use-No.*	Crop	Plant metabolism covered?	Sufficient residue trials?***	PHI sufficiently supported?	Sample storage covered by stability data?	MRL compliance	Chronic risk for consumers identified?	Acute risk for consumers identified?
29, 53, 65, 77, 33, 57, 69, 81, 37, 61, 73, 85, 89, 97, 105, 113, 93, 101, 109, 117, 129, 133, 137, 141, 30, 54, 66, 78, 34, 58, 70, 82, 38, 62, 74, 86, 90, 98, 106, 114, 94, 102, 110, 118, 130, 134, 138, 142, 31, 55, 67, 79, 35, 59, 71, 83, 39, 63, 75, 87, 91, 99, 107, 115, 95, 103, 111, 119, 131, 135, 139, 143, 32, 56, 68, 80, 36, 60, 72, 84, 40, 64, 76, 88, 92, 100, 108, 116, 96, 104, 112, 120, 132, 136, 140, 144	Winter wheat, winter triticale, winter barley, rye, durum wheat, spelt	Yes	Yes (23 trials for N-EU)	Not applicable**	Yes	Yes	No	No

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

** not applicable as the PHI is covered by the vegetation period of the crop

*** According to the 'guideline on comparability, extrapolation, group tolerances and data requirements for setting MRLs', SANTE/2019/12752 (01 January 2021, repealing SANCO 7525/VI/95 Rev. 10.3), extrapolation of residue data obtained from any of the crops (wheat, rye, barley, oats) for an active substance is possible if the use pattern involves treatments early in the growing season (last application before consumable parts of the crop have started to form). Therefore, combined data sets are considered adequate to support uses for FFA SC 508.8

In the EU peer review metabolism studies on maize (pre-emergence treatment) and pulses and oilseeds (soybean and cotton) have been evaluated.

Following the EU peer review three additional studies with [fluorophenyl-UL-^{14}C]flufenacet were conducted to investigate the metabolism after pre- and post-emergence use in potato and after post-emergence use in wheat and corn. The reports were submitted on national level in various countries and were reviewed by the RMS (France) in the framework of the review of existing MRLs. The studies were considered adequate and confirmed the established residue definition (flufenacet including all metabolites containing the N-fluorophenyl-N-isopropyl moiety, expressed as flufenacet). Relative to the supported uses within the present dossier also the study on post-emergence application on wheat is considered relevant and therefore reported.

The metabolism of flufenacet was found to be qualitatively similar in all the examined crops, which cover three crop groups: cereals (corn, wheat), pulses and oil seed (soybean, cotton), root and tuber vegetables

(potatoes) as well as in rotational crops.

For flufenacet, the GAP evaluated in the EU peer review involved pre-/early post-emergence application at 240 g a.s./ha on small grain cereals (wheat, rye, barley) in the northern climatic zone. All these studies (17 trials) involving application rates at 240 g a.s./ha (actual 220-254 g a.s./ha) are considered adequate to support the use of FFA SC 508.8 in the northern climatic region by means of a risk envelope. The data set was generated using a WG formulation, however, WG and SC formulations are known to produce comparable residues (SANCO 7525/VI/95 rev 10.2; 23 September 2016). Therefore, both formulation types can be used interchangeably to support either of the products.
In addition, with the present dossier 6 supplementary residue trials are reported on mixture products involving also SC formulations containing flufenacet and diflufenican.
The residue trials have been performed according to the critical GAP in the northern climatic zone and were also considered in the EFSA Reasoned Opinion (Article 12 review; EFSA Journal 2012;10(4):2689). In all 6 trials the residues in wheat and barley grain and straw were below the LOQ of 0.05 and 0.1 mg/kg, respectively, and thus confirm that the residue situation is covered by the established EU MRLs (Regulation (EC) No. 1127/2014).

The effects of processing on the nature of flufenacet residues have been investigated. As residues of flufenacet do not exceed the trigger values defined in Reg (EU) No 283/2013, there is no need to investigate the effect of industrial and/or household processing on the magnitude of residues in processed products from wheat or barley.

In the Monograph (France 1997), Report of ECCO 73 (1999) and in the EFSA Reasoned Opinion (EFSA 2012) further investigation of residue levels of flufenacet in succeeding crops was not considered necessary. However, 4 field rotational crops were performed which confirmed a 'no residue situation' in winter cereals when grown following a spring crop (e.g. potatoes) and both crops received the maximum registered rates.

In the EU peer review (Report of ECCO 73, 1999) and the EFSA Reasoned Opinion (EFSA 2012) it was concluded that on the basis of the dietary burden calculation and the animal metabolism studies residue levels in livestock commodities are expected to remain below the LOQ of the enforcement method and thus no livestock feeding studies are needed. Further investigation of residues as well as the modification of MRLs in commodities of animal origin is therefore not necessary. The dietary burdens calculated using the dietary burden calculation spreadsheet (animal model 2017) does not change the outcome of the evaluation.

When using the EFSA PRIMo rev 3.1 and based on an ADI of 0.005 mg/kg bw/day, the IEDI of flufenacet was calculated to be 35% of the ADI. The highest NESTI for children was 7% of the ARfD due to consumption of milk and 3% for adults due to consumption of poultry muscle. The highest NESTI arising from consumption of small grain cereals was 4% for children and 2% for adults, for both consumer groups based on consumption of wheat.
The use of FFA SC 508.8 in winter cereals does not imply any unacceptable chronic or acute dietary risk to consumers.

7.1.2.2 Summary for FFA SC 508.8 G

Table 7.1-4: Information on FFA SC 508.8 G (K.C.A 6.8)

Crop	PHI for FFA SC 508.8 proposed by applicant	PHI/ Withholding period* sufficiently supported for	PHI for FFA SC 508.8 proposed by zRMS	zRMS Comments (if different PHI proposed)
		FFA		
Winter wheat, winter triticale, winter barley, rye, durum wheat, spelt	Not specified, normal growth period**	NR	Not specified, normal growth period†	-

NR: not relevant
* Purpose of withholding period to be specified
** not applicable as the PHI is covered by the vegetation period of the crop
† Pre-emergence and early post-emergence treatment (BBCH ≤13). The PHI is defined by the growth stage at treatment (time elapsing between last treatment and harvest of the crop).

Table 7.1-5: Waiting periods before planting succeeding crops

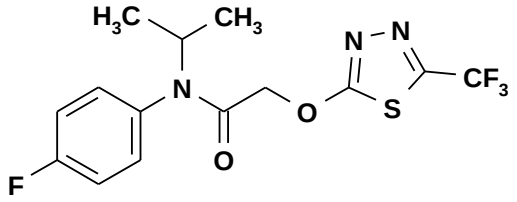
Waiting period before planting succeeding crops		**Overall waiting period proposed by zRMS for ACL+DFF+FFA SC 570 G**
Crop group	**Led by FFA**	
All	NR	NR

NR: not relevant

7.2 Flufenacet

General data on flufenacet are summarized in the table below (last updated 2020/12/05)

Table 7.2-1: General information on flufenacet

Active substance (ISO Common Name)	Flufenacet
IUPAC	N-(4-Fluoro-phenyl)-N-isopropyl-2-(5-trifluoromethyl[1,3,4]thiodiazol-2-yloxy)-acetanilide
Chemical structure	
Molecular formula	$C_{14}H_{13}F_4N_3O_2S$
Molar mass	363.34
Chemical group	Oxyacetamide
Mode of action (if available)	Selective with meristematic activity. Inhibition of cell division
Systemic	Yes
Company (ies)	Bayer AG*
Rapporteur Member State (RMS)	France (Annex I inclusion); Poland (for renewal of approval)
Approval status	Approved Commission Directive 2003/84/EC, dated 25th September 2003, entry into force 1st January 2004 and Reg (EU) No 540/2011, dated 25 May 2011, entry into force 14th June 2011 Reg (EU) No 823/2012, dated 14th September 2012, entry into force 5th October 2012 Reg (EU) 2019/1589, dated 26 September 2019, entry into force 17 October 2019 Commission Implementing Regulation (EU) 2020/1511 of 16 October 2020 Commission Implementing Regulation (EU) 2021/1449 of 3 September 2021 Commission Implementing Regulation (EU) 2022/1480 of 7 September 2022
Restriction (e.g. is restricted to use as "...")	Only uses as herbicide may be authorised.
Review Report	SANCO/7469/VI/98-Final, 03/07/2003
Current MRL regulation	Regulation (EC) No 1127/2014
Peer review of MRLs according to Article 12 of Reg No 396/2005 EC performed	Yes
EFSA Journal: Conclusion on the peer review	Not available
EFSA Journal: conclusion on Article 12	Yes, EFSA 2012**
Current MRL applications on intended uses	No (not by Bayer AG as notifier) Yes (According to EFSA register of Questions from other notifier, EFSA-Q-2019-00543, status additional data request; last updated 16/01/2020)

* Notifier in the EU process to whom the a.s. belong(s)
** If yes: EFSA, 2012 - see list of references

7.2.1 Stability of Residues (KCA 6.1)

7.2.1.1 Stability of residues during storage of samples

Available data

The freezer storage stability of flufenacet (FOE 5043) and 5 of its metabolites (FOE-oxalate, FOE sulfonic acid, FOE thioglycolate sulfoxide, FOE methylsulfoxide, and FOE methylsulfone) was examined in commodities of three different crops, representing oil-, starch- and water containing materials. Storage stability data were considered appropriate in the Monograph (Annex B 6) and in the EFSA Reasoned Opinion on existing MRLs (EFSA Journal 2012;10(4): 2689).
Storage stability data on commodities of high acid (orange fruit) and high protein content (dry bean seed) were also generated and submitted in the framework of the re-approval of the active substance. However, since the data are not relevant to the issue at hand they are not reported in the present document.

No new data submitted in the framework of this application.
A summary of the storage stability information is presented in the following table.

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

Matrix	Characteristics of the matrix	Acceptable maximum storage duration, months	Reference
Data relied on in EU for flufenacet (FOE 5043), FOE-oxalate, FOE sulfonic acid, FOE thioglycolate sulfoxide, FOE methylsulfoxide and FOE methylsulfone			
Plant products			
Corn forage	High water content	28	Monograh (Annex B 6), France 1997; EFSA, 2012 M-002426-01-1
Corn fodder		28	
Soybean forage		28	
Turnip tops		20	
Corn grain	High starch content	28	
Turnip roots		20	
Soybean hay	Dry commodity	28	
Soybean seed	High oil content	28	
Animal Products (investigated in livestock metabolism studies)*			
Goat for FOE-oxalate	Fat	20	Report of ECCO 73; Annex 2; LoEP, 1999 xxx 1995 M-004478-01-1
	Liver	21.5	
	Muscle	21.5	
	Milk	21.6	
	Kidney	18	

Matrix	Characteristics of the matrix	Acceptable maximum storage duration, months	Reference
Goat for flufenacet and other metabolites containing the fluorophenyl-isopropyl moiety	Fat	8	EU peer reviewed Report of ECCO 73; Annex 2; LoEP, 1999 xxx.; 1995 M-002250-01-1
	Liver	6	
	Muscle	8	
	Milk	8.5	
	Kidney	8.5	
New data **For flufenacet (FOE 5043), FOE sulfonic acid and FOE thioglycolate sulfoxide**			
Potato tuber	High starch content	20	Gould, T. J.; Murphy, I. M.; 2002; M-084449-01-1 Not reported in the present dossier
Flufenacet and a 1/1/1 mixture of its metabolites FOE oxalate hydrate, FOE thioglycolate sulfoxide, FOE sulfonic acid			
Dry bean seed	High protein content	24	Stuke, S., Ballmann, C. 2013; M-439517-02-1 Not reported in the present dossier
Orange fruit	High acid content	24	

Conclusion on stability of residues during storage

EU peer reviewed storage stability studies performed at ≤ -18°C covering the relevant matrix categories for cereals are available showing that flufenacet (FOE 5043) and its metabolites (FOE-oxalate, FOE sulfonic acid, FOE thioglycolate sulfoxide, FOE methylsulfoxide and FOE methylsulfone) are stable in all tested matrices under frozen conditions for at least as long as the storage stability studies lasted. Residues of flufenacet and its metabolites are stable up to 28 months in commodities with high oil content (soybean seed), in commodities of high water content (green plant material [forage/fodder] from soybean and corn) and in commodities of high starch content (corn grain). In addition, flufenacet residues proved to be stable in dry commodities like soybean hay.

The storage of residue samples of wheat/barley/rye green material, grain and straw (cf. chapter 7.2.3 and 7.2.6) was up to 371 days (12.4 months) for cereal green material, 234 days (7.8 months) for cereal grain and 256 days (8.5 months) for straw (all study RA-2020/06). The storage intervals are well covered by the maximum storage periods.
Data are adequate to cover the trials on small grain cereals supporting the intended GAPs of FFA SC 508.8.

zRMS comments:
Information given by the Applicant is acceptable and sufficient.

In EFSA Journal 2012;10(4):2689 it is stated that *The potential degradation of residues during storage of the residues trials samples was also assessed.*
In the framework of the peer review, storage stability of flufenacet was demonstrated for a period of 20 months at -21°C in commodities with high water content (turnip) (France, 1997). Also in the framework of the peer review, storage stability of flufenacet was demonstrated for a period of 28 months at -21°C in commodities with high oil content (soya bean) and dry commodities (maize grain) (France, 1997). The storage stability of flufenacet was not studied in commodities with high acid content. However, given that storage stability was demonstrated in the other three crop groups and that (currently) a total residue definition applies, and this moiety was found to be stable under several hydrolysis conditions, further investigation in cereal straw and commodities with high acid is not considered necessary.

According to the OECD 506: *If the stability of test substance in two diverse commodities in this category is confirmed, further examination with other commodities that belong to this category is unnecessary.*
Storage stability is demonstrated for two high starch commodities: in corn grain and turnip root, therefore stability can be supported for the entire high starch category in accordance with OECD guideline 506.
Stability data are cover the storage time for cereals.
No further data are requred.

7.2.1.2 Stability of residues in sample extracts (KCA 6.1)

Available data

Relevant information on the stability of flufenacet residues in the final extracts was investigated during development of method 00346 reported in the Annex II dossier (Monograph, Annex B 4, France, 1997). The analytical solution of control samples of wheat (green material, grain and straw) in tert-butyl methyl ether (MTBE) was fortified with the analytical target 4-fluoro-N-methylethyl benzenamine trifluoroacetamide (FOE5043 trifluoroacetamide) resulting from derivatisation. These solutions were analyzed on the day of preparation as well as four and eight weeks later. During this period the samples were stored in the refrigerator (about +4°C). The extracts have shown to be stable over these periods.

The more recent methods (01179, 01100, 01100/M001) do not require a derivatization step to obtain the analytical target FOE5043 trifluoroacetamide for determination by GC-MS; instead the common moiety compound 4-fluoro-N-isopropylaniline can be determined directly by HPLC-MS/MS. The analytical methods 01179 and 01100/M001 were validated for the determination of flufenacet residues in/on cereal grain, straw and green material by LC-MS/MS using matrix matched standards. The matrices to be analyzed are considered to be representative for the matrix groups of high starch content and high water content. In addition, straw was validated as a representative for dry matrices. All extraction and work-up steps are the same for both methods. The method 01100/M001 (Stuke, S., Bauer, J.; Ruhl, S.; 2012; M-433720-01-1) provides validation data on cereal matrices in addition to method 01179 (Class, Th.; Merdian, H.; 2010; M-362716-01-1) with only minor adaptations justified by different laboratory equipment and procedures.
During development of method 01100/M001 the stability in final plant extracts of wheat grain, wheat green material and straw was checked over a period of 14 to 23 days. During development of method 01179 stability in final extracts of the same cereal commodities was investigated over a 22-day interval. The recoveries for the stored extracts compared to the initial day of analysis did not indicate any degradation. Residues of the formed common moiety compound 4-fluoro-N-isopropylaniline were found to be stable in final plant extracts for at least 14 days (method 01100/M001) or 22 days (method 01179) when stored in a refrigerator at < 6 °C. During development of the ILV to these methods (Meyer, M.; 2011; M-405654-01-1) stability of the reference item in the final extracts of wheat green material and bean (dry seed) was investigated. Based on the recovery data obtained in the initial analysis and the reanalysis, the reference item was found to be stable in the extracts of wheat green plant material and bean seed (dry) for at least 21 and 19 days, respectively.
Method 01100, its modification 01100/M001, method 01179 and the corresponding ILV are reported in appendix 2 of section B5. These methods were not yet peer reviewed on EU level, however, are included in the DRAR (Poland 2017). The experimental extract stability data reported in method 01100/M001 covering cereal commodities are summarised in Appendix 2 of Section B7. Extract stability data for other commodity categories are not reported in the present section.

Conclusion on stability of residues in sample extracts

The analytical target FOE5043 trifluoroacetamide resulting from derivatisation (relevant to method 00346 and its modifications and extensions) as well as 4-fluoro-N-isopropylaniline which forms the analytical target from the more recent methods 01179 and 01100 (and modification) were found to be stable in commodities of high water and starch content and dry materials (straw) up to a minimum of 14 days.
In the residue reports the time between sample extraction and analysis is not reported. However, a time period exceeding the investigated minimum interval is unlikely. Relevant information on the stability of residues in the final or any intermediate extracts can also be derived from the fortification experiments performed during sample analysis. Every analytical batch does contain at least one freshly fortified sample for concurrent recovery determination. The extracts of the fortified samples and of the study samples are handled and stored in parallel. If the recoveries in the fortified samples are within acceptable ranges, the stability of the sample extracts is considered as sufficiently proven. In all studies, recovery experiments were performed concurrently with the analyzed samples. The recovery rates for the studies presented in this dossier were in the 70-110% range, concluding that residues were stable in the sample extracts.

zRMS comments:
Information given by the Applicant is acceptable.
No further data are requred.

7.2.2 Nature of residues in plants, livestock and processed commodities

7.2.2.1 Nature of residue in primary crops (KCA 6.2.1)

Available data

An overview of the metabolism studies evaluated in the EU peer review is given in the table below. Following the EU peer review supplementary metabolism studies were performed and were considered in EFSA's Reasoned Opinion on the existing MRLs (EFSA 2012) and evaluated on national level.

All supplementary studies are included in the DRAR (Poland 2017) but are not reported in detail in the present dossier except the study on wheat with post-emergence application. The studies are included in the table below for sake of completeness.

The detailed assessment of the supplementary study on wheat (post emergence treatment) with the Fluorophenyl-UL-^{14}C label is presented in Appendix 2 of this document.

Table 7.2-3: Summary of plant metabolism studies

Crop Group	Crop	Label position	Application and sampling details					Reference
			Method, F or G (a)	Rate (kg a.s./ ha)	No	Sampling (DAT)	Remarks	
EU data								
Cereals	Corn/ Maize	[Fluorophenyl-UL-^{14}C]	pre-emergence treatment, Soil, F	1.37	1	forage, fresh kernels 96 d; fodder and dry kernels 110 d	Baird, J. H.; 1994	EU peer reviewed Monograph (Annex B 6), France, 1997 EFSA, 2012
Pulses and oilseeds	Soybean	[Fluorophenyl-UL-^{14}C]	pre-emergence treatment, Soil, G	1.49	1	forage, fresh beans 66 d, dry hay, dry beans 80 d	Krolski, M. E.; Bosnak, L. L.; 1995	EU peer reviewed Monograph (Annex B 6), France, 1997 EFSA, 2012
		[Thiadiazole-2-^{14}C]	pre-emergence treatment, Soil, F/G	1.38	1	forage 48 d, dry hay, dry bean 91 d	Krolski, M. E.; Bosnak, L. L.; 1995	
	Cotton	[Fluorophenyl-UL-^{14}C]	pre-emergence treatment, Soil, G	1.42	1	forage 21, 43 156 d	Krolski, M. E.; Bosnak, L. L.; 1995	EU peer reviewed Monograph (Annex B 6), France, 1997 EFSA, 2012
New data								
Cereals	Wheat	[Fluorophenyl-UL-^{14}C]	post-emergence treatment, G	0.52	1	forage 18 d hay 33 d straw 66 d grain 59 d	Krolski, M. E.; Bosnak, L. L.; 1997; M-002275-01-1	EFSA, 2012 Suppl. dossier data point: KCA 6.2.1/05; Appendix 2
	Corn/ Maize	[Fluorophenyl-UL-^{14}C]	foliar treatment, G, post-emergence	1.5	1	forage 82 d, BBCH 85-87 fodder and grain 129 d, BBCH 97	Krolski, M. E.; Bosnak, L. L.; 1998 M-005755-01-1	EFSA, 2012, (not reported in the present dossier)
Root vegetables	Potato	[Fluorophenyl-UL-^{14}C]	pre-emergence	2.6	1	tubers: 40, 109 days after	Beedle, E. C.; Ying, S. L.;	EFSA, 2012 (not reported

Crop Group	Crop	Label position	Application and sampling details					Reference
			Method, F or G (a)	Rate (kg a.s./ ha)	No	Sampling (DAT)	Remarks	
			treatment, Soil, F/G			planting	2000; M-020428-01-1	in the present dossier)
			post-emergence treatment, Foliar, F	3.0		tubers:67 days		

Outdoor/field application (F) or glasshouse/protected/indoor application (G). Indoor application during the metabolism study does not preclude an outdoor/field GAP for the respective crops.

Summary of plant metabolism studies reported in the EU

The metabolism of flufenacet in plants after pre-emergence application was extensively addressed in the Monograph (France 1997). Three metabolism studies with the [fluorophenyl-UL-^{14}C]-labelled active substance were submitted for pre-emergence use in corn, soybean, and cotton. In a fourth study the metabolism of flufenacet in soybean was investigated after pre-emergence application of the [thiadiazole-2 ^{14}C]-labelled active substance.

