Bayer CropScience

Document Title

Summary of the residues in or on treated products, food and feed
Diflufenican+Flufenacet SC600 (200+400)G

Data Requirements

EU Regulation 1107/2009 & EU Regulation 284/2013
Document MCP
Section 8: Residues in or on treated products, food and feed

According to the guidance document, SANCO 10181/2013, for preparing dossiers for the approval of a chemical active substance

Date

2014-03-18

Author(s)

[redacted]

Bayer CropScience

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Version history

Date	Data points containing amendments or additions[1] and brief description	Document identifier and version number

[1] It is suggested that applicants adopt a similar approach to showing revisions and version history as outlined in SANCO/10180/2013 Chapter 4 How to revise an Assessment Report

CP 8 RESIDUES IN OR ON TREATED PRODUCTS, FOOD OR FEED

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CP 8 RESIDUES IN OR ON TREATED PRODUCTS, FOOD OR FEED

Guidance provided in Annex to SANCO/11803/2010/Rev.7-PPP states that data and information on residues in or on treated products, food and feed shall be submitted, unless it is justified that the data and information already submitted for the active substance can be applied.

All data and evaluation relative to the active substance flufenacet is provided in the KCA Section 6 and MCA Section 6 (Data Point CA 6) of the active substance dossier.
A brief summary and cross reference to the relevant active substance documentation is provided here.

Since the representative formulation is a mixture product (Flufenacet + Diflufenican SC 600), some basic information on the mixing partner is also provided here and can be used for easy reference is so desired. The representative formulation contains 400 g/L flufenacet and 200 g/L diflufenican.

Flufenacet was included in Annex I of Directive 91/414/EEC on 01/01/2004, as notified in Directive 2003/84/EC dated 25 September 2003 wherein there is no specific provision under Part B which needs to be considered related to the metabolism and residue data.
The Monograph prepared by the Rapporteur Member State France in the context of the inclusion of flufenacet in Annex 1 of the Council Directive 91/414/EEC, the Review Report for flufenacet (7469/VI/98-Final – 3rd, July 2003) and the EFSA's Reasoned Opinion on the review of existing maximum residue levels (MRLs) for flufenacet according to Article 12 of Regulation (EC) No 396/2005 (EFSA Journal 2012;10(4):2689) are considered to provide the relevant scientific information for the review of the active substance. Further information relative to the residue section can be taken from the Complete List of Endpoints, Report of ECCO 73, Annex 2, 5 Residue Section.

Diflufenican was included into Annex I of Directive 91/414 on 01/01/2009 (Directive 2008/66/EC). In the Annex I Inclusion Directive for diflufenican there are no specific provisions under Part B which need to be considered related to metabolism and residue section. The Review Report and EFSA Scientific Report for diflufenican (SANCO/3782/08 – rev. 1, 14th March 2008; and EFSA Scientific Report 122 (2007)) and the EFSA Reasoned Opinion on existing MRLs (EFSA Journal 2013;11(6):3281) are considered to provide the relevant scientific information for the review of the product.

The product 'Flufenacet + Diflufenican SC 600' was also the representative formulation for evaluation of diflufenican in the EU peer review process.

Stability of Residues

Stability of residues during storage of samples

Flufenacet

In the EU review process storage stability data were evaluated for flufenacet and 5 metabolites (FOE-oxalate, FOE-sulfonic acid, FOE-thioglycolate sulfoxide, FOE-methylsulfoxide, FOE-methylsulfone) in matrices of corn, soybean (up to 28 months) and turnips (20 months). In the supplementary dossier additional storage stability information is provided on wheat commodities (wheat forage, grain and

straw) for flufenacet and the 5 metabolites for up to 21 months and for additional commodity