As evident from the plant metabolism studies, the initial metabolic reaction is cleavage of the molecule into the thiadone and acetamide moiety. While the resulting thiadone (M09) itself was not observed, various conjugates were formed, the most important being the corresponding N-glucoside (M25). In soybeans, the malonylalanine conjugate (M34) predominated.

The fluorophenyl-acetamide portion is directly conjugated with glutathione (GSH) or homoglutathione (hGSH) and further metabolized yielding the transient FOE cysteine conjugate (M23). All subsequent metabolites can be considered as hydrolysis, oxidation and conjugation products of the glutathione pathway. However, the FOE oxalate (M01) most likely arose through direct oxidation of the transient hydrolysis product of flufenacet, the primary alcohol (FOE alc, M03).

From these studies a conclusion on the residue definition in food of plant origin was made: "The metabolism of the flufenacet results in a number of metabolites, which all have the common moiety N-isopropyl-4-fluorophenyl. Because no parent compound was found in any study and only three metabolites were of quantitative significance (M01: FOE oxalate; M02: FOE sulfonic acid, M04: FOE thioglycolate sulfoxide) a **"total residue" approach is proposed, based on the total amount of N-fluorophenyl-N-isopropyl derived residues."** (Monograph on FOE 5043 (flufenacet), France 1997, Annex B.6, Section B.6.3).

Additional plant metabolism studies were conducted later and thus not evaluated by a peer-review on EU level. These are studies of [fluorophenyl-UL-^{14}C]flufenacet on potato (pre-planting and post-emerging treatment) and on wheat and maize (both post-emerging treatment). The studies were submitted and evaluated in different EU Member States in support of uses in cereals, potatoes and maize. The studies were also evaluated by the previous RMS (France) and are considered in the EFSA reasoned opinion on existing MRLs (EFSA Journal 2012;10(4):2689)

EFSA Reasoned Opinion (2012):

Primary crop metabolism of flufenacet was investigated for pre-emergence treatment on cereals and pulses & oilseeds in the DAR using fluorophenyl-U-^{14}C labelled flufenacet. A study for pre-emergence treatment on pulses & oilseeds was conducted using thiadiazole-2-^{14}C labelled flufenacet. In addition pre-emergence and foliar treatment metabolism studies on root vegetables and cereals (foliar treatment only) using fluorophenyl-U-^{14}C labelled flufenacet were evaluated by the RMS, after the peer review was completed. The metabolism of the thiadiazole moiety of flufenacet is considered to be adequately understood on the basis of the available studies. It is also concluded that metabolites containing the thiadone moiety are not relevant and should not be included in the residue definition. The metabolism of the fluorophenyl moiety of flufenacet results in a number of metabolites which all have the N-isopropyl-4-flurophenyl moiety. A 'total residue' approach has been proposed and the current residue definition for risk assessment and enforcement is the sum of all compounds containing the N-fluorophenyl-N-isopropyl moiety expressed as

flufenacet equivalent.

Summary of new plant metabolism studies
Additional plant metabolism study on wheat with [fluorophenyl-UL-14C]flufenacet
The study is reported in detail in Appendix 2 (M-002275-01-1).
The additional plant metabolism study (Krolski, M. E.; Bosnak, L. L.; 1997; M-002275-01-1) was conducted on wheat for registration in the USA applying a higher application rate than used in Europe. The study investigated the post-emergence application on wheat as supported with the present dossier. The study was evaluated on national level and for the review of existing MRLs according to Article 12 of Regulation (EC) 396/2005 (EFSA 2012). The study is added to complete the picture on the metabolism of flufenacet in plants and to confirm common basic metabolic transformations.

The metabolism of [fluorophenyl-UL-^{14}C]flufenacet was investigated in spring wheat following post-emergent foliar application to young shoots (4-tiller growth stage) at a use rate of 0.46 lb. ai/acre (0.52 kg a.s./ha). Agricultural commodities of wheat were collected as immature forage, immature hay, mature straw and grain. All commodity samples were homogenized under liquid nitrogen and aliquots were radioassayed by combustion and liquid scintillation counting (LSC). The total radioactive residues (TRR) amounted to 1.93 mg equ/kg in forage, 3.50 mg equ/kg in hay, 2.04 mg equ/kg in straw and 0.62 mg equ/kg in grain. Extraction with methanol at ambient temperature and under reflux revealed a high extractability of the radioactive residues accounting for 92, 94, 86 and 80% of TRR for forage, hay, straw and grain, respectively. Following further acid and alkaline hydrolysis of the residues non-extractable residues from plant matrix were negligible (≤ 3 – 4% of TRR). The extracted residues were separated by reversed phase HPLC and identified by LC-MS/MS and co-elution with authentic reference standards.

The metabolism of flufenacet in wheat was extensive. While no parent substance was observed in any of the plant commodities 12 metabolites were detected in forage and straw, and 9 metabolites in hay and grain. FOE oxalate (FOEOX, M1) revealed to be a major metabolite in all commodities. It proved to be predominant in wheat grain amounting to 65% of TRR (corresponding to 0.40 mg equ/kg). Other metabolites in grain appeared at a very low level (≤ 2% of TRR). In forage, hay and straw two other major metabolites were identified as FOE sulfinyl lactic acid I (FAMSOL I, M33) and FOE sulfanyl lactic acid glucoside (FAMSL-Glu, M41). In straw, a further metabolite FOE sulfonic acid (FOESO3H, M2) amounted to 15% of TRR.

The major metabolite present in all commodities, i.e. FOE oxalate, most likely arose from oxidation of transient primary alcohol hydrolysis product. All other metabolites were formed by hydrolysis, oxidation and conjugation of a primary transient metabolite formed by initial conjugation with glutathione. The parent substance was not observed in any commodity of forage, hay, straw and grain. All major metabolites formed from the primary glutathionate conjugate in these commodities contained the common moiety fluorophenyl-N-isopropyl amine.
Comparative extraction of the residues using methanol (this metabolism study) and determination of the residues using the residue analytical method (oxidative acid hydrolysis and quantification of the hereby formed N-fluorophenyl-N-isopropyl amine) showed a good agreement of amount of residue compounds containing the common moiety.

Conclusion on metabolism in primary crops
From all the metabolism studies a common metabolic pathway of flufenacet in plants was concluded. The initial metabolic reaction is a cleavage of the molecule into the thiadone and acetamide moiety by glutathione (GSH) conjugation of the acetamide part resulting in the transient gluathionate conjugated FOE GSH (M22).

This transient glutathione conjugate is further metabolized by splitting off glycine and glutamine acid yielding the FOE cysteine conjugate (M23). All further metabolites can be considered as hydrolysis, oxidation and conjugation products of the FOE cysteine conjugate. However, the FOE oxalate (M01) most likely arose through direct oxidation of a transient primary alcohol hydrolysis product of flufenacet (FOE alcohol, M03).

Due to the initial cleavage of the parent molecule caused by glutathionate conjugation, trifluoromethyl thiadone (M09) was released. While this transient moiety was not observed, various conjugates were formed, the quantitatively most important being the corresponding N-glucoside (M 25). In soybeans, the malonylalanine conjugate (M34) predominated.
The additional studies with [fluorophenyl-UL-^{14}C] flufenacet on potato (pre- and post-emergence application), wheat and corn (both post-emergence application) confirmed this metabolic pathway.

The parent substance flufenacet did not occur in any crop. No metabolite was found which proved to be major in all crops and would qualify as marker substance. Therefore, the residue definition of flufenacet residues in plants was established as parent substance and all metabolites containing the N-fluorophenyl-N-isopropyl moiety. When summing up the metabolites with the common moiety the resulting sum represents the major portion of TRR in all examined raw agricultural commodities,

EFSA, in principle, agreed with the current residue definition in their "Reasoned opinion of the review of existing MRLs of flufenacet" (EFSA 2012). However, EFSA also mentioned that the 'common moiety residue definition' might be "not the most adequate for enforcement proposes" and therefore proposed to investigate the option to include six individual metabolites in a multi-residue method. New residue trials would not be needed as the current common moiety method includes all these metabolites.
Following the Article 12 review for flufenacet it was decided not to change the residue definition for enforcement: "Flufenacet (sum of all compounds containing the N fluorophenyl-N-isopropyl moiety expressed as flufenacet)" as published in Regulation (EU) No 1127/2014.

The intended GAPs of FFA SC 508.8 is defined as pre-emergence and/or early post-emergence application to wheat and barley at application rates up to 244 g a.s./ha. Thus, the uses are within the frame investigated in the metabolism studies on cereals evaluated in the EU peer review and the EFSA Art 12 review and the conclusions drawn in the Monograph (France 1997) and in the EFSA reasoned opinion (2012) are still considered valid.

zRMS comments:
Information given by the Applicant is sufficient and acceptable.
In EFSA Journal 2012;10(4):2689 it is stated that *Primary crop metabolism of flufenacet was investigated for pre-emergence treatment on cereals and pulses & oilseeds in the DAR using fluorophenyl-U-14C labelled flufenacet. A study for pre-emergence treatment on pulses & oilseeds was conducted using thiadiazole-2-14C labelled flufenacet. In addition pre-emergence and foliar treatment metabolism studies on root vegetables and cereals (foliar treatment only) using fluorophenyl-U-14C labelled flufenacet were evaluated by the RMS, after the peer review was completed. The metabolism of the thiadiazole moiety of flufenacet is considered to be adequately understood on the basis of the available studies. It is also concluded that metabolites containing the thiadone moiety are not relevant and should not be included in the residue definition. The metabolism of the fluorophenyl moiety of flufenacet results in a number of metabolites which all have the N-isopropyl-4-flurophenyl moiety.*

Plant residues definitions:
- for monitoring and risk assessment: Sum of all compounds containing the N fluorophenyl-N-isopropyl moiety expressed as flufenacet equivalent (EFSA 2012, Regulation (EC) No 1127/2014).

No further data are requred.

7.2.2.2 Nature of residue in rotational crops (KCA 6.6.1)

Available data
Confined rotational crop studies with flufenacet were conducted using the ^{14}C-labelled test substance, the radiolabel being in the [fluorophenyl-UL-^{14}C] and in the [thiadiazole-2-^{14}C] -position. These studies were already evaluated in the EU peer review and considered acceptable.
In the EFSA Reasoned Opinion (2012) it was concluded that "a study showed that metabolism in primary and rotational crops is comparable and significant residues in rotational crops are not expected, provided that flufenacet is applied according to the GAPs supported in the framework of this review."
No new data are submitted in the framework of this application.

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

Crop group	Crop	Label position	Application and sampling details					Reference
			Method, F or G *	Rate (kg a.s./ha)	Sowing intervals (DAT)	Harvest Intervals (DAT)	Remarks	
EU data								
Root and tuber vegetable	Turnip	Fluoro-phenyl-U-^{14}C	pre-emergence, G	0.9	1, 4-5 and 12 months	At harvest		Monograph (Annex B 6), France, 1997 EFSA, 2012 M-002369-01-1
		Thia-diazole-2-^{14}C	pre-emergence, G	0.9	4 and 12 months	At harvest	Crop failure due to phytotoxicity with 1st rotation	Monograph (Annex B 6), France, 1997 EFSA, 2012 M-002368-01-1

Crop group	Crop	Label position	Application and sampling details					Reference
			Method, F or G *	Rate (kg a.s./ha)	Sowing intervals (DAT)	Harvest Intervals (DAT)	Remarks	
Leafy vegetables	Kale	Fluoro-phenyl-U-^{14}C	pre-emergence, G	0.9	1, 4-5 and 12 months	At harvest		Monograph (Annex B 6), France, 1997 EFSA, 2012 M-002369-01-1
		Thia-diazole-2-^{14}C	pre-emergence, G	0.9	4 and 12 months	At harvest	Crop failure due to phytotoxicity with 1st rotation	Monograph (Annex B 6), France, 1997 EFSA, 2012 M-002368-01-1
Cereals	Wheat	Fluoro-phenyl-U-^{14}C	pre-emergence, G	0.9	1, 4-5 and 12 months	At harvest		Monograph (Annex B 6), France, 1997 EFSA, 2012 M-002369-01-1
		Thia-diazole-2-^{14}C	pre-emergence, G	0.9	4 and 12 months	At harvest	Crop failure due to phytotoxicity with 1st rotation	Monograph (Annex B 6), France, 1997 EFSA, 2012 M-002368-01-1

Outdoor/field application (F) or glasshouse/protected/indoor application (G). Indoor application during the metabolism study does not preclude an outdoor/field GAP for the respective crops.

Summary of the confined rotational crop studies reported in the EU

Evaluation in the EU peer review

Excerpt from Monograph (Annex B 6, France, 1997):

"The results of the confined rotational crop studies demonstrate that the metabolic pattern after application of FOE 5043 (flufenacet) is similar in target crops and crops grown in rotation. No active ingredient was found, and all metabolites are derived by the same metabolic pathway via glutathione and homoglutathione, which is common to all plant species. Although several additional compounds were only observed in rotational crops, they are considered as products of further metabolism of known metabolites. Most of them should be detectable with the total residue method developed for plant residue analysis and/or are considered of being of no relevance because they are not expected to appear in significant amounts.

After normal agricultural use of FOE 5043 no significant residues are to be expected in leafy or root crops grown in rotation with the target crops, even at rates which are considerably higher than the highest recommended field application in Europe. According to the above-mentioned studies the only exception would be wheat (which at the same time is also a target crop). However, a comparison with the results from field trials in cereals and maize at recommended application rates of 240 ai/ha and 600 g a.i./ha (see Chapter 6.3 [of the AII dossier] *reveals that no residues were detected. Therefore, it is concluded, that the high residue levels in the confined rotational crop study are a consequence of the experimental design and do not reflect normal practice relevant conditions. Consequently, a field rotational crop study is considered*

as not being necessary".

The conclusions drawn in the Monograph (Annex B 6, France, 1997) were confirmed in the EFSA Reasoned Opinion on existing MRLs (EFSA Journal 2012;10(4):2689).

Excerpt from the EFSA Reasoned Opinion which makes reference to the Monograph

A specific residue definition for rotational crops is not considered necessary as metabolism in primary and rotational crops was found to be similar and very low residue levels are expected. (p.25)

In the DAR it was concluded that after use of flufenacet according to the GAPs (…), no significant residues are expected in leafy or root crops grown in rotation with the primary crops. According to the confined rotational crop metabolism studies the only exception to this would be wheat. However an assessment of the results from field trials in cereals and maize (…) shows that no residues are detected in any trial, except in green material sampled within 40 days of application and therefore it was concluded in the DAR that the high residue levels seen in wheat were a consequence of the experimental design and do not reflect normal practice. Considering, also, that the application rate of flufenacet within the EU ranges between 0.15-0.6 kg a.s./ha it can be concluded that flufenacet residue levels in rotational commodities are not expected to exceed 0.01 mg/kg, provided flufenacet is applied in compliance with the GAPs reported in Appendix A. (p.26)

Summary of new plant metabolism studies
No new studies are submitted with this submission

Conclusion on metabolism in rotational crops
The supported use pattern and application rates for the product FFA SC 508.8 G (*i.e.* 244 g a.s./ha) are within the frame evaluated in the EU peer review (Monograph (Annex B 6), France, 1997) and therefore the conclusions drawn in the Monograph and in the EFSA reasoned opinion (EFSA 2012) are still valid.

zRMS comments:
Information given by the Applicant is sufficient and acceptable. Residue levels in rotational commodities are not expected to exceed 0.01 mg/kg after the use of Flufenacet SC 508.8 G (i.e. 244 g a.s./ha) in compliance with the proposed GAP. No further data are requred.

7.2.2.3 Nature of residues in processed commodities (KCA 6.5.1)

Available data
The data on hydrolytic degradation of flufenacet is summarised in the following table. No new data is submitted in the framework of this application.

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

Conditions (Duration, Temperature, pH)	Identified compound(s) (%)	Reference
EU data		
Hydrolytic degradation (30 days, 25°C, pH 5, 7, 9), simulation of relevant hydrolytic conditions	parent flufenacet and all its derivatives and metabolites which comprise the *N*-fluorophenyl-*N*-isopropyl functional group	Monograph (Annex B 6), France,1997 EFSA, 2012 M-002203-01-1

The effect of processing on the nature of flufenacet was evaluated in the framework of the peer review.

Excerpt from Monograph B.6.7.1:
"Experiments conducted to study the hydrolytic degradation of FOE 5043 [flufenacet] *at pH values 5, 7 and 9 showed that the parent compound is not significantly affected by this process (see chapter B.7.4* [hydrolytic behaviour]*). It is therefore unlikely that processing will affect the nature of FOE 5043 residue. In addition, the analytical method used for raw and processed commodities determines the total residue of*

FOE 5043 by converting the relevant residue into a common derivate. Therefore, any minor changes of the molecule would not influence the residue determined. Due to these facts, it is not considered necessary to conduct special radioactive studies on the nature of FOE 5043 residues in processed products."

Conclusion on nature of residues in processed commodities
The residue definition in plants consists of parent flufenacet and all its derivatives and metabolites which comprise the N fluorophenyl-N-isopropyl functional group. These residues are determined by means of the common moiety method covering all the metabolites derived from the fluorophenyl acetamide moiety.

All residues containing the N-fluorophenyl-N-isopropyl group in the RACs as well as each potential breakdown product containing this moiety resulting from processing of these RACs are captured by the residue analytical methods for determination of flufenacet residues. By application of these residue methods all N-fluorophenyl-N-isopropyl containing residues are hydrolysed to the analytical target 4-fluoro-N-isopropylaniline that is quantified by GC-MS after derivatization with TFAA or directly by HPLC-MS/MS determination. Therefore, a study on the nature of processed residues (high temperature hydrolysis according to OECD 507) resulting from use of flufenacet in crops does not provide any new information and can thus be omitted.

zRMS comments:
Information given by the Applicant is acceptable and sufficient.
Studies on the hydrolytic degradation of flufenacet and studies on the magnitude of residues in processed commodities of maize and soya bean indicate that processing is not expected to have a significant impact on the composition or magnitude of residues in matrices of plant origin.
zRMS agrees with the above conclusion.

7.2.2.4 Conclusion on the nature of residues in commodities of plant origin (KCA 6.7.1)

Table 7.2-3: Summary of the nature of residues in commodities of plant origin

Endpoints	
Plant groups covered	Cereals (maize, wheat) Pulses and oilseeds (soybean, cotton) Root vegetables (potato)
Rotational crops covered	Root and tuber vegetables (turnip) Leafy vegetables (kale/Swiss chard) Cereals (wheat)
Metabolism in rotational crops similar to metabolism in primary crops?	Yes
Processed commodities	Flufenacet and all its derivatives and metabolites which comprise the *N*-fluorophenyl-*N*-isopropyl functional group which may originate during processing are covered by the residue definition of the primary crop
Residue pattern in processed commodities similar to pattern in raw commodities?	Yes
Plant residue definition for monitoring	Flufenacet (sum of all compounds containing the N fluorophenyl-N-isopropyl moiety expressed as flufenacet equivalent (Regulation n°1127/2014)
Plant residue definition for risk assessment	Flufenacet (sum of all compounds containing the N fluorophenyl-N-isopropyl moiety expressed as flufenacet equivalent (Monograph Annex B 6, France, 1997; EFSA, 2012)
Conversion factor from enforcement to RA	not needed

7.2.2.5 Nature of residues in livestock (KCA 6.2.2-6.2.5)

Available data

The nature of flufenacet resides in goat and hen was investigated in the framework of Directive 91/414/EEC. The studies used [fluorophenyl-UL-^{14}C] flufenacet, [thiadiazole-2-^{14}C] flufenacet and [fluorophenyl-UL-^{14}C] flufenacet oxalate, the latter one being the main plant metabolite in poultry and ruminant feed. The studies were reviewed in the Monograph (Annex B 6, France, 1997).
No new data are submitted in the framework of this application.

Since the parent compound degrades rapidly in plants and is not detectable in animal feeding items the metabolism study using [fluorophenyl-UL-^{14}C] FOE oxalate provides the most relevant information. Oral administration of [fluorophenyl-U-^{14}C] flufenacet oxalate to ruminant and poultry showed its metabolic stability. Flufenacet oxalate is essentially not metabolised by the animal. The low residue levels in tissue, milk and eggs suggest that flufenacet oxalate is minimally absorbed and rapidly excreted. This metabolic stability was confirmed by a bio-availability study of flufenacet oxalate in rats. Following oral administration of radiolabeled flufenacet oxalate to three rats at a dose rate of approx. 1 mg/kg bw 19 – 37% of the dose was excreted with urine and 61 – 80% was excreted with faeces as unchanged flufenacet oxalate.

The metabolism studies performed with flufenacet indicate a wide range of metabolites are formed containing the N-fluorophenyl-N-isopropyl moiety. Therefore, EFSA (2012) concluded that for commodities of animal origin, it is desirable to include all metabolites containing the N-fluorophenyl-N-isopropyl moiety in the residue definition, both for enforcement and risk assessment.

Table 7.2-7: Summary of animal metabolism studies

Group	Species	Label position	No of animal	Application details		Sample details		Reference
				Rate (mg/kg bw/d)	Duration (days)	Commodity	Time of sampling	
EU data								
Lactating ruminants	Goat	[Fluorophenyl-UL-^{14}C] FOE 5043	1	5	3	Milk	Daily[1]	xxx, 1995, M-002250-01-1 Monograph, France,1997 EFSA, 2012
						Urine and faeces	not sampled	
						Tissues	at sacrifice (4 hours after final dose)	
		[Thiadiazole-2-^{14}C] FOE 5043	1	5	3	Milk	Daily[1]	xxx 1995, M-002248-01-1 Monograph, France,1997 EFSA, 2012
						Urine and faeces	not sampled	
						Tissues	at sacrifice (4 hours after final dose)	
		[Fluorophenyl-UL-^{14}C] FOE oxalate	1	5.12	3	Milk	Daily[1]	xxx 1995, M-004478-01-1 Monograph, France,1997 EFSA, 2012
						Urine and faeces	not sampled	
						Tissues	at sacrifice (4 hours after final dose)	
Laying poultry	Hens	[Fluorophenyl-UL-^{14}C] FOE 5043	10	5	3	Eggs	daily, 2 days after first dose	xxx, 1995, M-002251-01-1 Monograph, France,1997 EFSA, 2012
						Excreta	not sampled	
						Tissues	3-4 hours after last dose	
		[Thiadiazole-2-^{14}C] FOE 5043	10	5	3	Eggs	daily, 2 days after first dose	xxx 1995, M-002253-01-1 Monograph, France,1997 EFSA, 2012
						Excreta	not sampled	
						Tissues	4 hours after last dose	
		[Fluorophenyl-UL-^{14}C] FOE oxalate	10	5	3	Eggs	daily	xxx 1995, M-004474-01-1 Monograph, France,1997 EFSA, 2012
						Excreta	not sampled	
						Tissues	4 hours after last dose	

[1] Milk collected within 24 hours after each dosing was combined in one sample

Summary of animal metabolism studies reported in the EU

Excerpt from EFSA Reasoned Opinion (2012):

"The metabolism studies with the fluorophenyl-U-^{14}C labelled flufenacet on both ruminant and poultry show that the flufenacet glutathione conjugate[1] (58% TRR in goat liver), the cysteine conjugate (55% TRR in goat fat), the N-acetyl conjugate[2] (24% TRR in goat kidney), flufenacet methylsulfone (17% TRR in hen fat), 4-fluoroaniline methylsulfonyl acetamide[3] (22% TRR in goat muscle), N-(4-fluorophenyl) acetamide[4](19% TRR in hen muscle), N-(4-fluorophenyl)-N-(2-hydroxy-1-methyl-ethyl)-2-(methylsulfinyl)

[1] Flufenacet glutathione conjugate: N-(4-fluorophenyl)-N-isopropyl-2-(S-glutationyl)acetamide.
[2] Flufenacet N-acetyl conjugate: N-acetyl-S-[2-[(4-fluorophenyl)(1-methylethyl)amino]-2-oxoethyl]cysteine
[3] 4-fluoroaniline methylsulfonyl acetamide: N-(4-fluorophenyl)-2-methylsulfonyl-acetamide
[4] N-(4-fluorophenyl) acetamide: N-(4-fluorophenyl) acetamide

acetamide[5] (8% TRR in hen muscle), N-(4-fluorophenyl)-N-(2-hydroxy-1-methyl-ethyl)-2-(methylsulfonyl) acetamide[6] (22% TRR in hen muscle) and N-(4-fluorophenyl)-N-(1-methylethyl) acetamide[7] (3% TRR in hen liver) are the main components of the residue in animal tissues and milk products. Parent flufenacet was detected in small amounts (2% of TRR) in the fat and muscle of ruminants and in the fat (up to 55% TRR), muscle (3% TRR) and eggs (7% TRR) of poultry.
*The metabolism studies with the thiadiazole-2-^{14}C labelled flufenacet on both ruminant and poultry show that flufenacet is rapidly cleaved at the ether bond yielding thiadone (89% TRR in goat kidney and fat) which is then, primarily, conjugated to glucuronic acid (to form thiadone glucoronide[8]) (9% TRR in goat kidney) prior to elimination. Parent flufenacet was not detected at all in ruminants and was only found in the fat (15% TRR [*with thiadiazole-2-^{14}C label; 55% TRR with F-phenyl-^{14}C label*]) of poultry. It is noted that the studies in ruminant and poultry show that the residue levels after administration of thiadiazole-2-^{14}C labelled flufenacet are approximately 3 to 14 times higher than after administration of fluorophenyl-U-^{14}C labelled flufenacet. This is to be expected as the products of the initial cleavage reaction undergo further metabolism and elimination at different rates, due to the different polarities of the metabolites. However, metabolites containing the thiadiazole moiety are anyhow not expected to occur in commodities of animal origin because parent flufenacet is rapidly hydrolysed in plants and metabolites included in the plant residue definition no longer contain this moiety. The metabolism studies with fluorophenyl-U-^{14}C labelled flufenacet oxalate on ruminant and poultry show that flufenacet oxalate is essentially not metabolised by the animal. The low levels in tissue, milk and eggs suggest that flufenacet oxalate is minimally absorbed and rapidly excreted after oral administration. This was confirmed by a bio-availability study of flufenacet oxalate in rats which also found that the compound is not metabolised and is rapidly excreted as flufenacet oxalate in the faeces and urine.*
The general metabolic pathways in rodents and ruminants were found to be comparable; the findings in ruminants can therefore be extrapolated to pigs.
Consequently, for commodities of animal origin, it is desirable to include all metabolites containing the N-fluorophenyl-N-isopropyl moiety. The metabolism studies performed with flufenacet indicate a wide range of metabolites containing the N-fluorophenyl-N-isopropyl moiety are formed. These studies were not considered to be fully representative because in practice livestock will not be exposed to flufenacet but to a mixture of flufenacet oxalate, flufenacet sulfonic acid and flufenacet thioglycolate sulfoxide and other metabolites. Nevertheless, the additional metabolism studies with flufenacet oxalate indicate that flufenacet oxalate is the only relevant compound in all matrices and although it is not completely clear how the other plant metabolites will be metabolised in livestock, a residue definition including all metabolites with the N-fluorophenyl-N-isopropyl moiety is expected to be the most appropriate, both for enforcement and risk assessment.
Since log Po/w of flufenacet is 3.2 at 24 °C, which is only slightly above 3 (France, 1997); it was concluded in the peer review that the residue in commodities of animal origin is not fat soluble".

Summary of new animal metabolism studies
No new data are submitted with this application.

Conclusion on metabolism in livestock
Livestock metabolism data were evaluated on EU level for Annex I inclusion of Directive 91/414 and in the framework of the review of existing MRLs (EFSA, 2012). No new studies were submitted within the present dossier and the conclusions drawn in the Monograph (France 1997) and the EFSA Reasoned Opinion (EFSA 2012) are still valid.

zRMS comments:
Information given by the Applicant is acceptable and sufficient. zRMS agrees with the conclusion.
In EFSA Journal 2012;10(4):2689 it is stated that *Based on the uses reported by the RMS, significant intakes were calculated for ruminants, poultry and pigs. Metabolism studies on lactating goats and laying hens using fluorophenyl-U-14C, flufenacet oxalate and thiadiazole-2-14C labelled flufenacet were reported. In consideration*

[5] N-(4-fluorophenyl)-N-(2-hydroxy-1-methyl-ethyl)-2-(methylsulfinyl) acetamide
[6] N-(4-fluorophenyl)-N-(2-hydroxy-1-methyl-ethyl)-2-(methylsulfonyl) acetamide
[7] N-(4-fluorophenyl)-N-(1-methylethyl) acetamide
[8] Thiadone glucoronide: IUPAC name not reported

of the available animal metabolism studies the residue definition proposed for plants is also proposed for animal matrices.

Animal residues definitions:

- for monitoring and risk assessment: Sum of all compounds containing the N fluorophenyl-N-isopropyl moiety expressed as flufenacet equivalent (EFSA 2012, Regulation (EC) No 1127/2014).

7.2.2.6 Conclusion on the nature of residues in commodities of animal origin (KCA 6.7.1)

Table 7.2-8: Summary on the nature of residues in commodities of animal origin

	Endpoints
Animals covered	Lactating goats
	Laying hens
Time needed to reach a plateau concentration	[Fluorophenyl-UL-^{14}C] flufenacet & [Thiadiazole-2-^{14}C] flufenacet & [Fluorophenyl-UL-^{14}C] FOE oxalate: ≥3 days in milk; (Monograph, Annex B 6, France 1997); at a high overdose (> 100N)
	Fluorophenyl-UL-^{14}C] flufenacet & [Thiadiazole-2-^{14}C] flufenacet & [Fluorophenyl-UL-^{14}C] FOE oxalate: ≥ 3 days in eggs (Monograph, Annex B 6, France 1997); at a high overdose (> 100N)
Animal residue definition for monitoring	Flufenacet (sum of all compounds containing the N fluorophenyl-N-isopropyl moiety expressed as flufenacet equivalent), (Regulation n°1127/2014)
Animal residue definition for risk assessment	Flufenacet (sum of all compounds containing the N fluorophenyl-N-isopropyl moiety expressed as flufenacet equivalent), (Report of ECCO 73, 1999; EFSA, 2012)
Conversion factor	not needed (Monograph Annex B 6, France 1997; Report of ECCO 73, 1999; EFSA, 2012)
Metabolism in rat and ruminant similar	Yes (Monograph Annex B 6, France 1997; Report of ECCO 73, 1999; EFSA, 2012) The same metabolic reactions (or metabolic stability) were observed in rat, goat and hen when feeding the parent substance flufenacet or the main residue components of flufenacet in animal feed, i.e. FOE oxalate. Therefore, an extra metabolism study in pigs is unlikely to provide new information on the nature of residues in food of animal origin and is not required.
Fat soluble residue	No (Monograph Annex B 6, France 1997; Report of ECCO 73, 1999; EFSA, 2012) Since log Po/w of flufenacet is 3.2 at 24°C, which is only slightly above 3 (France, 1997); it was concluded in the peer review that the residue in commodities of animal origin is not fat soluble.

7.2.3 Magnitude of residues in plants (KCA 6.3)

7.2.3.1 Summary of European data and new data supporting the intended uses

The use patterns for FFA SC 508.8 G involve autumn uses (pre- or early post-emergence up to BBCH 13) at application rates up to 0.48 L/ha (corresponding to 244 g flufenacet/ha) in/on winter wheat (including triticale) and barley. The post-emergence treatment is considered to form the critical residue GAP.

In the Monograph (France, 1997) and in the EFSA Reasoned Opinion on existing MRLs (2012) the critical GAPs for flufenacet have been evaluated involving an application rate of 240 g a.s./ha. The critical GAP considered in the EU peer review was based on northern European data while the critical GAPs evaluated by EFSA (2012) concerned northern and southern Europe. The southern European data were identified to form the basis for MRL setting for wheat and barley. The data evaluated in the EU peer review and for setting MRLs according to Art 12 of Reg 396/2005 are considered to establish the risk envelope for the supported uses of FFA SC 508.8 G.

The Monograph (France 1997) reported 18 trials in small grain cereals, however, only from 17 trials grain and straw were sampled. In the EFSA reasoned opinion (EFSA 2012), 24 individual results are reported for wheat/barley grain. Six additional results are reported in the EFSA document, thus leading to an overall number of 23 trials. The six additional trials are submitted as new studies by the applicant in the framework of this application. It is not clear to the applicant why the same number is not reflected for straw. The supplementary studies were conducted using WG and SC formulations with mixtures of flufenacet and diflufenican. The detailed assessment of the studies considered as new studies is included in Appendix 2.

According to the ‘guideline on comparability, extrapolation, group tolerances and data requirements for setting MRLs’, SANTE/2019/12752 (01 January 2021, repealing SANCO 7525/VI/95 Rev. 10.3), extrapolation of residue data obtained from any of the crops (wheat, rye, barley, oats) for an active substance is possible if the use pattern involves treatments early in the growing season (last application before consumable parts of the crop have started to form). Therefore, combined data sets obtained from residue studies on wheat, barley and rye are considered adequate to support uses for FFA SC 508.8 G.

Table 7.2-4: Summary of EU reported and new data supporting the intended uses of FFA SC 508.8 G and conformity to existing MRL

Commodity	Source	Residue zone (N-EU, S-EU, EU, outside EU)	Evaluation GAP Residue levels (mg/kg) E = according to enforcement residue definition RA = according to risk assessment residue definition	STMR (mg/kg)	HR (mg/kg)	Unrounded OECD calculator MRL (mg/kg)	Current EU MRL (mg/kg)** Reg 1127/2014	MRL compliance
Small grain cereals (wheat, barley, rye) Grain	Monograph France, 1997 (RA-2054/93 RA-2008/94) (M-002284-01-2 + M-002280-01-2)	N-EU	GAP on which EU a.s. assessment is based: 1 x 0.24 kg a.s./ha, early post emergence up to BBCH 25. The pre-harvest interval covers the vegetation period of the crop until harvest. Outdoor *grain E/RA:* 17x<0.05	E/RA: <0.05	E/RA: <0.05	0.05	0.1 for wheat and barley (based on S-EU data) 0.05 for rye	Yes
	EFSA 2012 New trials (RA-2010/94 M-004451-01-2 RA-2144/00 M-058156-01-1)	N-EU	Trials GAP: 1 x 0.24 kg a.s./ha, BBCH 13-25, The pre-harvest interval covers the vegetation period of the crop until harvest. Outdoor *grain E/RA:* 6x<0.05	E/RA: <0.05	E/RA: <0.05	0.05		Yes
	EFSA 2012 (= Overall supporting data for cGAP*)	N-EU	Combined dataset on barley (8), rye (3) and wheat (13) early post-emergence up to BBCH 25; supporting the GAPs for all small grain cereals (except rice). *grain E/RA:* 23x<0.05	E/RA: <0.05	E/RA: <0.05	0.05	0.1 (based on S-EU data)	Yes
Small grain cereals (wheat, barley, rye) Straw	Monograph France, 1997 (RA-2054/93 RA-2008/94) (M-002284-01-2 + M-002280-01-2)	N-EU	GAP on which MRL/EU a.s. assessment is based: 1 x 0.24 kg a.s./ha, early post emergence up to BBCH 25. The pre-harvest interval covers the vegetation period of the crop until harvest. Outdoor *straw E/RA*: 17x<0.1	E/RA: <0.1	E/RA: <0.1		N/A	N/A
	EFSA 2012 New trials (RA-2010/94 M-004451-01-2 RA-2144/00 M-058156-01-1)	N-EU	Trials GAP: 1 x 0.24 kg a.s./ha, BBCH 13-25, The pre-harvest interval covers the vegetation period of the crop until harvest. Outdoor *straw E/RA:* 6x<0.1	E/RA: <0.1	E/RA: <0.1		N/A	N/A
	EFSA, 2012 (= overall supporting data for cGAP)*	N-EU	Combined dataset on barley (8), rye (3) and wheat (13) early post-emergence up to BBCH 25; supporting the GAPs for all small grain cereals (except rice). *straw E/RA*: 23x <0.1	E/RA <0.1	E/RA <0.1		N/A	N/A

*In the EFSA Reasoned Opinion (2012) erroneously 24 results for grain were reported. However, for one trial only green material could be sampled reducing the overall number of results for grain and straw to 23. For straw, 18 trials were reported by EFSA (2012) which were included in the Monograph (<0.1 mg/kg). For the same reason the actual number was 17.
N/A = not applicable
** Source of EU MRL: Regulation (EC) 1127/2014

7.2.3.2 Conclusion on the magnitude of residues in plants

The intended uses on wheat (including triticale) and barley are adequately supported by the available data and considered acceptable.
The GAPs for FFA SC 508.8 G are considered to be covered by the critical EU GAPs for flufenacet establishing the risk envelope.

The trials reviewed in the Monograph (France, 1997) of flufenacet were performed using a WG formulation which is known to produce comparable residue levels to SC formulations. The supplementary trials for the northern zone were conducted with mixtures of flufenacet and diflufenican as WG and SC formulated products. Both formulation types can be used interchangeably to support either of the formulations.

According to the 'guideline on comparability, extrapolation, group tolerances and data requirements for setting MRLs', SANTE/2019/12752 (01 January 2021 repealing SANCO/7525/VI/95 rev 10.3), extrapolation of residue data obtained from any of the crops (wheat, rye, barley, oats) for an active substance is possible if the use pattern involves treatments early in the growing season (last application before consumable parts of the crop have started to form). Therefore, combined data sets obtained from residue studies on wheat, rye and barley are adequate to support uses for FFA SC 508.8 G.

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

zRMS comments:
Cereals
Wheat, rye and barley are the major crops in northern Europe (Technical Guidelines SANTE/2019/12752). A minimum of eight independent trials representative of the proposed growing area for outdoor are required.
According to the SANTE/2019/12752 the residue trials on wheat or barley may be extrapolated to rye, when application is done before or after the forming of the edible part in cereals.

Regarding the magnitude of residues in cereals crops, a sufficient number of supervised residue trials is available to support the uses. 17 residue trials on cereals are available (France 1997). The six additional trials are submitted as new studies by the applicant in the framework of this application. The supplementary studies were conducted using WG and SC formulations with mixtures of flufenacet and diflufenican.

The trials were performed within the GAP: 1 x 0.24 kg a.s./ha, BBCH 13-25, the pre-harvest interval covers the vegetation period of the crop until harvest and therefore can be used to support the registration of Flufenacet SC 508.8 G. Grain and straw samples were taken at normal harvest.

The residues of flufenacet (sum of all compounds containing the N fluorophenyl-N-isopropyl moiety expressed as flufenacet) in wheat, raye and barley grain at harvest were <0.05 mg/kg.

Available results show that the in force MRL on wheat and barley of 0.1 mg/kg and on rye of 0.05* mg/kg (Reg. (EU) No 1127/2014) will not be exceeded.
Therefore, sufficient residue trials are available to support the intended GAP uses on cereals (wheat, triticale, barley, rye, durum wheat and spelt).

Maximum storage period was 224 days (7.5 months) for grain and straw and 237 days (~8 months) for whole plant.
According to the OECD 506 wheat grain and straw belongs to dry commodity and whole plant belongs to high water commodity.
The stability data cover the storage storage period of the field samples: grain, straw and whole plant of cereals.

No further data are required to support the proposed uses on wheat, triticale, barley, rye, durum wheat and spelt.

7.2.4 Magnitude of residues in livestock

7.2.4.1 Dietary burden calculation

Evaluation in the EFSA Reasoned Opinion on the review of the existing maximum residue levels (MRLs) for flufenacet according to Art 12 of Regulation (EC) No 396/2005 (EFSA Journal 2012;10(4):2689):

Based on the uses reported by the RMS, significant intakes were calculated for ruminants, poultry and pigs using the feedstuff table reported in the EU guideline 7031/VI/95 rev.4. EFSA calculated the dietary burden based on all authorized uses for crops that might be fed to livestock (potatoes, sunflower seed, soya bean, barley, maize, rye, wheat) and the corresponding by-products which may be used as feeding items (cereal bran, oilseed meals). The median and maximum dietary burdens were calculated for different groups of livestock using the agreed European methodology. The input values for all relevant commodities are summarised in Table 7.4-10 (corresponds to Table 3-4 of the Reasoned Opinion). For cereal bran and sunflower seed meal default processing factors of 8 and 2, respectively, have been included in the calculation in order to consider potential concentration of residues in these commodities. The default processing factor for soya bean has not been applied as processing studies evaluated in the Monograph show that residues of flufenacet are below the LOQ in both the RACs and the processed products and no concentration of flufenacet is observed. The results of dietary burden calculation as described by EFSA are presented in Table 7.4-11 (corresponds to Table 3-5 of the Reasoned Opinion).

In addition, the dietary burden is calculated using the dietary burden calculation spreadsheet animal model 2017. According to the new calculation sheet uses on cereals are – by default – understood as 'uses on cereals for grain production' and therefore, feeding items from immature cereals are disregarded for the calculation. Relative to small grain cereals only residues in grains (median) and straw (HR) from cereals are considered for the animal dietary burden calculation. Input values and results of the dietary burden calculation according to the animal model 2017 are presented in Table 7.2-12 and 7.2-13.

Dietary burdens for all groups of livestock were found to exceed the trigger value of 0.004 mg/kg bw/d as set under Reg. (EU) No 283/2013.

Table 7.2-10: EU methodology (EFSA Reasoned Opinion , 2012): Input values for the dietary burden calculation (considering the uses authorised in the country of the zRMS/authorized within the zone/evaluated in Art. 12 procedure and the uses under consideration)

Feed Commodity	Median dietary burden		Maximum dietary burden	
	Input value (mg/kg)	Comment	Input value (mg/kg)	Comment
Enforcement residue definition = Risk assessment residue definition: Sum of all compounds containing the N fluorophenyl-N-isopropyl moiety expressed as flufenacet equivalent (EFSA Journal 2012;10(4):2689)				
Cereal grain (small)	0.05	Median residue	0.05	Median residue
Maize grain	0.05	Median residue	0.05	Median residue
Cereal bran	0.4	Median residue × PF (8)	0.4	Median residue × PF (8)
Cereal straw	0.1	Median residue	0.11	Highest residue
Potatoes	0.05	Median residue	0.11	Highest residue
Sunflower seed	0.05	Median residue	0.05	Median residue
Sunflower seed meal	0.1	Median residue × PF (2)	0.1	Median residue × PF (2)
Soya bean	0.05	Median residue	0.05	Median residue
Soya bean meal	0.05	Median residue	0.05	Median residue

PF: Processing Factor

Table 7.2-11: Results of the dietary burden calculation (EFSA Reasoned Opinion , 2012)

	Median dietary burden (mg/kg bw/d)	Maximum dietary burden (mg/kg bw/d)	Highest contributing commodity	Max dietary burden (mg/kg DM)	Trigger exceeded(Y/N)
Enforcement residue definition = Risk assessment residue definition: Sum of all compounds containing the N fluorophenyl-N-isopropyl moiety expressed as flufenacet equivalent (EFSA Journal 2012;10(4):2689)					
Dairy ruminants	0.0090	0.0135	Potatoes	0.3704	Y
Meat ruminants	0.0134	0.0238	Potatoes	0.5555	Y
Poultry	0.0092	0.0143	Wheat bran	0.2257	Y
Pigs	0.0125	0.0221	Potatoes	0.5531	Y

Table 7.2-12: Animal model 2017: Input values for the dietary burden calculation

1 - Forages		**STMR**	**HR**	**PF**	**CF**	**Default PF**	**STMR by-P**	**HR by-P**	**Souce/ remark**
Barley	straw	0.10	0.11	-	-	-	0.10	0.11	EFSA 2012
Corn. field	stover (fodder)	0.05	0.05	-	-	-	0.05	0.05	EFSA 2012
Corn. pop	stover (fodder)	0.05	0.05	-	-	-	0.05	0.05	Default
Oat	straw	0.10	0.11	-	-	-	0.10	0.11	EFSA 2012
Rye	straw	0.10	0.11	-	-	-	0.10	0.11	EFSA 2012
Triticale	straw	0.10	0.11	-	-	-	0.10	0.11	EFSA 2012
Wheat	straw	0.10	0.11	-	-	-	0.10	0.11	EFSA 2012
2 - Roots & Tubers		**STMR**	**HR**	**-**	**CF**	**-**	**STMR**	**HR**	
Potato	culls	0.05	0.11				0.05	0.11	EFSA 2012
3 - Cereal grains/Crop seeds		**STMR**	**Post-h?**	**HR**	**CF**	**-**	**STMR**	**HR**	
Barley	grain	0.05	N	-	-	-	0.05		EFSA 2012
Corn. field (Maize)	grain	0.05	N	-	-	-	0.05		EFSA 2012
Corn. pop	grain	0.05	N	-	-	-	0.05		Default -
Oat	grain	0.05	N	-	-	-	0.05		EFSA 2012
Rye	grain	0.05	N	-	-	-	0.05		EFSA 2012
Soybean	seed	0.05	N	-	-	-	0.05		EFSA 2012
Triticale	grain	0.05	N	-	-	-	0.05		EFSA 2012
Wheat	grain	0.05	N	-	-	-	0.05		EFSA 2012
4 - By-products		**STMR**	**-**	**PF**	**CF**	**Default PF**	**STMR by-P**	**-**	
Brewer's grain	dried	0.05			-	3.3	0.17		Default in template if entry for barley grain
Corn. field	milled by-pdts	0.05			-	1	0.05		Default in template if entry for corn grain
Corn. field	hominy meal	0.05			-	6	0.30		
Corn. field	gluten feed	0.05			-	2.5	0.13		
Corn. field	gluten. meal	0.05			-	1	0.05		

Distiller's grain	dried	0.05			-	3.3	0.17		Default in template
Potato	process waste	0.05			-	20	1.0		Default in template
Potato	dried pulp	0.05				38	1.9		Default in template
Soybean	meal	0.05		1.0		1.3	0.05		EFSA 2012
Soybean	hulls	0.05				13	0.65		Default in template
Sunflower	meal	0.05				2	0.10		Default in template
Wheat gluten	meal	0.05				1.8	0.05		Default in template
Wheat	milled by-pdts	0.05				7	0.22		Default in template

Table 7.2-13: Results of the dietary burden calculation (Animal model 2017)

Relevant groups	**Dietary burden expressed in**				**Most critical diet (a)**	**Most critical commodity (b)**		Trigger exceeded (Yes/ No)
	mg/kg bw per day		mg/kg DM					0.004
	Median	Maximum	Median	Maximum				mg/kg bw
Cattle (all diets)	0.101	0.104	3.44	3.54	Dairy cattle	Potato	process waste	Yes
Cattle (dairy only)	0.101	0.104	2.61	2.71	Dairy cattle	Potato	process waste	Yes
Sheep (all diets)	0.115	0.118	3.44	3.54	Ram/Ewe	Potato	process waste	Yes
Sheep (ewe only)	0.115	0.118	3.44	3.54	Ram/Ewe	Potato	process waste	Yes
Swine (all diets)	0.042	0.045	1.81	1.96	Swine (breeding)	Potato	process waste	Yes
Poultry (all diets)	0.035	0.037	0.50	0.53	Poultry broiler	Potato	dried pulp	Yes
Poultry (layer only)	0.027	0.029	0.40	0.43	Poultry layer	Potato	dried pulp	Yes

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

zRMS comments:
The dietary burdens calculated for all animal groups were found to exceed the trigger value of 0.004 mg/kg bw/d (0.1 mg/kg DM). Therefore, further investigation of residues is therefore required in all commodities of animal origin.

7.2.4.2 Livestock feeding studies (KCA 6.4.1-6.4.3)

Available data

Evaluation in the EU peer review (Monograph (Annex B 6), France 1997)

In the EU peer review the dietary burden for livestock was assessed based on uses in cereals, corn, sunflower and soybean as relevant feeding items. Since i) no residues above the LOQ (0.05 mg/kg in green material of plants (at forage stage), cereal grain, sunflower and soybean seed, maize kernel and 0.1 mg/kg in straw) were determined and ii) the data from metabolism studies do not indicate a significant transfer from residues in feeding items to food of animal origin, it was concluded in the Monograph that livestock feeding studies are not required. However, a cow feeding study conducted for the US was submitted and has been evaluated. In this study, cows were administered highly exaggerated doses of FOE5043-oxalate which constitutes the main plant metabolite (M-002268-01-1). The results show that even at an exaggerated dose of 7.8 ppm (1N dose in the study) no flufenacet derived residues

can be expected in tissues or products of ruminants which have been fed flufenacet treated crops.

In the Report of ECCO 73, Annex 2, Complete List of Endpoints (1999) it is concluded that no residues are anticipated in animal tissues or products

Evaluation of the magnitude of residues in livestock (EFSA, 2012):
"On the basis of the animal metabolism studies it is concluded that, after exposure to the maximum dietary burden (about 200 times lower than the dose level in the metabolism studies, [5 mg/kg bw/d]*), residue levels in livestock commodities are expected to remain below the enforcement LOQ of 0.01 mg/kg in milk, 0.02 mg/kg in liver and 0.05 mg/kg in fat, eggs, kidney and muscle. Hence, no livestock feeding study is needed; MRLs and risk assessment values for the relevant commodities in ruminants, pigs and poultry can be established at the LOQ level."*

The cow feeding study conducted for the US and evaluated in the EU peer review used highly exaggerated dose levels of 7.8, 24.7 and 82.4 ppm. The lowest dose rate corresponds to 0.22 mg/kg bw/day. This dose corresponds to 1.9N of the anticipated maximum dietary burden ruminants (sheep) (Table 7.2-13), calculated using the spreadsheet for animal model 2017.
The results show that even at this exaggerated rate no flufenacet-derived residues can be expected in tissues or products of animals which have been fed flufenacet treated crops.

It has to be noted that high default processing factors have been used in the calculation, in particular for potatoes. Processing studies show that these factors are a high overestimate for flufenacet (PF = <0.6 for potato waste and 3.5 for dried pulp). For wheat, processing factors for meal and milled by-products are also significantly less than the default value as evaluated in the DRAR, List of endpoints (Poland 2017).

The results of the already evaluated feeding study on dairy cows are presented in the table below. Data for ruminants can also be considered applicable to pigs.

No new data on the magnitude of residues in livestock were submitted in the framework of this application.

Table 7.2-14: Overview of the values derived from livestock feeding studies

Commodity	Dietary burden		Results of the livestock feeding study						Median residue (mg/kg)(b)	Highest residue (mg/kg)(c)	Calculated MRL (mg/kg) Reg. (EU) 1127/2014	CF for RA(d)
	Med. (mg/kg bw/d)	Max. (mg/kg bw/d)	Dose Level (mg/kg bw/d)(a)	No	Result for enforcement		Result for RA					
					Mean h) (mg/kg)	Max. (mg/kg)	Mean h) (mg/kg)	Max. (mg/kg)				
EU data (France, 1997; EFSA, 2012); (Duah, 1995, M-002268-01-1)												
Enforcement residue definition = Residue definition for risk assessment::Flufenacet (sum of all compounds containing the N fluorophenyl-N-isopropyl moiety expressed as flufenacet equivalent)												
Ruminant meat	0.115 g)	0.118 g)	0.22	3	<0.05	<0.05	<0.05	<0.05	<0.05	<0.05	0.05*	1
			0.71	3	<0.05	<0.05	<0.05	<0.05				
			2.43	3	0.075	0.090	0.075	0.090				
Ruminant fat			0.22	3	n.a.	n.a.	n.a.	n.a.	<0.05	<0.05	0.05*	
			0.71	3	<0.05	<0.05	<0.05	<0.05				
			2.43	3	0.080	0.103	0.080	0.103				
Ruminant liver			0.22	3	<0.05	<0.05	<0.05	<0.05	<0.05	<0.05	0.02*	
			0.71	3	0.053	0.056	0.053	0.056				
			2.43	3	0.150	0.183	0.150	0.183				
Ruminant kidney			0.22	3	0.053	0.057	0.053	0.057	<0.05	<0.05	0.05*	
			0.71	3	0.179	0.306	0.179	0.306				
			2.43	3	0.531	0.629	0.531	0.629				
Milk			0.22	3	n.a.	N/A	n.a.	n.a.	<0.01	N/A	0.01*	
			0.71	3	<0.01 (f)	N/A	<0.01 (f)	<0.01				
			2.43	3	<0.01 (e)	N/A	<0.01 (e)	0.01				

N/A: Not applicable – only the mean values are considered for calculating MRLs in milk.
n.a.: Not analysed due to residues < LOQ in the higher dose level
(*): Indicates that the MRL is set at the limit of analytical quantification.
(F): MRL is expressed as mg/kg of fat contained in the whole product.
(a): Based on an average animal weight of 468, 429 and 395 kg for the low, mid and high dose group receiving 104.6, 306.4 or 959.1 mg/day (as capsule) resulting in dose levels of 0.22, 0.71 and 2.43 mg/kg bw/day, respectively.
(b): Median residue value according to the enforcement residue definition, derived by interpolation/extrapolation from the feeding study for the median dietary burden (FAO, 2009).
(c): Highest residue value (tissues, eggs) or mean residue value (milk) according to the enforcement residue definition, derived by interpolation/extrapolation of the maximum dietary burden between the relevant feeding groups of the study (FAO, 2009).
(d): The median conversion factor for enforcement to risk assessment.

(e): Mean residue level from day 7 until day 29 (3 cows, 5 sampling days). Residue of 0.01 mg/kg was for a day 7 sample dropping to < 0.01 mg/kg at the later sampling intervals
(f): Mean residue level from day 29. Since the residues were below the LOQ at day 29 and at the highest dosing level, no residues before day 29 could be expected.
(g): Dietary burden for sheep (all diets) – highest dietary burden
(h): Mean values calculated taking into account all animals and all replicates per feeding level.

The highest poultry exposure is calculated for poultry (all diets) (0.037 mg/kg bw/d); which is 100 times less than the dose level in the metabolism studies, [5 mg/kg bw/d].
The results already show that residue levels in poultry commodities are expected to remain below the enforcement LOQ of 0.02 mg/kg in liver and 0.05 mg/kg in fat, eggs, kidney and muscle.

Conclusion on feeding studies

The dietary burden arising from the supported uses on small grain cereals has been evaluated by EFSA (2012) for use pattern at a dose rate of 240 g as/ha.

The new mode of calculation based on the OECD feedstuff tables and using the calculation spreadsheet "animal model 2017" modifies the theoretical maximum daily intake for farm animals. However, the dietary burden for ruminants is still less than the lowest dose level tested in the feeding study – even when using the worse case default processing factors. The results show that residues are not anticipated in animal tissues and milk. The conclusions drawn in the EFSA Reasoned Opinion (EFSA, 2012) are still valid and no new data are required.

There is no risk that the MRLs set at the LOQ level in Reg. (EC) 1127/2014 will be exceeded.

zRMS comments:
Information given by the Applicant is sufficient and acceptable. zRMS agrees with above conclusion.
There is no risk for MRLs to be exceeded in animal commodities.
No further data are requred.

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

Based on European residue data evaluated in the EU peer review, processing studies were not considered necessary for all the evaluated crops since residue levels for all edible commodities were below the threshold of 0.1 mg/kg (France 1997; EFSA 2012).

However, in the EU peer review processing studies on maize and soybean were evaluated which were conducted according to US requirements and at exaggerated rates. For maize it could be shown that although residues in the raw agricultural commodities were still below the validated LOQ of 0.05 mg/kg no concentration of residues in any of the tested commodities occurs. The tested procedures included wet and dry milling (tested commodities starch, crude oil and refined-bleached-deodorized oil for wet milling and germs, grits, meal, flour, crude oil and refined-bleached-deodorized oil for dry milling). In soybean at the 8N rate, residues were obtained in seed. It was demonstrated that no concentration occurs in the investigated commodities meal, hulls, crude oil and refined bleached deodorized oil (France 1997; Report of ECCO 73; LoEP, 1999, EFSA, 2012; Grace, 1995, M-002412-01-1 and Grace, 1995, M-002420-01-1).

Since processing studies on these crops are not relevant to this submission they are not summarized in detail in the present document. Also, due to the low residue levels present in small cereal grain processing studies on wheat or barley are not reported within the present dossier.

The processing studies evaluated on EU level are summarized in the table below.

Table 7.2-15: Overview of the processing studies evaluated in the EU peer review

Processed commodity	Number of studies	Median PF *	Median CF **	Comments	Reference
EU data					
Enforcement residue definition = Risk assessment residue definition: *The sum of all compounds containing the N-fluorophenyl-N-isopropyl moiety expressed as flufenacet equivalent*					
Wet milling (maize)					France, Monograph (Annex B 6),1997 Report of ECCO 73; LoEP, 1999, EFSA, 2012 M-002412-01-1
corn, starch	1	<1	--		
corn, crude oil	1	<1	--		
corn, oil refined-bleached-deodorized	1	<1	--		
Dry milling (maize)					
corn, grits	1	1.6†	--		
corn, meal	1	1	--		
corn, flour	1	<1	--		

Processed commodity	Number of studies	Median PF *	Median CF **	Comments	Reference
corn, crude oil	1	<1	--		
corn, oil refined-bleached deodorized	1	<1	--		
Soybean					France, Monograph (Annex B 6),1997 Report of ECCO 73; LoEP, 1999, EFSA, 2012 M-002420-01-1
soybean, meal	1	<1 [0.8] ††	--		
soybean, hulls	1	<1 [0.66] ††	--		
soybean, crude oil	1	<1 [0.1] ††	--		
soybean, refined bleached deodorised oil	1	<1 [<0.1] ††	--		

† corn grits were not considered in the list of endpoints provided by ECCO 73. Residues were below the validated level.
†† Values in brackets were re-calculated from study results.
* The median processing factor is obtained by calculating the median of the individual processing factors of each processing study.
** The median conversion factor for enforcement to risk assessment is obtained by calculating the median of the individual conversion factors of each processing study.

No new data were submitted in the framework of this application since residues in small cereal grain were always below the threshold of 0.1 mg/kg.

Table 7.2-56: Overview of the available processing studies

Processed commodity	Number of studies	Median PF	Median CF	Comments	Reference
EU data					
No processing data were evaluated for small grain cereals					
New data					
No new data are submitted with this submission					

7.2.5.1 Conclusion on processing studies

Since the threshold of 0.1 g/kg is not exceeded in all the residue trials on small grain cereals and the ADI or ARfD is not exhausted by more than 10% studies on the magnitude of the residues in processed cereal grain are not necessary and no new data are included in this submission.

zRMS comments:
As residues of flufenacet exceeding 0.1 mg/kg are not expected in the treated crops, there is no need to conduct processing studies.
No further data are required.

7.2.6 Magnitude of residues in representative succeeding crops

The crop under consideration can be grown in rotation. According to the evaluation in the Monograph (1997) and by EFSA (2012), in principle, no field rotational crop trials with flufenacet are deemed necessary to support the critical GAP of flufenacet in small grain cereals (up to 0.24 kg a.s./ha) or any of the GAPs evaluated in the frame of the Art 12 review which involves application rates in the range of 0.15 – 0.6 kg a.s./ha .
However, field rotational crop studies were conducted at four different locations in northern Europe on request of UK CRD to investigate the residues in treated winter cereals which are sown following the preceding crop potatoes which also received an application of a flufenacet containing product within the same calendar year. The potato crop can be considered as a representative for any possible spring crop that might be grown as a preceding crop to winter cereals.

This study has already been evaluated by UK CRD in support of flufenacet containing products to be used in cereals and was considered appropriate. The study was also submitted in France and was evaluated in the DRAR (Poland 2017). The study is summarised hereafter.

7.2.6.1 Field rotational crop studies (KCA 6.6.2)

Available data
A new study for residues in succeeding crops has been submitted by the applicant in the framework of this application. This study is summarized in the table below. The detailed results are presented in Appendix 2.

Table 7.2-67: Summary of available studies in field rotational crops

Primary crop	Rate (kg a.s./ha) (GS at application or PHI)	Residue levels in succeeding crops				
		Succeeding crop group	Succeeding crop	Sowing intervals (DAT)	Residue	Reference / Remarks
EU data						
Field rotational crop studies were not considered necessary in the EU peer review						
New data						
Potato	Preceding crop potato: 0.6 kg a.s./ha, BBCH 00 Succeeding crop winter cereals: 0.24 kg a.s./ha, BBCH 12-21, not later than November	Cereals	Wheat	145, 133	grain: <0.01; <0.01 straw: <0.1; <0.1 green material: <0.05, <0.05	Melrose, I.; Erler, S.; 2008; M-306269-01-1, Appendix 2
		Cereals	Barley	146, 158	grain: <0.01; <0.01 straw: <0.1; <0.1 green material: <0.05, <0.05	

Four field residue trials were conducted in northern Europe (the United Kingdom, Germany and France) in order to determine the magnitude of flufenacet derived residues in/on cereals (winter wheat and winter barley) grown as succeeding crops following the preceding crop potatoes. Potatoes and cereals were both treated with one spray application of a flufenacet containing product (at the maximum rates of 0.6 kg a.s./ha for potatoes and 0.24 kg a.s./ha for cereals).
No residues were apparent in green material of cereals collected at growth stage BBCH 29 – 30 or grain and straw sampled at harvest (BBCH 89). The findings show that treatment of the preceding crop with flufenacet at the maximum registered field rate does not impact residue levels in/on cereals grown as succeeding crops. No uptake from the soil into the following crop has been observed. This scenario reflects a worst-case rotation with regard to potential uptake from soil. Shorter plant back intervals (e.g. 30 days) were not investigated since the time for sowing spring cereals has already passed in case of failure of other spring crops (i.e. potatoes, maize) that may have received a treatment with flufenacet. The absence of residues in cereals when sown as following crop is considered to be representative for all other rotational crop situations where the preceding crop is treated with an application rate up to 0.6 kg a.s./ha.
The need to consider rotational crop scenarios for MRL setting does not arise.

Conclusion on rotational crops studies
The highest supported application rate with FFA SC 508.8 G in small grain cereals is comparable to the application rate investigated in the field rotational crop studies (0.244 vs. 0.240 kg a.s./ha). Therefore, the use supported in the present dossier is covered by the reported data. The rotational crop study demonstrated that treatment of the preceding crop with a flufenacet containing product at the maximum field rate of 0.6 kg a.s./ha does not result in residues in/on cereals when grown as succeeding crops.

See EFSA, 2012:

In the DAR (Monograph) it was already concluded that after use of flufenacet according to the GAPs, no significant residues are expected in leafy or root crops grown in rotation with the primary crops. According to the confined rotational crop metabolism studies the only exception to this would be wheat. However an assessment of the results from field trials in cereals and maize including pre-emergence applications shows that no residues are detected in any trial, except in green material sampled within 40 days of application and therefore it was concluded in the DAR that the high residue levels seen in wheat were a consequence of the experimental design and do not reflect normal practice. Considering also, that the application rate of flufenacet within the EU ranges between 0.15-0.6 kg a.s./ha (which covers the highest intended application rate = 0.244 kg sa/ha) it can be concluded that flufenacet residue levels in rotational commodities are not expected to exceed the LOQ of the analytical method (0.05 mg/kg) mg/kg, provided flufenacet is applied in compliance with the intended GAPs.

This conclusion also applies to the use evaluated in this dossier.

zRMS comments:
Information given by the Applicant is sufficient and acceptable.
Residue levels in rotational commodities are not expected to exceed 0.01 mg/kg after the use of Flufenacet SC 508.8 G (i.e. 244 g a.s./ha) in compliance with the proposed GAPs.
Waiting periods for avoiding residues in succeeding crops are not required.
No further data are requred.

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

The available data for the active substance sufficiently addresses aspects of the residue situation that might arise from the use of FFA SC 508.8 G. Therefore, other special studies are not needed.

Wheat and barley are not considered as melliferous crops (SANTE/11956/2016 rev. 9), therefore investigation of residue levels in honey is not necessary.

zRMS comments:
Information given by the Applicant is sufficient and acceptable.
No further data are requred.

7.2.8 Estimation of exposure through diet and other means (KCA 6.9)

Toxicological reference values relevant for dietary risk assessment are reported in the summary of the evaluation (see 7.1.2).

7.2.8.1 Input values for the consumer risk assessment

In order to evaluate the potential chronic and acute exposure to flufenacet residues through the diet, the respective International Estimated Daily Intakes (IEDI) and International Estimated Short-Term Intakes (IESTI) were estimated using the EFSA PRIMo model (revision 3.1).

The calculation of the IEDI was performed based on the median residue values from all the authorised uses of flufenacet and reported in the framework of the MRL review (EFSA 2012 - Table 4-1). The median residues calculated from the supervised field residue trials submitted in this dRR to support the uses in small grain cereals do not result in any modification. For calculation the refined mode was used including those food commodities for which a GAP is authorised.

The input value for the acute consumer exposure calculation for the crops under consideration (wheat, barley) is also included in the table below. The acute exposure calculation is performed taking into account the highest residue level (0.05 mg/kg) for small cereal grain and the MRLs for commodities of animal origin (MRLs corresponding to the LOQs of the analytical method).

The input values are presented in the table below.

Table 7.2-78: Input values for the consumer risk assessment

Commodity	Chronic risk assessment		Acute risk assessment	
	Input value (mg/kg)	Comment	Input value (mg/kg)	Comment
Risk assessment residue definition: the sum of all compounds containing the N-fluorophenyl-N-isopropyl moiety expressed as flufenacet equivalent				
Strawberries	0.05	STMR (EFSA, 2012)	-	-
Blueberries, cranberries, currants, gooseberries	0.05	STMR (EFSA, 2012)	-	-
Potatoes	0.05	STMR (EFSA, 2012)	-	-
Celeriac	0.02	STMR (EFSA, 2012)	-	-
Onions	0.02	STMR (EFSA, 2012)	-	-
Tomatoes, cucumbers, courgettes, pumpkins	0.05	STMR (EFSA, 2012)	-	-
Sweetcorn	0.05	STMR (EFSA, 2012)	-	-
Lettuce, scarole (broad-leaf endive)	0.01	STMR (EFSA, 2012)	-	-
Beans (with pods)	0.05	STMR (EFSA, 2012)	-	-
Asparagus	0.05	STMR (EFSA, 2012)	-	-
Leeks	0.01	STMR (EFSA, 2012)	-	-
Sunflower seed	0.05	STMR (EFSA, 2012)	-	-
Soybean	0.05	STMR (EFSA, 2012)	-	-
Barley, wheat	0.05	STMR (EFSA, 2012)	0.05	HR (EFSA, 2012)
Oats, rye	0.05	STMR (EFSA, 2012)	-	-
Rice	0.05	STMR (EFSA, 2012)	-	-
Maize	0.05	STMR (EFSA, 2012)	-	-
Ruminant: muscle, fat, kidney	0.05*	MRL (Reg. (EC) 1127/2014)	0.05*	MRL (Reg. (EC) 1127/2014)
Ruminant: liver	0.02*	MRL (Reg. (EC) 1127/2014)	0.02*	MRL (Reg. (EC) 1127/2014)
Ruminant: milk	0.01*	MRL (Reg. (EC) 1127/2014)	0.01*	MRL (Reg. (EC) 1127/2014)
Birds' eggs	0.05*	MRL (Reg. (EC) 1127/2014)	0.05*	MRL (Reg. (EC) 1127/2014)
Honey	0.05*	MRL (default)		

(*): Indicates that the MRL is set at the limit of analytical quantification.

Chronic consumer exposure resulting from all the authorized uses of flufenacet and reported in the framework of the MRL review **(**EFSA 2012**)** was calculated using the EFSA PRIMo model (rev 3.1). The total calculated intake values accounted up to 35% of the ADI (NL toddler). No long-term consumer intake concerns were identified for any of the European diets.

The acute consumer exposure to flufenacet was calculated for small grain cereals using the EFSA PRIMo model (rev 3.1). Taking into account the ARfD of 0.017 mg/kg, the highest IESTI was estimated 4% of ARfD for children and 2% of ARfD for adults for wheat.

Outputs of the calculation sheets are reported in Appendix 3.

7.2.8.2 Conclusion on consumer risk assessment

Extensive calculation sheets for IEDI are presented in Appendix 3.
EFSA PRIMo rev 3.1: The IEDI estimates for the various diets were found at 35% of ADI at maximum (NL toddler). For this diet, milk (cattle) was the highest contributor to the residue intake, representing 12% of ADI.
The highest IESTI of flufenacet was 7% for children (consumption of milk, cattle) and 3% of ARfD for adults (consumption of poultry muscle) based on the MRL (LOQ of the analytical method). For the uses under consideration the IESTI was highest for wheat (4% ARfD, based on children diet).

Table 7.2-89: Consumer risk assessment

TMDI (% ADI) according to EFSA PRIMo rev.3.1	Not calculated
IEDI (% ADI) according to EFSA PRIMo ††rev.3.1	Max 35% ADI
IESTI (% ARfD) according to EFSA PRIMo* rev.3.1	Commodities of animal origin: 7% for children (consumption of milk, cattle) 3% of ARfD for adults (consumption of poultry muscle) based on the MRL (LOQ of the analytical method) Wheat: 4% (based on children diet) 2% (based on adult diet) 4% (wheat / milling (flour) for children's diet Barley: 2% (based on children diet) 1% (based on adult diet) 1% barley cooked (children's diet) 2% beer for adult's diet

* include raw and processed commodities if both values are required for PRIMo
† Input values are entered into the calculation spreadsheet at the lowest level of aggregation.
†† Chronic consumer exposure resulting from all the authorized uses of flufenacet and reported in the framework of the MRL review (EFSA Journal 2012; 10(4):2689) was calculated

The proposed uses of flufenacet in the formulation FFA SC 508.8 G do not represent unacceptable acute and chronic risks for the consumer.

7.3 Combined exposure and risk assessment

From a scientific point of view it is regarded necessary to take into account potential combination effects. However, the evaluation of cumulative or synergistic effects as requested by Art. 4 (3b) of Regulation (EC) No. 1107/2009 should only be performed when harmonised "scientific methods accepted by the Authority to assess such effects are available."
Currently, no EU-harmonized guidance is available on the risk assessment of combined exposure to multiple active substances; this approach is not mandatory at EU level.

Concerning the assessment of the product any evaluation of combined exposure is not relevant as the product contains only one active substance.

7.3.1 Acute consumer risk assessment from combined exposure

Refer to 7.3

7.3.2 Chronic consumer risk assessment from combined exposure

The uses under consideration provide only a minor contribution to the overall chronic exposure of consumers to pesticide residues. The issue requires a more universal consideration and possibly the generic usage of monitoring data. A harmonised approach is not yet available, and currently no specific consideration is warranted in the scope of this evaluation.

zRMS comments:

zRMS agrees with the conclusion.
The proposed uses of Flufenacet SC 508.8 G (i.e. 244 g a.s./ha) do not represent unacceptable acute and chronic risks for the consumer.

7.4 References

Flufenacet

EC (European Commission), 2003. Review report for the active substance flufenacet. Finalised in the Standing Committee on the Food Chain and Animal Health at its meeting on 4 July 2003 in view of the inclusion of flufenacet in Annex I of Council Directive 91/414/EEC. SANCO/7469/VI/98-Final, 3 July 2003.

France, 1997. Draft assessment report (monograph) on the active substance flufenacet prepared by the rapporteur Member State France in the framework of Council Directive 91/414/EEC, August 1997.

Report of ECCO, 1999. Complete List of Endpoints: flufenacet. Annex 2, p. 37-57.

France, 2000. Draft assessment report on the active substance flufenacet prepared by the rapporteur Member State France in the framework of Council Directive 91/414/EEC, February 2000.

EC (European Commission), 2004. Review report for the active substance flufenacet. Finalised in the Standing Committee on the Food Chain and Animal Health at its meeting on 13 February 2004 in view of the inclusion of clomazone in Annex I of Council Directive 91/414/EEC. SANCO/4347/2000 - final, 13 February 2004. Available online:
http://ec.europa.eu/sanco_pesticides/public/index.cfm?event=activesubstance.selection

EFSA (European Food Safety Authority), 2012. Reasoned opinion on the review of the existing maximum residue levels (MRLs) for flufenacet according to Article 12 of Regulation (EC) No 396/2005, EFSA Journal 2012; 10(4):2689

DRAR, Poland 2017

Appendix 1 Lists of data considered in support of the evaluation

List of data submitted by the applicant and relied on

Data Point	Author(s)	Year	Title Company Report No. Source GLP or GEP status published or not	Vertebrate study Y/N	Owner
KCA 6.1 / 01 **... also filed:** **KCP 5.2.1 / 03**	Stuke, S.	2018	Amendment no. 01 to final report: Modification M001 of the residue analytical method 01100 for the determination of residues of flufenacet (FOE5043) and its metabolites in/on cereals (straw, grain, and green material) at a LOQ of 0.01 mg/kg for grain and green material and at a LOQ of 0.05 mg/kg for straw by HPLC-MS/MS Report No.: 01100/M001, Edition Number: M-433720-02-1 Method Report No.: MR-11/011 Bayer AG, Crop Science Division, Monheim, Germany **... amended: 2018-09-20** GLP/GEP: Yes unpublished	No	Bayer
KCA 6.2.1 / 01 **... also filed:** **KCP 5.2.1 / 06**	Krolski, M. E.; Bosnak, L. L.	1997	The metabolism of [Fluorophenyl-UL-^{14}C] FOE 5043 in wheat after postemergent foliar spray application Report No.: 107399, Edition Number: M-002275-01-1 Bayer Corporation, Stilwell, KS, USA GLP/GEP: Yes unpublished	No	Bayer
KCA 6.3.1.1 / 01 **... also filed:** **KCP 5.1.2.5 / 01**	Seym, M.	1996	Determination of residues of FOE 5043 & Diflufenican 60 WG in/on winter barley, winter rye and winter wheat following early post-emergence spray application in Germany Report No.: RA-2010/94, Edition Number: M-004451-01-2 Bayer AG, Leverkusen, Germany GLP/GEP: Yes unpublished	No	Bayer
KCA 6.3.1.1 / 02 **... also filed:** **KCP 5.1.2.5 / 02**	Hoffmann, M.	2002	Determination of residues of FOE 5043 in/on wheat and barley following spray application of FOE 5043 & Diflufenican (600 SC) to winter wheat and winter barley in the field in Northern and Southern France, Germany and Spain Report No.: RA-2144/00, Edition Number: M-058156-01-1 Bayer AG, Leverkusen, Germany GLP/GEP: Yes unpublished	No	Bayer
KCA 6.6.2 / 01 **... also filed:** **KCP 5.1.2.5 / 04**	Melrose, I.; Erler, S.	2008	Determination of the residues of FOE 5043 in/on the rotational crops cereals after spraying of Artist (41.5 WG) and Liberator (500 SC) in the field in the United Kingdom, Germany and Northern France Report No.: RA-2020/06, Edition Number: M-306269-01-1 Bayer CropScience S.A., Lyon, France GLP/GEP: Yes unpublished	No	Bayer

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

Please note that all data mentioned as part of DAR, RAR, or EFSA journals are considered as 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 submitted by the applicant and not relied on

Data point	Author(s)	Year	Title Company Report No. Source (where different from company) GLP or GEP status Published or not	Vertebrate study Y/N	Owner
-	-	-	-	-	-

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

Data point	Author(s)	Year	Title Company Report No. Source (where different from company) GLP or GEP status Published or not	Vertebrate study Y/N	Owner
-	-	-	-	-	-

Appendix 2 Detailed evaluation of the additional studies relied upon

A 2.1 Flufenacet

A 2.1.1 Stability of residues

A 2.1.1.1 Stability of residues during storage of samples

A 2.1.1.1.1 Storage stability of residues in plant products

No additional study has been submitted.

A 2.1.1.1.2 Storage stability of residues in animal products

No additional study has been submitted.

A 2.1.1.2 Stability of residues in sample extracts

A 2.1.1.2.1 Storage stability of residues in plant sample extracts

A 2.1.1.2.1.1 Study 1 (method 01100/M001; MR-11/011

Comments of zRMS:	The study has already been evaluated in the Draft Renewal Assessment Report by RMS Poland (DRAR, 2018). It should be noted that no publication by EFSA have been published yet. The study is acceptable.

Reference:	**KCA 6.1/01**
Title:	Amendment no. 01 to final report: Modification M001 of the residue analytical method 01100 for the determination of residues of flufenacet (FOE5043) and its metabolites in/on cereals (straw, grain, and green material) at a LOQ of 0.01 mg/kg for grain and green material and at a LOQ of 0.05 mg/kg for straw by HPLC-MS/MS
Report:	Stuke, S.; 2018; 01100/M001; M-433720-02-1
Authority registration No:	
Guideline(s):	EC Guidance Document SANCO/825/00 rev. 8.1 of November 16, 2010 EC Guidance Document for Generating and Reporting Methods of Analysis in Support of Pre-Registration Data Requirements for Annex II (part A, Section 4) and Annex III (part A, section 5) of Directive 91/414, SANCO 3029/99 Commission Regulation (EU) No 544/2011 of 10 June 2011 implementing Regulation (EC) No 1107/2009 of the European Parliament and of the Council as regards the data requirements for active substances OECD Guideline, ENV/JM/MONO(2007)17, August 13, 2007 U.S. EPA Guideline, OPPTS 850.7100 Data Reporting for Environmental Chemistry Methods of April 1996 U.S. EPA Guideline, OPPTS 860.1340 Residue Analytical Method of August 1996
Deviations:	None
GLP/GEP:	yes
Acceptability:	yes
Duplication (if vertebrate study):	

Materials and methods

The analytical method 01100/M001 was validated for the determination of flufenacet residues in/on cereal grain, straw and green material by LC-MS/MS using matrix matched standards. The matrices to be analyzed are considered to be representative for the matrix groups of high starch content and high water content. In addition straw was validated as a representative for dry matrices.

All extraction and work-up steps are the same for method 01100/M001 and 01179 used for the analysis of the residue trials with sequential application. The method 01100/M001 provides validation data on cereal matrices in addi-tion to method 01179 (Class, Th.; Merdian, H.; 2010; M-362716-01-1) with only minor adaptations justified by different laboratory equipment and procedures.
The analytical method was validated for the determination of residues of flufenacet and three main metabolites (FOE-thioglycolate sulfoxide, FOE-oxalate, FOE-sulfonic acid) as the common moiety compound 4-fluoro-N-isopropylaniline (FOE 5043 aniline) in/on samples of plant origin. Details on the method are reported in Section B5.
During method development the stability in final plant extracts was checked for the tested sample materials over a period of 14 to 23 days.

Results and discussions
In the table below the recoveries for the stored extracts compared to the initial day of analysis are shown. Residues of the formed common moiety compound FOE 5043-aniline were found to be stable in final plant extracts for at least 14 days when stored in a refrigerator at < 6 °C.

Table A 1:Stability of Flufenacet and Metabolites in Plant Extracts.

Fortified Analyte(s) / Sample Material	FL* [mg/kg]		Recovery rates [%]					Mean
flufenacet** / wheat grain	0.1	Day 0 (initial analysis)	79	78	84	75	73	
		14 days reanalyses	90	91	97	99	96	
		deviation day 0/14 days	13.9	16.7	15.5	32.0	31.5	21.9***
flufenacet** / wheat green material	0.1	Day 0 (initial analysis)	90	80	72	66	83	
		20 days reanalyses	86	72	72	67	87	
		deviation day 0/20 days	4.4	10.0	0.0	1.5	4.8	4.2
flufenacet** / wheat straw	0.5	Day 0 (initial analysis)	88	82	79	79	81	
		23 days reanalyses	92	88	89	87	83	
		deviation day 0/23 days	4.5	7.3	12.7	10.1	2.5	7.4

FL = Fortification level RSD = relative standard deviation
* Expressed as parent equivalents.
** Fortified as flufenacet, determined as FOE 5043-aniline, calculated and expressed as flufenacet.
*** This value was accepted since the values after 14 day reanalysis were increased compared to day 0 analysis and therefore do not indicate a degradation of flufenacet.

A 2.1.1.2.2 Storage stability of residues in animal sample extracts

No additional study has been submitted.

A 2.1.2 Nature of residues in plants, livestock and processed commodities

A 2.1.2.1 Nature of residue in primary crops

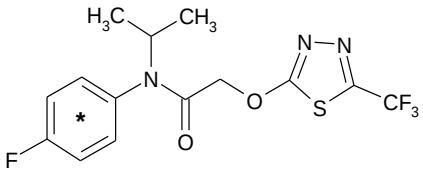
A 2.1.2.1.1 Study report 107399

Comments of zRMS:	The study has already been evaluated in the Draft Renewal Assessment Report by RMS Poland (DRAR, 2018). It should be noted that no publication by EFSA have been published yet. The study is acceptable.

Reference:	**KCA 6.2.1/01**
Title:	The metabolism of [Fluorophenyl-UL-14C] FOE 5043 in wheat after postemergent foliar spray application
Report:	Krolski, M. E.; Bosnak, L. L.; 1997; 107399; M-002275-01-1
Authority registration No:	
Guideline(s):	EPA Ref: 860.1300, Nature of the Residue - Plants
Deviations:	not specified
GLP/GEP:	yes
Acceptability:	yes
Duplication (if vertebrate study):	

Materials and methods

Test Material

Structural formula	 * denotes the ^{14}C label
Chemical name	N-(4-Fluorophenyl)-N-isopropyl-2-(5-trifluoromethyl-[1,3,4]thiadiazol-2-yloxy)-acetamide (IUPAC); Acetamide, N-(4-Fluorophenyl)-N-(1-methylethyl)-2-[[5-(trifluoromethyl)-1,3,4-thiadiazol-2-yl]oxy]- (9Cl; CAS)
Common name	Flufenacet
CAS RN	142459-58-3
Empirical formula	$C_{14}H_{13}F_4N_3O_2S$
Company code	FOE 5043
Molar mass (non-labelled)	363.34 g/mol
Label	[fluorophenyl-UL-^{14}C]Flufenacet
Specific radioactivity	47.9 mCi/mmol (0.132 mCi/mg, 4.878 MBq/mg)
Radiochemical purity	96% (radio-HPLC), 92% after formulation with slight degradation to FOE alcohol (FOEALC, M3, identified by HPLC-MS)

Test Plants

Test plant	Spring wheat (*Triticum vulgare*)
Origin	Farmers Union Cooperative, Spring Hill, Kansas, USA
Growth stage at application	4-tiller growth stage, 46 days after seeding
Harvested commodities	Forage, hay, straw, grain

Planting of wheat grain, preparation and application of the test mixture

Loam soil (49.2% sand, 32.8% silt, 18.0% clay, 2.51% organic matter, pH 6.4) was filled in a trough with a surface area of 18.4 ft^2 (1.70 m^2) and a depth of 14 inches (35 cm). Wheat seeds were placed in furrows on the soil surface, approx. 6 inches (15 cm) apart, at approx. 1-cm intervals. The furrows were finally covered with a 0.5 cm soil layer. The wheat was grown outdoors in spring and summer 1995 at the Bayer Research Park in Stilwell, Kansas, USA.

The radiolabelled test substance was mixed with 60WP blank formulation and water resulting in the spraying mixture. This spraying mixture was evenly sprayed across the surface of the trough with the wheat plants in the 4-tillering stage (46 days after sowing) using a plastic pump sprayer. The actual application rate corresponded to 0.461 lb. a.s./acre (0.52 kg a.s./ha).

Harvest, processing and extraction

The wheat plants were harvested at the following growth stages:

Forage:	at BBCH 26, 6-tillering growth stage, 64 days after sowing
Hay:	at BBCH 85, soft dough growth stage
Straw and grain:	at full maturity, 105 and 112 days after sowing

Plants were cut off at the soil surface level. They were cut into 1-inch (2.54 cm) pieces and homogenized under liquid nitrogen using a high-speed tissue mixer. The liquid nitrogen was allowed to evaporate in a freezer at < -10°C. Aliquots of the resulting tissue powder were radioassayed and the remainder stored in the freezer for later analysis.

In case of grain and straw sampling, ripe heads were first cut from the stalks using scissors. Then, the remaining plant (straw) was cut above the soil. The wheat heads were rubbed across a No. 10 soil sieve to remove the seeds. The sifted and winnowed (using a gentle nitrogen stream) grain was pulverized in a Warring blender. The straw was cut into pieces and homogenized under liquid nitrogen as done with forage and hay.

Homogenized forage was extracted with methanol (3x) at ambient temperature followed by refluxing with methanol. Aliquots of the methanol extracts were evaporated to dryness, re-dissolved in 0.1% acetic acid and analyzed by radio-HPLC. Each fraction was radioassayed.

Homogenized hay was extracted with methanol/water (3/1, 1x) and pure methanol (3x) at room temperature followed by refluxing with methanol. The methanol extracts were concentrated, and analyzed by radio-HPLC. The remaining solids were suspended successively in 1 N hydrochloric acid and in 2 N aqueous sodium hydroxide, both at ambient temperature. The aqueous phases were neutralized and partitioned against chloroform. The remaining solids were refluxed successively with 6 N aqueous hydrochloric acid and 6 N aqueous sodium hydroxide. All fractions/phases were radioassayed.

Homogenized straw and grain were extracted separately with methanol/water (4/1, 1x) following steeping at room temperature for half an hour. Extraction was continued with pure methanol (2x) at ambient temperature and under reflux, with hydrochloric acid and sodium hydroxide at room temperature and under reflux as done with hay. The aqueous phases were neutralized and partitioned against chloroform. Between acid/basic hydrolysis at room temperature and under reflux an additional extraction step with methanol/water (3/1) under ultrasonication was inserted. All fractions/phases were radioassayed.

Extraction efficiency of the residue analytical method[9]

Samples of grain and straw were processed and analyzed according to the analytical residue method for flufenacet in plants. This is a common moiety method with analysis for split-off “N-fluorophenyl-N-isopropyl amine”.

The sample was hydrolyzed and oxidized with sulfuric acid and potassium permanganate. Surplus permanganate was reduced by added sodium bisulfite. The hydrolysis was completed by addition of concentrated sulfuric acid and refluxing for 24 hours. The resulting mixture was cooled down, made strongly basic with sodium hydroxide and the formed N-fluorophenyl-N-isopropyl amine distilled off together with water (steam distillation). This amine was purified by partitioning with methylene chloride, derivatized with trifluoroacetic anhydride in pyridine. The final reaction mixture was radioassayed and analyzed by HPLC.

[9] KIIA, 4.2.1/02: Gould, T. J., Lemke, V. J. (1995). An analytical method for the determination of FOE 5043 residues in plant matrices, report 106406 of Bayer Corp., Stilwell, KS, USA, Comp. No. M-041601-01-1 – submitted in Annex II dossier, evaluated in the Monograph (France 1997)

Radioassaying and analysis

Radioassaying (measurement of the radioactivity) was conducted by liquid scintillation counting (LSC). Quenching was automatically compensated using an external standard. Solid samples were firstly combusted and the formed $^{14}CO_2$ absorbed in an alkaline scintillation liquid. The limit of quantification (LOQ) was set to twice the background radioactivity for radioassaying of solid samples. Given the aliquot amount of combustion and the specific radioactivity used in this study the LOQ for radioassaying was 0.00077 mg parent equivalents/kg (0.00077 mg equ/kg) for liquid samples and 0.0011 mg equ/kg for solid samples.

Radio-HPLC was conducted on a RP8 or RP18 column (250 x 10 mm, 5 µm particle size) operated with a gradient mixture of water and methanol (both containing 0.1% acetic acid). The HPLC system was equipped with a radiomonitor with a glass scintillator. The linearity of the radiomonitor response was examined by injection of various amounts of radioactivity. The limit of detection was derived from detector-response curve and the specific radioactivity of the test substance. It amounted to 0.0093 µg of the test substance.

Radio-TLC of the straw hydrolysis fraction was conducted on TLC plates (5 x 20 cm) coated with Silicagel 60 F254. The plates were developed with tetrahydrofuran/methanol (9/1). Radioactive zones were detected using a radio-TLC-scanner.
LC-MS/MS analyses were performed with a combination of a mass spectrometer connected to a HPLC system. The MS system was operated in both the positive and negative ion electrospray ionization (ESI) mode.

Results and discussions

Total radioactive residues and their extractability in wheat commodities

The total radioactive residues (TRR) amounted to 1.93 mg equ/kg in wheat forage 18 days post treatment, to 3.50 mg equ/kg in wheat hay 33 days post treatment, to 2.04 mg equ/kg in wheat straw 66 days post treatment and to 0.62 mg equ/kg in grain 59 - 66 days post treatment (Table A 1).

The extractable portions of TRR using the different techniques are shown in Table A 2 for wheat forage and hay and in Table A 3 for wheat straw and grain. Most the residues could already be released by conventional extraction with methanol at ambient temperature accounting for 64 (grain) - 92% (forage) of TRR. Refluxing with methanol released additional 4 - 16% of TRR resulting in a total of 80 (grain) – 96% (forage) of TRR. Sonication with methanol/water released an additional portion of 8% of TRR from wheat grain. Since most of the residues had already been released by the previous extraction steps succeeding acid and basic hydrolysis were not efficient. The portion of non-extractable residues finally was negligible amounting to 4% of TRR in forage (no acid or basic hydrolysis of the matrix performed), to <1% of TRR in hay, to 3% of TRR in straw and to 2% of TRR in grain samples.

Residues in wheat commodities originating from foliar application of ^{14}C-flufenacet

The composition of the radioactive residues in wheat forage and hay following foliar treatment of [fluoro-phenyl-UL-^{14}C]flufenacet are summarized in Table A 4. The respective composition of residues in wheat straw and grain is shown in Table A 5. A total of 12 metabolites were detected in forage and straw and 9 metabolites in hay and grain. The metabolites were identified by comparison of their HPLC retention to those of authentic reference standards and by individual collection following HPLC separation and identification by HPLC-MS.
The chromatographic profiles of the methanol extracts of forage, hay and straw were very similar. Common major metabolites were identified as FOE oxalate, M1 (14 – 36% of TRR) and FOE sulfinyl lactic acid I, M33 (20 – 26% of TRR). At the earlier growth stages forage and hay two additional metabolites were observed at relevant amounts, i.e. FOE sulfanyl lactic acid glucoside, M41 (8 – 21% of TRR) and FOE sulfinyl lactic acid glucoside, M37 (6 – 10% of TRR), whereas at maturity FOE sulfonic acid, M2 (15% of TRR) was found in straw. Other metabolites appeared at a minor extent (<10% of TRR).
The grain extract comprised mainly of a single component (65% of TRR corresponding to 0.40 mg equ/kg) which was identified as FOE oxalate, M1. Other metabolites were quantified as very minor (≤ 2% of TRR). The parent substance was not observed in any commodity of forage, hay, straw and grain. All major metabolites in these commodities contained the common moiety “fluorophenyl-N-isopropyl amine”. The proposed metabolic pathway of flufenacet in wheat is shown in Figure A 1.

Extraction efficiency of the residue analytical method

The extraction efficiency of the analytical method (accountability of residue method) was examined using grain and straw with incurred residues from the current wheat metabolism study. TRR levels of grain and straw samples used for this test amounted to 0.55 and 1.96 mg equ/kg. These levels were slightly lower than the initial levels, probably due to hydration of the dried grain and straw during freezer storage.

Following oxidation, hydrolysis and steam distillation of formed common moiety N-fluorophenyl-N-isopropyl amine from wheat grain the distillate contained 97% of TRR in the original grain sample. 84% of TRR partitioned into the organic phase after addition of sodium hydroxide. Subsequent derivatisation revealed the analytical target N-4-fluorophenyl-N-isopropyl-trifluoroacetamide representing 81% of TRR in the original grain sample. Compared to the total extractability with methanol determined in the metabolism experiment (80% of TRR extractable at room temperature and under reflux conditions, with 66% of TRR identified as metabolites containing the common moiety) this figure represented a complete extraction of those residue components that contain the respective N-fluorophenyl-N-isopropyl amine moiety.

Applying the same method to a straw sample resulted in 86% of TRR in the distillate with 76% of TRR in the organic phase prior to derivatisation. The derivatized sample contained 70% of TRR in the original straw sample, which was identified as N-4-fluorophenyl-N-isopropyl-trifluoroacetamide. Compared to the total extractability with methanol determined in the metabolism experiment (86% of TRR extractable at room temperature and under reflux conditions, with 74% of TRR identified as metabolites containing the common moiety, Table A 4) this figure represented also a complete extraction of those residue components that contain the respective N-fluorophenyl-N-isopropyl amine moiety.

Storage stability of residues in the freezer

Initial extraction of all commodities was made one month after sample collection. All extractions and quantitative measurements were completed within 6 months of sample collection. Therefore, no additional storage stability data are required according to OECD Guideline 501 (2007) on “Metabolism in Crops” to support this study.

Table A 2: Total Radioactive Residues (TRRs) in wheat matrices after post-emergence treatment.

Matrix	Timing and Applic. No.	PHI (days) DAT	TRR (mg equ/kg)
			[Fluorophenyl-UL-^{14}C]
wheat forage	single post-emergence treatment at BBCH 24 at the rate of 0.52 kg a.s./ha	18	1.93
wheat hay		33	3.50
wheat straw		66	2.04
wheat grain		59	0.62

mg equ/kg = mg parent equivalents/kg

Table A 3: Extractability of radioactive residues from wheat forage and hay following foliar treatment with [fluorophenyl-UL-^{14}C]flufenacet at a use rate of 0.52 kg a.s./ha

Agricultural commodity	Wheat forage		Wheat hay	
TRR [mg equ/kg]	1.93		3.50	
Extraction with	[% of TRR]	[mg equ/kg]	[% of TRR]	[mg equ/kg]
Methanol, room temperature	92	1.78	88	3.01
Methanol, refluxing	4	0.08	6	0.21
1N HCl, room temperature				
- Partition into chloroform	-	-	<1	<0.01
- Partition into water	-	-	2	0.02
2 N NaOH, room temperature				
- Partition into chloroform	-	-	<1	<0.01
- Partition into water	-	-	<1	<0.01

Agricultural commodity	**Wheat forage**		**Wheat hay**	
TRR [mg equ/kg]	1.93		3.50	
Extraction with	[% of TRR]	[mg equ/kg]	[% of TRR]	[mg equ/kg]
Methanol/water sonication	-	-	<1	0.01
6 N HCl, reflux	-	-	<1	<0.01
6 N NaOH, reflux	-	-	<1	<0.01
Non-extractable (solids)	4	0.08	<1	<0.01
Total*	100	1.94	100	3.37

* slight differences from TRR determination measured by combustion due to rounding of subfractions
mg equ/kg = mg parent equivalents/kg

Table A 4: Extractability of radioactive residues from wheat straw and grain following foliar treatment with [fluorophenyl-UL-^{14}C]flufenacet at a use rate of 0.52 kg a.s./ha

Agricultural commodity	**Wheat straw**		**Wheat grain**	
TRR [mg equ/kg]	2.04		0.62	
Extraction with	[% of TRR]	[mg equ/kg]	[% of TRR]	[mg equ/kg]
Methanol, room temperature	76	1.51	64	0.36
Methanol, refluxing	10	0.20	16	0.09
1N HCl, room temperature	-			
- Partition into chloroform	<1	<0.01	<1	<0.01
- Partition into water	3	0.06	3	0.02
2 N NaOH, room temperature	-			
- Partition into chloroform	1	0.02	1	<0.01
- Partition into water	4	0.08	3	0.02
Methanol/water sonication	2	0.04	8	0.04
6 N HCl, reflux				
- Partition into chloroform	<1	<0.01	2	<0.01
- Partition into water	<1	<0.01	1	<0.01
6 N NaOH, reflux	<1	<0.01	<1	<0.01
Non-extractable (solids)	3	0.06	2	0.01
Total*	100	1.97	100	0.54

* slight differences from TRR determination measured by combustion due to rounding of subfractions
mg equ/kg = mg parent equivalents/kg

Table A 5: Distribution of the parent and the metabolites in plant matrices when dosed with [fluorophenyl-UL-^{14}C]flufenacet at a use rate of 0.52 kg a.s./ha.

Compound	Wheat forage TRR = 1.93 ppm		Wheat hay TRR = 3.50 ppm	
	[% of TRR]	**[mg equ/kg]**	**[% of TRR]**	**[mg equ/kg]**
Organosoluble *Metabolites extracted with MeOH at RT and MeOH refluxing*				
Unknown 1	<1	<0.02	-	-
FOE oxalate (FOEOX, M1)	19	0.37	36	1.26
Unknown 2	-	-	<1	<0.04
FOE sulfinyl lactic acid glucoside I (FAMSOL-Glu I, M37)	6	0.12	10	0.35
FOE sulfinyl lactic acid glucoside II (FAMSOL-Glu II, M37)	6	0.12	5	0.18
FOE thioglycolate sulfoxide (FAMSOC, M4)	2	0.04	4	0.14
FOE sulfinyl lactic acid I (FAMSOL I, M33)	23	0.44	20	0.70
FOE sulfinyl lactic acid I I (FAMSOL II, M33)	7	0.14	4	0.14
Unknown 3	3	0.06	2	0.07
Unknown 4	2	0.04	-	-
FOE sulfanyl lactic acid glucoside (FAMSL-Glu, M41)	21	0.21	8	0.28
Unknown 5	<1	<0.02	-	-
Unknown 6	<1	<0.02	-	-
Total	**89**	**1.74**	**89**	**3.12**

mg equ/kg = mg parent equivalents/kg

Table A 6: Distribution of the parent and the metabolites in plant matrices using [fluorophenyl-UL-^{14}C]flufenacet at a use rate of 0.52 kg a.s./ha.

Compound	Wheat straw TRR = 2.04 ppm		Wheat grain TRR = 0.62 ppm	
	[% of TRR]	**[mg equ/kg]**	**[% of TRR]**	**[mg equ/kg]**
Organosoluble *Metabolites extracted with MeOH at RT and MeOH refluxing*				
Unknown 1	-	-	1	<0.01
FOE sulfonic acid (FASO3H, M2)	15	0.31	-	-
FOE oxalate (FOEOX, M1)	14	0.29	65	0.40
Unknown 2			2	0.01
FOE sulfinyl lactic acid glucoside I (FAMSOL-Glu I, M37)	2	0.04	<1	<0.01
FOE sulfinyl lactic acid glucoside II (FAMSOL-Glu II, M37)	1	0.02	1	<0.01
FOE thioglycolate sulfoxide (FAMSOC, M4)	7	0.14	-	-
Unknown 3	1	0.02	<1	<0.01
FOE sulfinyl lactic acid I (FAMSOL I, M33)	26	0.53	-	-
FOE sulfinyl lactic acid I I (FAMSOL II, M33)	9	0.18	-	-
Unknown 4	1	0.02	<1	<0.01
Unknown 5	-	-	<1	<0.01
FOE sulfanyl lactic acid glucoside (FAMSL-Glu, M41)	<1	0.02	-	-
Unknown 6	<1	<0.02	<1	<0.01
Unknown 7	2	0.04	<1	<0.01
Total	**78**	**1.61**	**69**	**0.41**

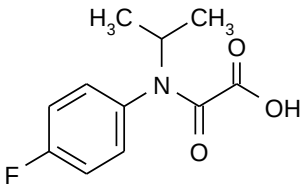
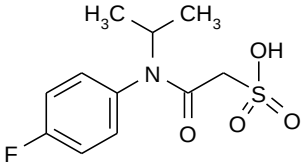
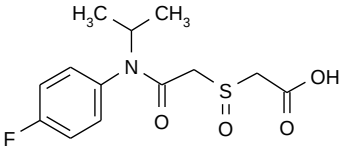
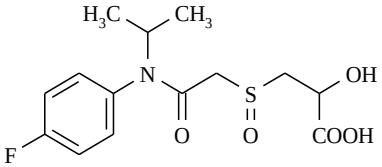
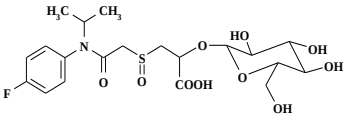
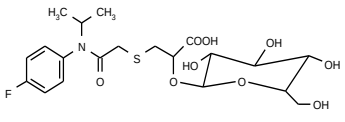
mg equ/kg =mg parent equivalents/kg

Table A 7: Summary of characterization and identification of radioactive residues in plant matrices following application of [fluorophenyl-UL-^{14}C]flufenacet at a use rate of 0.52 kg a.s./ha.

Compound	Wheat forage TRR = 1.93 ppm		Wheat hay TRR = 3.50 ppm		Wheat straw TRR = 2.04 ppm		Wheat grain TRR = 0.62 ppm	
	[% of TRR]	[mg equ/kg]	[% of TRR]	[mg equ/kg]	[% of TRR]	[mg equ/kg]	[% of TRR]	[mg equ/kg]
TRR** (mg equ/kg)	1.93		3.50		2.04		0.62	
Flufenacet	--	--	--	--	--	--	--	--
FOE oxalate (FOEOX, M1)	19	0.37	36	1.26	14	0.29	65	0.40
FOE sulfonic acid (FASO3H, M2)	--	--	--	--	15	0.31	--	--
FOE thioglycolate sulfoxide (FAMSOC, M4)	2	0.04	4	0.14	7	0.14	--	--
FOE sulfinyl lactic acid I (FAMSOL I, M33)	23	0.44	20	0.70	26	0.53	--	--
FOE sulfinyl lactic acid I I (FAMSOL II, M33)	7	0.14	4	0.14	9	0.18	--	--
FOE sulfinyl lactic acid glucoside I (FAMSOL-Glu I, M37)	6	0.12	10	0.35	2	0.04	<1	<0.01
FOE sulfinyl lactic acid glucoside II (FAMSOL-Glu II, M37)	6	0.12	5	0.18	1	0.02	1	<0.01
FOE sulfanyl lactic acid glucoside (FAMSL-Glu, M41)	21	0.21	8	0.28	<1	0.02	--	--
Unknown 1	<1	<0.02	-	-	-	-	1	<0.01
Unknown 2	-	-	<1	<0.04	-	-	2	0.01
Unknown 3	3	0.06	2	0.07	<1	<0.01	<1	<0.01
Unknown 4	2	0.04	-	-	1	0.02	<1	<0.01
Unknown 5	<1	<0.02	-	-	-	-	<1	<0.01
Unknown 6	<1	<0.02	-	-	<1	<0.02	<1	<0.01
Unknown 7	--	--	--	--	2	0.04	<1	<0.01
Total identified	**84**	**1.64**	**87**	**1.68*** **	**74**	**1.53**	**66**	**0.40**
Total characterized	**5**	**0.1**	**2**	**1.44**	**4**	**0.08**	**3**	**0.01**
Total extractable	**89**	**1.74**	**89**	**3.12**	**78**	**1.61**	**69**	**0.41**
Unextractable (PES)*	**4**	**0.08**	**<1**	**<0.01**	**3**	**0.06**	**2**	**0.01**

* Residues remaining after exhaustive extractions.
** TRR determined in a separate measurement .
*** FAMSOL I and II (M33) and FAMSOL-Glu I and II (M37) not included.

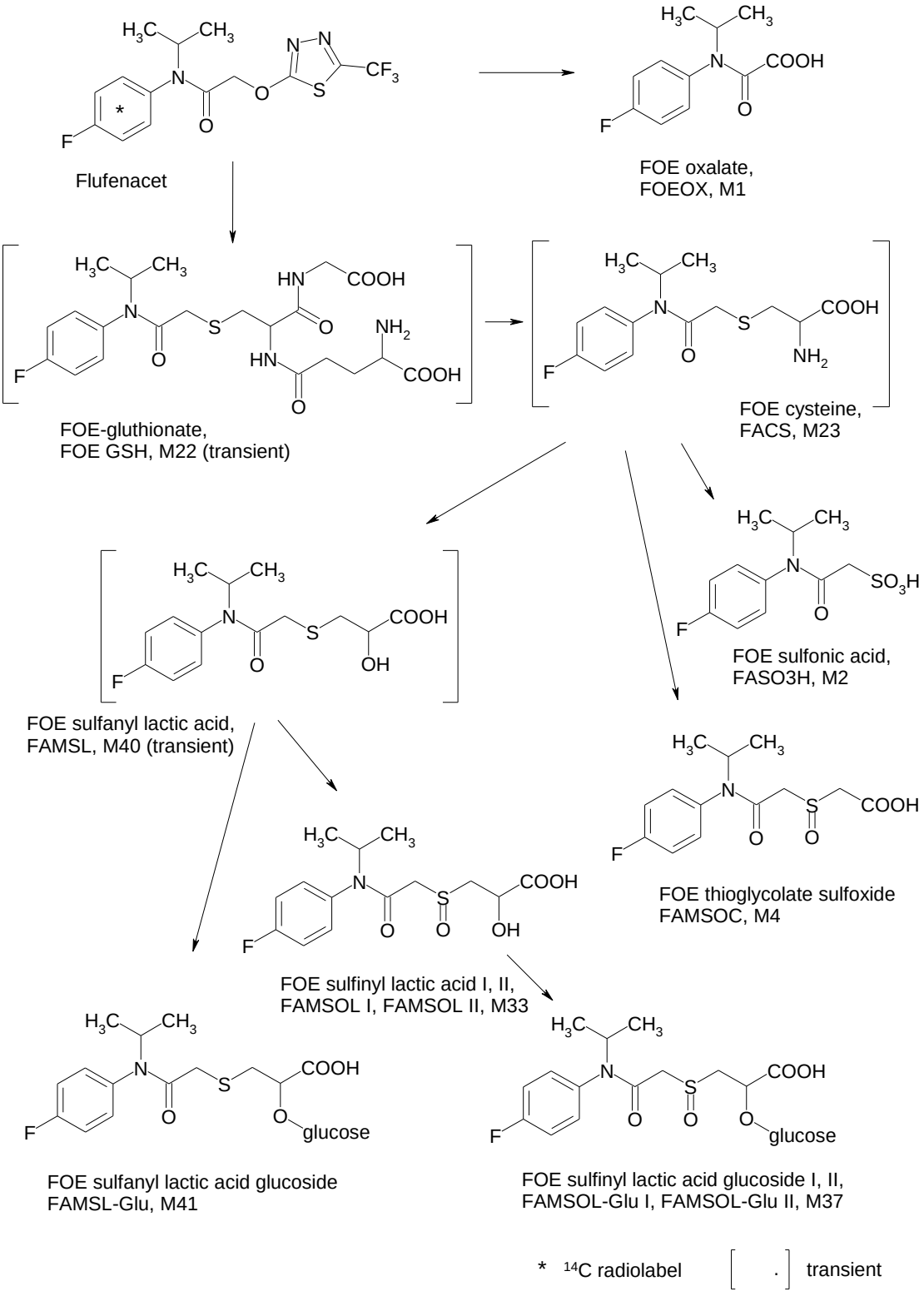
Table A 8: Identification of compounds from metabolism study

Common name/code	Chemical name	Chemical structure
FOE-oxalate (FOEOX, M1)	FOEOXALATE, FOEACID OXALATE AE 0841913 BCS-AB16305 IUPAC: [(4-fluorophenyl)(isopropyl)amino](oxo)acetic acid (generated by ICS Naming) CAS: Acetic acid, 2-[(4-fluorophenyl)(1-methylethyl) amino]-2-oxo-	
FOE sulfonic acid (FASO3H, M2)	FASO3H AE 0841914 KTS 9465 (sodium salt) BCS-AZ23374 (sodium salt) WAK 6222 (acid) ethanesulfonic acid sodium salt IUPAC: 2-[(4-fluorophenyl)(isopropyl)amino]-2-oxoethanesulfonic acid sodium 2-[(4-fluorophenyl)(isopropyl)amino]-2-oxoethanesulfonate (both generated by ICS Naming) CAS: sodium salt: (2-[(4-fluorophenyl)(1-methylethyl)amino]-2-oxo-ethanesulfonic acid sodium salt)	
FOE thioglycolate sulfoxide (FAMSOC, M4)	FAMSOC TGS FOE mercapto acetic acid sulfoxide AE 0841915 BCS-AB68868 IUPAC: ({2-[(4-fluorophenyl)(isopropyl)amino]-2-oxoethyl}sulfinyl)acetic acid (generated by ICS Naming)	
FOE sulfinyl lactic acid I &II (FAMSOL I, FAMSOL II, M33)	FAMSOL FAMSOL-I FAMSOL-II (diastereomeric pair) IUPAC: 3-({2-[(4-fluorophenyl)(isopropyl)amino]-2-oxoethyl}sulfinyl)-2-hydroxypropanoic acid (generated by ICS Naming)	
FOE sulfinyl lactic acid glucoside I &II (FAMSOL-Glu I and FAMSOL-Glu II, M37)	FAMSOL-Glu FAMSOL-Glu-I FAMSOL-Glu-II IUPAC: 3-({2-[(4-fluorophenyl)(isopropyl)amino]-2-oxoethyl}sulfinyl)-2-(hexopyranosyloxy) propanoic acid (generated by ICS Naming)	
FOE sulfanyl lactic acid glucoside (FAMSL-Glu, M41)	FAMSL-Gl, FAMSL-Glu IUPAC: 3-({2-[(4-fluorophenyl)(isopropyl)amino]-2-oxoethyl}sulfanyl)-2-(hexopyranosyloxy) propanoic acid	

Common name/code	Chemical name	Chemical structure
	(generated by ICS Naming)	

Figure A 1: Proposed metabolic pathway of flufenacet in wheat following post-emergent foliar application

Conclusion



The metabolism of [fluorophenyl-UL-^{14}C]flufenacet was investigated in spring wheat following post-emergent foliar application to young shoots (4-tiller growth stage) at an use rate of 0.46 lb. ai/acre (0.52 kg a.s./ha). The following crop commodities were collected and analysed: immature forage, immature hay, mature straw and grain. The total radioactive residues (TRR) amounted to 1.93; 3.50; 2.04 and 0.62 mg equ/kg in forage, hay, straw and grain. Extraction with methanol at ambient temperature and under reflux

revealed a high extractability of the radioactive residues accounting for 92, 94, 86 and 80% of TRR for forage, hay, straw and grain, respectively. Following additional acid and alkaline hydrolysis of the plant matrix the non-extractable residues were negligible (≤ 1– 4% of TRR).

The metabolism of flufenacet was extensive in wheat. While no parent substance was observed in any of the plant commodities 12 metabolites were detected in forage and straw, and 9 metabolites in hay and grain. FOE oxalate (FOEOX, M1) revealed to be a major metabolite in all commodities. It proved to be predominant in wheat grain amounting to 65% of TRR (corresponding to 0.40 mg equ/kg). Other metabolites in grain appeared at a very low level (≤ 2% of TRR). In forage, hay and straw two other major metabolites were identified as FOE sulfinyl lactic acid I (FAMSOL I, M33) and FOE sulfanyl lactic acid glucoside (FAMSL-Glu, M41). In straw, a further metabolite FOE sulfonic acid (FOESO3H, M2) amounted to 15% of TRR.

The main metabolite present in all commodities, i.e. FOE oxalate, most likely arose from oxidation of transient primary alcohol hydrolysis product. All other metabolites were formed by hydrolysis, oxidation and conjugation of a primary transient metabolite formed by initial conjugation with glutathione. A similar metabolic pathway of flufenacet was also found in soybeans, corn and cotton. All of these metabolism studies were conducted with [fluorophenyl-UL-^{14}C]flufenacet. From the pattern of detected metabolites a metabolic pathway of flufenacet in wheat is proposed in Figure A1.

Comparative extraction of the residues using methanol (this metabolism study) and determination of the residues using the residue analytical method (oxidative acid hydrolysis and quantification of the hereby formed N-fluorophenyl-N-isopropyl amine) showed a good agreement of amount of residue compounds containing the common moiety.

A 2.1.2.2 Nature of residue in rotational crops

No new study submitted.

A 2.1.2.3 Nature of residues in processed commodities

No new study submitted.

A 2.1.2.4 Nature of residues in livestock

No new study submitted.

A 2.1.2.4.1 Poultry

No new study submitted.

A 2.1.2.4.2 Lactating ruminants

No new study submitted.

A 2.1.2.4.3 Pigs

No new study submitted.

A 2.1.2.4.4 Fish

No new study submitted.

A 2.1.3 Magnitude of residues in plants

A 2.1.3.1 Small grain cereals (wheat and barley)

Table A 9: Comparison of intended and critical EU GAPs

Type of GAP	Number of applications	Application rate per treatment (precise unit)	Interval between application	Growth stage at last application	PHI (days)
Wheat and barley cGAP EU (France, 1997)/ (Art. 12, EFSA, 2012) EU-N	1	240 g a.s./ha	--	early post emergence up to BBCH 25.	a)
Wheat and barley cGAP EU (Art. 12, EFSA, 2012) EU-S	1	240 g a.s./ha	--	BBCH 13	a)
Wheat , triticale, durum wheat, spelt (30, 34, 54, 58, 66, 70, 78, 82, 94, 102, 110, 118, 130, 134, 138, 142*) Intended cGAP EU-N	1	244 g a.s./ha	--	BBCH 13	a)
Barley, rye (38, 62, 74, 86, 90, 98, 106, 114*) Intended cGAP EU-N	1	244 g a.s./ha	--	BBCH 13	a)

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

a) not applicable; the PHI is covered by the vegetation period of the crop

A 2.1.3.1.1 Study 1 (RA-2010/94)

Comments of zRMS:	The study has already been evaluated in the Draft Renewal Assessment Report by RMS Poland (DRAR, 2018). Four trials on winter cereals have been conducted to determine residues of flufenacet in green material, grain and straw after early postemergence application of FOE 5043 & Diflufenican 60 WG at rate of 0.6 kg product. Four field tests were done at different test locations in Germany. The analytical method 00346 to determine residues of FOE 5043 60 WG is a total residue method. The reliability of the method is shown by mean recoveries between - 85% and 95% for the individual sample materials with relative standard deviations between 4% and 13% and a limit of quantitation (LOQ) of 0.05 mg/kg for green material and grain and 0.1 mg/kg for straw. No residues were detected both in grain and straw samples of winter barley, winter rye and winter wheat. The study is acceptable.

Reference:	**KCA 6.3.1.1/01**
Title:	Determination of residues of FOE 5043 & Diflufenican 60 WG in/on winter barley, winter rye and winter wheat following early post-emergence spray application in Germany
Report:	Seym, M.; 1996; RA-2010/94; M-004451-01-2
Authority registration No:	
Guideline(s):	not specified
Deviations:	not specified
GLP/GEP:	yes
Acceptability:	yes
Duplication (if vertebrate study):	

Material and methods

Four trials on winter cereals (1 trial on barley, 1 trial on winter rye, and 2 trials on winter wheat) were conducted during the 1994-1995 growing season in Germany using a WG formulation containing 20% diflufenican + 40% flufenacet. The plants were treated in autumn (November), at growth stages ranging from BBCH 13 (3 leaves unfolded) to BBCH 25 (5 tillers detectable). The application rate was 240 g flufenacet/ha.

Green plant samples were taken for analysis at the growth stages BBCH 29 (end of tillering) and BBCH 51 (beginning of heading). Grain and straw samples were taken at normal harvest, which was between 246 and 253 days after application.

All samples were analysed for residues of flufenacet according to the method 00346 (Seym, M.; 1995, M-018864-02-1) which yields the combined level of the parent compound and all its metabolites containing the N-fluorophenyl-N-isopropyl functional group. The method was assessed in the Monograph (France 1997). Residues are expressed as parent flufenacet.

Recovery rates were determined prior to analysis and concurrently with the sample analysis. Fortification was performed by spiking control samples with one of the following compounds or a mixture thereof: parent flufenacet, flufenacet oxalate, flufenacet sulfonic acid, flufenacet thioglycolate sulfoxide. The recovery rates and corresponding relative standard deviations (RSD) obtained during the conduct of this study were acceptable with a mean value in the range of 70-110 % and RSD < 20%.
The limit of quantification was 0.05 mg/kg in green material and grain, and 0.1 mg/kg in straw.
No apparent residues were found in any of the untreated samples.

Table A 10: Summary of the study RA-2010/94 trials

Analyte 1: Total residue flufenacet (determined as FOE 5043 trifluoro acetamide, calculated as flufenacet)

Trial No./ Location/ EU zone/ Year	Commodity/ Variety	Date of 1.Sowing or planting 2.Flowering 3. Harvest	Application rate per treatment			Dates of treatment or no. of treatments and last date	Growth stage at last treatment or date	Portion analyzed	Residues (mg/kg)	PHI (days)	Details on trial
			kg a.s./ ha	Water (l/ha)	kg a.s./hl				Total residue flufenacet		
	(a)	(b)				(c)				(d)	(e)
RA-2010/94 40044/0 0044-94-T1 Germany Versuchsgut Höfchen, D-51399 Burscheid Europe, North, F 1994	Barley, winter Loreley	1) 22.09.1994 2) 29.05.1995 - 04.06.1995 3) 13.07.1995	0.2400	300	0.080	02.11.1994/0	3 leaves unfolded BBCH 13	green material grain straw	<0.05 <0.05 <u><0.05</u> <u><0.1</u>	124 201 253 253	(f) RA-2010/94 (g) Flufenacet & Diflufenican 60 WG, (h) Spraying, (i) Total residue flufenacet: 00346 (j) Total residue flufenacet, green material, grain and straw: 0.05 mg/kg, 0.05 mg/kg and 0.1 mg/kg, respectively (k) method 00346, method validation was also done in the study RA-2010/94 prior to analysis (l) green material and grain/straw: 234 and 105 days, respectively
RA-2010/94 40045/9 0045-94-T1 Germany Versuchsgut Laacherhof, D-40789 Monheim Europe, North, F 1994	Rye, winter Gambit	1) 10.10.1994 2) 24.05.1995 - 30.05.1995 3) 25.07.1995	0.2400	300	0.080	21.11.1994/0	Beginning of tillering BBCH 21	green material grain straw	0.06 <0.05 <u><0.05</u> <u><0.1</u>	94 172 246 246	(f) RA-2010/94 (g) Flufenacet & Diflufenican 60 WG, (h) Spraying, (i) Total residue flufenacet: 00346 (j) Total residue flufenacet, green material, grain and straw: 0.05 mg/kg, 0.05 mg/kg and 0.1 mg/kg, respectively (k) method 00346, method validation was also done in the study RA-2010/94 prior to analysis (l)) green material and grain/straw: 237 and 85 days, respectively

Trial No./ Location/ EU zone/ Year	Commodity/ Variety	Date of 1.Sowing or planting 2.Flowering 3. Harvest	Application rate per treatment			Dates of treatment or no. of treatments and last date	Growth stage at last treatment or date	Portion analyzed	Residues (mg/kg)	PHI (days)	Details on trial
			kg a.s./ ha	Water (l/ha)	kg a.s./hl				Total residue flufenacet		
	(a)	(b)				(c)				(d)	(e)
RA-2010/94 40046/7 0046-94-T1 Germany Versuchsgut Höfchen, D-51399 Burscheid Europe, North, F 1994	Wheat, winter Contra	1) 30.09.1994 2) 10.06.1995 - 18.06.1995 3) 26.07.1995	0.2400	300	0.080	21.11.1994/0	5 tillers detectable BBCH 25	green material grain straw	<0.05 <0.05 <u><0.05</u> <u><0.1</u>	119 191 247 247	(f) RA-2010/94 (g) Flufenacet & Diflufenican 60 WG, (h) Spraying, (i) Total residue flufenacet: 00346, (j) Total residue flufenacet, green material, grain and straw: 0.05 mg/kg, 0.05 mg/kg and 0.1 mg/kg, respectively (k) method 00346, method validation was also done in the study RA-2010/94 prior to analysis (l)) green material and grain/straw: 234 and 106 days, respectively
RA-2010/94 40047/5 0047-94-T1 Germany Versuchsgut Laacherhof, D-40789 Monheim Europe, North, F 1994	Wheat, winter Contra	1) 12.10.1994 2) 10.06.1995 - 17.06.1995 3) 25.07.1995	0.2400	300	0.080	21.11.1994/0	Beginning of tillering BBCH 21	green material grain straw	0.10 <0.05 <u><0.05</u> <u><0.1</u>	133 190 246 246	(f) RA-2010/94 (g) Flufenacet & Diflufenican 60 WG, (h) Spraying, (i) Total residue flufenacet: 00346 (j) Total residue flufenacet, green material, grain and straw: 0.05 mg/kg, 0.05 mg/kg and 0.1 mg/kg, respectively (k) method 00346, method validation was also done in the study RA-2010/94 prior to analysis (l)) green material and grain/straw: 225 and 112 days, respectively

- (a) According to CODEX Classification / Guide
- (b) Only if relevant
- (c) Year must be indicated
- (d) Days after last application (Label pre-harvest interval, PHI, underline)
- (e) Remarks may include: Climatic conditions; Reference to analytical method and information which metabolites are included
- (f) Study reference
- (g) Formulation type
- G greenhouse F field
- (h) Application method
- (i) Method information
- (j) LOQ
- (k) Method validation
- (l) Storage (max)
- * prior to last treatment
- ** residue in control
- # no data available

A 2.1.3.1.2 Study 2 (RA-2144/00)

Comments of zRMS:	The study has already been evaluated in the Draft Renewal Assessment Report by RMS Poland (DRAR, 2018). Two trials on cereals have been conducted in northern Europe to determine residues of flufenacet in grain and straw after one application of Flufenacet& Diflufenican 600 SC at rate of 0.6 L/ha (240 g flufenacet /ha). The applications were carried out at growth stage 13. The analytical method 00346 was used to determine the total residues of flufenacet. The Limit of Quantitation (LOQ) was 0.05 mg/kg for FOE 5043 total residue in grain and 0.10 mg/kg in straw. The single recovery values for all analytes and matrices examined range from 72 to 111% and the overall revoceries for each sample material are in the range of 84 to 85% with relative standard deviations between 8.0 and 15.0% (n=12). All results of the method validation are in accordance with the general requirements for residue analytical methods, therefore the method was validated successfully. No residues were detected in grain samples of barley and wheat. In straw, the residues ranged from <0.10 mg/kg to 0.11 mg/kg. The study is acceptable.

Reference:	**KCA 6.3.1.1/02**
Title:	Determination of residues of FOE 5043 in/on wheat and barley following spray application of FOE 5043 & Diflufenican (600 SC) to winter wheat and winter barley in the field in Northern and Southern France, Germany and Spain
Report:	Hoffmann, M.; 2002; RA-2144/00; M-058156-01-1
Authority registration No:	
Guideline(s):	EU-Ref: Council Directive 91/414/EEC Residues in or on treated products, food and feed; not stated fulfils EU 7029/VI/95 rev.5 dated 22 July 1997
Deviations:	none
GLP/GEP:	yes
Acceptability:	yes
Duplication (if vertebrate study):	

Material and methods

Two trials on winter wheat and two trials on winter barley were conducted during the 2000/2001 growing season in northern and southern France, Germany and Spain using 'Flufenacet + Diflufenican SC 600'. The plants were treated at the growth stage BBCH 13 (3 leaves unfolded), which was usually in autumn (October - December), except in the Spanish trial, in which treatment was in February. The application rate was 240 g flufenacet /ha, except in the Spanish trial, in which the applied rate was slightly higher (254 g flufenacet/ha).

Grain and straw samples were taken at normal harvest, which was between 148 and 254 days after application.

All the samples were analysed for residues of flufenacet according to the method 00346 (Seym, M.; 1995, M-018864-02-1) which yields the combined level of the parent compound and all its metabolites containing the N fluorophenyl-N-isopropyl functional group. Residues are expressed as parent flufenacet. The method was evaluated in the Monograph (France 1997).

Recovery rates were determined prior to and concurrently with the sample analysis in order to check the performance of the method. Fortification was performed by spiking control samples with one of the following compounds or a mixture thereof: parent flufenacet, flufenacet oxalate, flufenacet sulfonic acid, flufenacet thioglycolate sulfoxide. The recovery-rates and corresponding relative standard deviations

(RSD) obtained during the conduct of this study were acceptable with mean value in the range of 70-110% and RSD < 20%.
No residues were found in any of the untreated samples, i.e. residues were < LOQ for flufenacet.

Table A 11: Summary of the study RA-2144/00 trials

Total residue flufenacet (determined as FOE 5043 trifluoro acetamide, calculated as flufenacet)

Trial No./ Location/ EU zone/ Year	Commodity/ Variety	Date of 1.Sowing or planting 2.Flowering 3. Harvest	Application rate per treatment			Dates of treatment or no. of treatments and last date	Growth stage at last treatment or date	Portion analyzed	Residues (mg/kg)	PHI (days)	Details on trial
			kg a.s./ ha	Water (l/ha)	kg a.s./hl				Total residue flufenacet		
	(a)	(b)				(c)				(d)	(e)
RA-2144/00 R 2000 0568/7 0568-00-T1 Germany Versuchsgut Höfchen, D-51399 Burscheid Europe, North, F 2000	Barley, winter Theresa	1) 29.09.2000 2) 15.05.2001 - 21.05.2001 3) 23.07.2001	0.2400	300	0.080	31.10.2000/0	3 leaves unfolded	grain straw	<0.05 <0.10	254 254	(f) RA-2144/00 (g) Flufenacet & Diflufenican 600 SC, (h) Spraying, (i) Total residue flufenacet: 00346 (j) Total residue flufenacet, grain and straw: 0.05 mg/kg and 0.1 mg/kg, respectively (k) method 00346, method validation was also done in the study RA-2144/00 prior to analysis (l) grain and straw: 216 days
RA-2144/00 R 2000 0566/0 0566-00-T1 France, north F-37310 Chambourg sur Indre Europe, North, F 2000	Wheat, winter Isengrain	1) 14.10.2000 2) 16.05.2001 - 25.05.2001 3) 12.07.2001	0.2400	300	0.080	15.11.2000/0	3 leaves unfolded	grain straw	<0.05 <0.10	243 243	(f) RA-2144/00 (g) Flufenacet & Diflufenican 600 SC, (h) Spraying, (i) Total residue flufenacet: 00346 , (j) Total residue flufenacet, grain and straw: 0.05mg/kg and 0.1 mg/kg, respectively (k) method 00346, method validation was also done in the study RA-2144/00 prior to analysis (l) grain and straw: 211 days

Trial No./ Location/ EU zone/ Year	Commodity/ Variety	Date of 1.Sowing or planting 2.Flowering 3. Harvest	Application rate per treatment			Dates of treatment or no. of treatments and last date	Growth stage at last treatment or date	Portion analyzed	Residues (mg/kg)	PHI (days)	Details on trial
			kg a.s./ ha	Water (l/ha)	kg a.s./hl				Total residue flufenacet		
	(a)	(b)				(c)				(d)	(e)
RA-2144/00 R 2000 0570 9 0570-00 Spain E-08289 Veciana 2001	Barley, winter Graphic	1) 29.11.2000 3) 03.07.2001	0.2540	317.5	0.0800	05.02.2001/0	3 leaves unfolded	grain straw	<0.05 0.11	148 148	(f) RA-2144/00 (g) Flufenacet & Diflufenican 600 SC, (h) Spraying, (i) Total residue flufenacet: 00346 , (j) Total residue flufenacet, grain and straw: 0.05 mg/kg and 0.1 mg/kg, respectively (k) method 00346, method validation was also done in the study RA-2144/00 prior to analysis (l) grain and straw: 224 days
RA-2144/00 R 2000 0567 9 0567-00 France F-31620 Gargas 2000	Wheat, winter Soissons	1) 11.11.2000 2) 03.05.2001 - 15.05.2001 3) 02.07.2001	0.2400	300	0.0800	18.12.2000/0	3 leaves unfolded	grain straw	<0.05 <0.10	196 196	(f) RA-2144/00 (g) Flufenacet & Diflufenican 600 SC, (h) Spraying, (i) Total residue flufenacet: 00346 (j) Total residue flufenacet, grain and straw: 0.05mg/kg and 0.1 mg/kg, respectively (k) method 00346, method validation was also done in the study RA-2144/00 prior to analysis (l) grain and straw: 196 days

Abreviations:

- (a) According to CODEX Classification / Guide
- (b) Only if relevant
- (c) Year must be indicated
- (d) Days after last application (Label pre-harvest interval, PHI, underline)
- (e) Remarks may include: Climatic conditions; Reference to analytical method and information which metabolites are included
- (f) Study reference
- (g) Formulation type
- G greenhouse F field
- (h) Application method
- (i) Method information
- (j) LOQ
- (k) Method validation
- (l) Storage (max)
- * prior to last treatment
- ** residue in control
- # no data available

A 2.1.4 Magnitude of residues in livestock

A 2.1.4.1 Livestock feeding studies

No additional study has been submitted.

A 2.1.4.1.1 Poultry

No additional study has been submitted.

A 2.1.4.1.2 Ruminants

No additional study has been submitted.

A 2.1.4.1.3 Pigs

No additional study has been submitted.

A 2.1.4.1.4 Fish

No additional study has been submitted.

A 2.1.5 Magnitude of residues in processed commodities (Industrial Processing and/or Household Preparation)

A 2.1.5.1 Distribution of the residue in peel/pulp

No additional study has been submitted.

A 2.1.5.2 Processing studies on a core set of representative processes

No additional study has been submitted.

A 2.1.6 Magnitude of residues in representative succeeding crops

Comments of zRMS:	The study has already been evaluated in the Draft Renewal Assessment Report by RMS Poland (DRAR, 2018). Four field residue trials were conducted in Northern Europe (United Kingdom, Germany and France). The purpose of this study was to determine the magnitude of the total residue of flufenacet (FOE 5043) in/on cereals (winter wheat and winter barley) grown as rotational crops following the preceding crop potatoes. Potatoes and cereals were both treated with one spray application with a flufenacet containing product (Artist 41.5 WG for poatoes and Liberator 500 SC for cereals). No residues were apparent in green material of cereals collected at growth stage BBCH 29 - 30 or grain and straw sampled at harvest (BBCH 89). The findings show that treatment of the preceding crop with a flufenacet containing product at the maximum field rate does not result in measurable residue levels in/on cereals grown as rotational crops. No uptake from the soil into the following crop has been observed. Analytical Method 00346/E004: The Limit of Quantification (LOQ) for total residues of flufenacet was 0.01 mg/kg for grain, 0.05 mg/kg for green material and 0.10 mg/kg for straw. No residues of flufenacet were determined in any of the control samples. The mean of the concurrent recoveries was for all matrices and for all fortification levels within the acceptable range of 70 - 110%. The study is acceptable.

Reference:	**KCA 6.6.2/01**
Title:	Determination of the residues of FOE 5043 in/on the rotational crops cereals after spraying of Artist (41.5 WG) and Liberator (500 SC) in the field in the United Kingdom, Germany and Northern France
Report:	Melrose, I.; Erler, S.; 2008; RA-2020/06; M-306269-01-1
Authority registration No:	
Guideline(s):	EU-Ref: Council Directive 91/414/EEC of July 15, 1991, Annex II, part A, section 6 and Annex III, part A, section 8 Residues in or on Treated Products, Food and Feed EC guidance working document 7524/VI/95 rev. 2 (1997-07-22) OECD Guideline for testing of Chemicals; Residues in rotational crops (limited field studies), No. 504, 8 Jan. 2007
Deviations:	not specified
GLP/GEP:	yes
Acceptability:	yes
Duplication (if vertebrate study):	

The purpose of this study was to determine the magnitude of flufenacet residues in cereals (winter wheat and winter barley) grown as rotational crops following the preceding crop potato. Potatoes and cereals were both treated with one spray application with a flufenacet containing product within the same calendar year. The study objective was to investigate whether treatment of the preceding crop with a flufenacet containing product has an impact on the residue levels determined in cereals grown as the following crop. The application rates for flufenacet correspond to the maximum registered rates for a spring crop (potatoes, maize, *i.e.* 600 g a.s./ha) and cereals (240 g a.s./ha). The trials were performed in northern Europe (the United Kingdom, Germany and Northern France).

Material and methods

This study comprises four supervised residue trials with potatoes followed by cereals (2 trials on barley and wheat, each). All plots received the application of 'Flufenacet + Metribuzin 41.5 WG' to potato plants pre emergence with an application rate of 2.5 kg/ha of test item, corresponding to 0.6 kg flufenacet /ha. The water rate was 300 L/ha. After harvesting potatoes, the aerial parts of the plants were incorporated into soil in order not to remove potential residues from the plot. Cereals were sown 133 - 158 days after application on potatoes. The application of 'Flufenacet + Diflufenican 500 SC' on cereals (wheat or barley) was performed between growth stages BBCH 12-22 but not later than November. The application rate was 0.6 L/ha of test item, corresponding to 0.24 kg flufenacet/ha. The water rate was also 300 L/ha.
For residue analysis, samples were taken from the treated and the control plots. Only the rotational crops (cereals) were sampled for analysis and the samples were analysed for flufenacet residues. Samples were collected at growth stage BBCH 30 (green material) and at harvest (BBCH 89, grain and straw).

The total residue of flufenacet in/on the collected samples was determined according to the method 00346 which yields the combined level of the parent compound and all its metabolites containing the N-fluorophenyl-N-isopropyl functional group. The total residue flufenacet is determined as FOE 5043 trifluoro acetamide and the residue is expressed as flufenacet equivalents. For grain, supplement E004 (Rzepka, S.; 2006; M-277805-01-1, Section 5) was applied which provides a lower LOQ for grain than the basic method. The method was modified for the clean-up of grain samples since SPE clean-up was not necessary.

Findings

Recovery rates were determined prior to analysing the samples in order to validate the method and concurrently with the sample analysis. Fortification was performed by spiking control samples with one of the following compounds or a mixture thereof: parent flufenacet, flufenacet oxalate, flufenacet sulfonic acid, flufenacet thioglycolate sulfoxide. The recovery-rates and corresponding relative standard deviations (RSD) were satisfactory, as shown in Table A for pre-validation recoveries and Table for concurrent recoveries.

No flufenacet residues were found in any of the untreated samples. Tables compiles the residue levels found in samples of treated cereals sown after a normal re-planting interval following potatoes which were also treated with a flufenacet containing product. The total residue of flufenacet was found to be less than the LOQ in green material (< 0.05 mg/kg), grain (< 0.01 mg/kg) and straw (< 0.1 mg/kg) in all treated samples.

Table A 12: Pre validation data for flufenacet and its metabolites on wheat grain

Analyte	FL [mg/kg]	Single Values [%]	Mean Value [%]	RSD [%]	LOQ [mg/kg]
Flufenacet (FOE 5043)	0.01	107; 102; 99; 90; 70	94	16	0.01
FOE 5043 Oxalate Hydrate	0.01	70; 90; 78; 61	75	16	0.01
FOE 5043 Sulfonic Acid Sodium Salt	0.01	71; 67; 64; 74	69	6	0.01
FOE 5043 Thioglycolate Sulfoxide	0.01	70; 78; 71; 74	73	5	0.01

FL = Fortification Level RSD = Relative Standard Deviation, LOQ = Practical Limit of Quantification
Residues were determined as FOE 5043 trifluoroacetamide and expressed as flufenacet (FOE 5043) equivalents

Table A 13: Procedural recovery data for flufenacet
The LOQ is marked in bold.

Study Trial No. Plot No. GLP Year	Crop	Portion analysed	a.s./metabolite	n	Fortification level (mg/kg)	Recovery (%)				
						Individual recoveries	Min	Max	Mean	RSD
RA-2020/06 R 2006 0420/3 0420-06/01 R 2006 0418/1 0418-06/01 R 2006 0003/8 0003-06/01 R 2006 0046/1 0046-06/01 GLP: yes 2006	Barley, winter Wheat, winter (R1)	green material	FOE 5043 metabolite mix	3	**0.050**	107; 93; 82	82	107	94	13.3
		straw	FOE 5043 metabolite mix	2	**0.10**	113; 113	113	113	113	
				2	1.00	101; 87	87	101	94	
				4	overall		87	113	104	12.0
		grain	FOE 5043 metabolite mix	2	**0.010**	87; 91	87	91	89	
				2	0.40	84; 81	81	84	83	
				4	overall		81	91	86	5.0

FL = Fortification Level; RSD = Relative Standard Deviation, LOQ = Practical Limit of Quantification
Residues were determined as FOE 5043 trifluoroacetamide and expressed as flufenacet (FOE 5043) equivalents
FOE 5043 Mix : ¼ of FOE 5043, ¼ FOE 5043 Oxalate Hydrate, ¼ of FOE 5043 Sulfonic Acid Sodium Salt, ¼ of FOE 5043 Thioglycolate Sulfoxide.

Table A 14: Summary of the rotational crop trials for cereals, potato as preceding crop

Reference	**:**	**flufenacet** **RA-2020/06**		
GLP	**:**	yes	**Sample storage conditions**	**:** green material, grain and straw: 371, 234 and 256 days, respectively at <-18°C
Crop group/ Preceeding Crop	**:**	Root and tuber/potato	**Analytical method**	**:** 00346 (green material , straw) validated in method report 00346/E004 (grain); validated in method report and residue report RA-2020/06
Crop Group/ Succeding Crop		Cereal/wheat and barley	**Limit of quantification (mg/kg)**	**:** total residue flufenacet (00346/E004): 0.01 mg/kg grain, total residue flufenacet (00346): 0.05 mg/kg green material, 0.10 mg/kg straw
Indoor/Outdoor	**:**	Outdoor		
Formulation	**:**	FFA+MRB WG 41.5 (preceding crop) DFF+FFA SC 500 (following crop)	**Limit of detection (mg/kg)**	**:** 0.3 × LOQ
Content of active substance (g/kg or g/l)	**:**	WG 41.5: 240 g/kg SC 500: 400 g/L	**Residues calculated as**	**:** total residue flufenacet determined as the derivative 2,2,2-trifluoro-N-(4-fluorophenyl)-N-isopropylacetamide (also called 4-fluoro-N-methylethyl benzenamine trifluoroacetamide or FOE 5043 trifluoroacetamide in the documentation)

Analyte: Total residue flufenacet (determined as FOE 5043 Trifluoro acetamide, calculated as flufenacet)

Trial No./ Location/ EU zone/ Year	Commodity/ Variety	Date of 1.Sowing or planting 2.Flowering 3. Harvest	Application rate per treatment			Dates of treatment or no. of treatments and last date	Growth stage at last treatment or date	Portion analyzed	Residues (mg/kg)	PHI (days)	Details on trial
			kg a.s./ ha	Water (l/ha)	kg a.s./hl				Total residue flufenacet		
	(a)	(b)				(c)				(d)	(e)
RA-2020/06 R 2006 0003 8 0003-06-T1 United Kingdom GB-SG8 85S Great Chishill	Potato Maris Peer (Rotation: 0)	1) 28.04.2006 2) 13.07.2006 - 15.07.2006 3) 01.09.2006 - 15.09.2006	A: 0.60	A: 300	A: 0.20	03.05.2006/0	End of dormancy				(f) RA-2020/06 (g) A: Flufenacet & Metribuzin WG 41.5, B: Flufenacet & Diflufenican SC 500, (h) Spraying, (i) Total residue flufenacet:for grain in method 00346/E004; for green material and straw in method 00346 (j) Total residue flufenacet, green material, 0.05 mg/kg, grain 0.01 mg/kg , straw 0.1 mg/kg (k) 00346, for grain in 00346/E004 and RA-2020/06 (l) green material, grain and straw: 323, 192 and 214 days, respectively Plant-back interval 145 days
Europe, North, F 2006	Wheat, winter Consort (Rotation: 1)	1) 25.09.2006 2) 15.06.2007 - 20.06.2007 3) 15.08.2007 - 25.08.2007	B: 0.24	B: 300	B: 0.080	27.10.2006/177	3 leaves unfolded	green material grain straw	<0.05 <u>≤0.01</u> <u>≤010</u>	179 294 294	
RA-2020/06 R 2006 0046 1 0046-06-T1 Germany D-51799 Burscheid	Potato Cilena (Rotation: 0)	1) 09.05.2006 2) 12.06.2006 - 28.06.2006 3) 13.09.2006	A: 0.60	A: 300	A: 0.20	17.05.2006/0	End of dormancy				(f) RA-2020/06 (g) A: Flufenacet & Metribuzin WG 41.5, B: Flufenacet & Diflufenican SC 600, (h) Spraying, (i) Total residue flufenacet:for grain in method 00346/E004; for green material and straw in method 00346 (j) Total residue flufenacet, green material, 0.05 mg/kg, grain 0.01 mg/kg , straw 0.1 mg/kg (k) 00346, for grain in 00346/E004 and RA-2020/06 (l) green material, grain and straw: 369, 223 and 245 days, respectively Plant-back interval 133 days
Europe, North, F 2006	Wheat, winter Limes (Rotation: 1)	1) 27.09.2006 2) 17.06.2007 - 21.06.2007 3) 17.07.2007	B: 0.24	B: 300	B: 0.080	13.10.2006/149	2 leaves unfolded	green material grain straw	<0.05 <u>≤0.01</u> <u>≤010</u>	147 277 277	

Trial No./ Location/ EU zone/ Year	Commodity/ Variety	Date of 1.Sowing or planting 2.Flowering 3. Harvest	Application rate per treatment			Dates of treatment or no. of treatments and last date	Growth stage at last treatment or date	Portion analyzed	Residues (mg/kg)	PHI (days)	Details on trial
			kg a.s./ ha	Water (l/ha)	kg a.s./hl				Total residue flufenacet		
	(a)	(b)				(c)				(d)	(e)
RA-2020/06 R 2006 0418 1 0418-06-T1 Germany D-49377 Vechta-Langenförden	Potato Cilena (Rotation: 0)	1) 04.05.2006 2) 29.06.2006 - 19.07.2006 3) 18.09.2006 - 22.09.2006	A: 0.60	A: 300	A: 0.20	16.05.2006/0	Beginning of root formation				(f) RA-2020/06 (g) A: Flufenacet & Metribuzin WG 41.5, B: Flufenacet & Diflufenican SC 600, (h) Spraying, (i) Total residue flufenacet:for grain in method 00346/E004; for green material and straw in method 00346 (j) Total residue flufenacet, green material, 0.05 mg/kg, grain 0.01 mg/kg , straw 0.1 mg/kg (k) 00346, for grain in 00346/E004 and RA-2020/06 (l) green material, grain and straw: 331, 224 and 246 days, respectively Plant-back interval 146 days
Europe, North, F 2006	Barley, winter Franziska (Rotation: 1)	1) 09.10.2006 2) 26.05.2007 - 02.06.2007 3) 16.07.2007 - 17.07.2007	B: 0.24	B: 300	B: 0.080	03.11.2006/171	3 leaves unfolded	green material grain straw	<0.05 <u>≤0.01</u> <u>≤010</u>	164 255 255	
RA-2020/06 R 2006 0420 3 0420-06-T1 France F-80700 Champien	Potato Pomme Fine (Rotation: 0)	1) 25.04.2006 2) 01.07.2006 - 25.07.2006 3) 15.09.2006 - 30.09.2006	A: 0.60	A: 300	A: 0.20	05.05.2006/0	Beginning of root formation				(f) RA-2020/06 (g) A: Flufenacet & Metribuzin WG 41.5, B: Flufenacet & Diflufenican SC 600, (h) Spraying, (i) Total residue flufenacet:for grain in method 00346/E004; for green material and straw in method 00346 (j) Total residue flufenacet, green material, 0.05 mg/kg, grain 0.01 mg/kg , straw 0.1 mg/kg (k) 00346, for grain in 00346/E004 and RA-2020/06) (l) green material, grain and straw: 371, 234 and 256 days, respectively Plant-back interval 158 days
Europe, North, F 2006	Barley, winter Colibri (Rotation: 1)	1) 10.10.2006 3) 06.07.2007 - 14.07.2007	B: 0.24	B: 300	B: 0.080	30.11.2006/209	2 tillers detectable	green material grain straw	<0.05 <u>≤0.01</u> <u>≤010</u>	97 218 218	

Abbreviations:

(a) According to CODEX Classification / Guide
(b) Only if relevant
(c) Year must be indicated
(d) Days after last application (Label pre-harvest interval, PHI, underline)
(e) Remarks may include: Climatic conditions; Reference to analytical method and information which metabolites are included
(f) Study reference
(g) Formulation type
(i) Method information
(j) LOQ
(k) Method validation
(l) Storage (max)

A 2.1.7 Other/Special Studies (KCA 6.10)

No additional study has been submitted.

Appendix 3 Pesticide Residue Intake Model (PRIMo)

A 3.1 TMDI calculations

Not performed for flufenacet.

A 3.2 IEDI calculations

Refined calculation mode

Chronic risk assessment: JMPR methodology (IEDI/TMDI)

No of diets exceeding the ADI : ---

	Calculated exposure (% of ADI)	MS Diet	Expsoure (µg/kg bw per day)	Highest contributor to MS diet (in % of ADI)	Commodity / group of commodities	2nd contributor to MS diet (in % of ADI)	Commodity / group of commodities	3rd contributor to MS diet (in % of ADI)	Commodity / group of commodities	Exposure resulting from MRLs set at the LOQ (in % of ADI)	Exposure resulting from commodities not under assessment (in % of ADI)
TMDI/NEDI/IEDI calculation (based on average food consumption)	35%	NL toddler	1,75	12%	Milk: Cattle	7%	Maize/corn	4%	Potatoes	27%	
	23%	DK child	1,16	6%	Rye	4%	Wheat	3%	Milk: Cattle	16%	
	20%	GEMS/Food G10	1,01	4%	Wheat	3%	Soyabeans	3%	Potatoes	12%	
	20%	GEMS/Food G06	1,01	7%	Wheat	4%	Tomatoes	2%	Potatoes	11%	
	20%	UK infant	0,98	8%	Milk: Cattle	3%	Potatoes	3%	Wheat	14%	
	19%	GEMS/Food G08	0,97	4%	Wheat	4%	Potatoes	2%	Soyabeans	10%	
	19%	FR child 3 15 yr	0,97	5%	Wheat	5%	Milk: Cattle	2%	Potatoes	13%	
	19%	GEMS/Food G15	0,96	5%	Wheat	4%	Potatoes	2%	Soyabeans	10%	
	19%	NL child	0,95	5%	Milk: Cattle	4%	Wheat	3%	Potatoes	11%	
	19%	GEMS/Food G11	0,94	4%	Potatoes	4%	Soyabeans	4%	Wheat	10%	
	19%	RO general	0,93	5%	Wheat	4%	Potatoes	2%	Milk: Cattle	10%	
	19%	GEMS/Food G07	0,93	4%	Wheat	4%	Potatoes	2%	Soyabeans	10%	
	18%	SE general	0,89	4%	Bovine: Muscle/meat	4%	Potatoes	3%	Wheat	10%	
	18%	DE child	0,89	4%	Wheat	4%	Milk: Cattle	3%	Potatoes	11%	
	17%	FR toddler 2 3 yr	0,87	6%	Milk: Cattle	3%	Wheat	2%	Potatoes	12%	
	16%	ES child	0,82	4%	Wheat	2%	Milk: Cattle	2%	Potatoes	10%	
	16%	UK toddler	0,81	4%	Milk: Cattle	4%	Wheat	3%	Potatoes	9%	
	12%	PT general	0,62	5%	Potatoes	4%	Wheat	0,9%	Tomatoes	3%	
	11%	NL general	0,53	2%	Potatoes	2%	Wheat	2%	Milk: Cattle	6%	
	10%	DE general	0,52	2%	Milk: Cattle	2%	Wheat	1%	Potatoes	7%	
	10%	IE adult	0,51	2%	Wheat	2%	Potatoes	0,9%	Milk: Cattle	5%	
	10%	FI 3 yr	0,51	5%	Potatoes	1%	Wheat	1%	Cucumbers	4%	
	10%	DE women 14-50 yr	0,50	2%	Milk: Cattle	2%	Wheat	1%	Potatoes	6%	
	10%	IT toddler	0,49	7%	Wheat	1%	Tomatoes	0,9%	Potatoes	2%	
	10%	LT adult	0,48	3%	Potatoes	1%	Rye	1%	Wheat	5%	
	9%	ES adult	0,47	2%	Wheat	1,0%	Milk: Cattle	0,9%	Potatoes	6%	
	9%	FR infant	0,44	3%	Milk: Cattle	2%	Potatoes	0,8%	Wheat	6%	
	8%	FI 6 yr	0,40	4%	Potatoes	1,0%	Wheat	0,7%	Cucumbers	3%	
	8%	FR adult	0,38	2%	Wheat	0,9%	Milk: Cattle	0,7%	Potatoes	5%	
	7%	DK adult	0,37	1%	Potatoes	1%	Wheat	1%	Milk: Cattle	5%	
	7%	IT adult	0,33	4%	Wheat	1%	Tomatoes	0,6%	Potatoes	2%	
	6%	UK adult	0,31	2%	Wheat	1%	Potatoes	0,7%	Bovine: Muscle/meat	3%	
	6%	UK vegetarian	0,30	2%	Wheat	1%	Potatoes	0,7%	Milk: Cattle	3%	
	5%	PL general	0,23	3%	Potatoes	0,9%	Tomatoes	0,1%	Onions	1%	
	4%	FI adult	0,19	1%	Potatoes	0,7%	Rye	0,6%	Tomatoes	2%	
	4%	IE child	0,19	1%	Wheat	0,7%	Milk: Cattle	0,6%	Potatoes	2%	

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

A 3.3 IESTI calculations - Raw commodities

Table A 15: IESTI calculated for flufenacet using PRIMo (rev 3.1)

Results for children No. of commodities for which ARfD/ADI is exceeded (IESTI): ---				**Results for adults** No. of commodities for which ARfD/ADI is exceeded (IESTI): ---			
IESTI				**IESTI**			
Highest % of ARfD/ADI	Commodities	MRL / input for RA (mg/kg)	Exposure (µg/kg bw)	Highest % of ARfD/ADI	Commodities	MRL / input for RA (mg/kg)	Exposure (µg/kg bw)
4%	Wheat	0.1 / 0.05	0.72	2%	Wheat	0.1 / 0.05	0.42
2%	Barley	0.1 / 0.05	0.28	1%	Barley	0.1 / 0.05	0.24
0.4%	Rye	0.05 / 0.01	0.06	0.3%	Rye	0.05 / 0.01	0.05
0.07%	Oat	0.05 / 0.01	0.01	0.04%	Oat	0.05 / 0.01	0.01
Expand/collapse list							
Total number of commodities exceeding the ARfD/ADI in children and adult diets (IESTI calculation)							

A 3.4 IESTI calculations - Processed commodities

Table A 16: IESTI calculated for flufenacet using PRIMo (rev 3.1)

Results for children				**Results for adults**			
No of processed commodities for which ARfD/ADI is exceeded (IESTI):			---	No of processed commodities for which ARfD/ADI is exceeded (IESTI):			---
IESTI				**IESTI**			
Highest % of ARfD/ADI	Processed commodities	MRL / input for RA (mg/kg)	Exposure (µg/kg bw)	Highest % of ARfD/ADI	Processed commodities	MRL / input for RA (mg/kg)	Exposure (µg/kg bw)
4%	Wheat / milling (flour)	0,1 / 0,05	0,60	2%	Barley / beer	0,1 / 0,01	0,36
2%	Wheat / milling (wholemea	0,1 / 0,05	0,28	1%	Wheat / bread/pizza	0,1 / 0,05	0,22
1%	Rye / boiled	0,05 / 0,05	0,18	1%	Wheat / pasta	0,1 / 0,05	0,19
1%	Oat / boiled	0,05 / 0,05	0,18	0,5%	Wheat / bread	0,1 / 0,05	0,08
1%	Barley / cooked	0,1 / 0,05	0,18				
1%	Rye / milling (wholemeal)-I	0,05 / 0,05	0,18				
0,9%	Oat / milling (flakes)	0,05 / 0,05	0,15				
0,5%	Barley / milling (flour)	0,1 / 0,05	0,09				

Appendix 4 Additional information provided by the applicant

Not relevant.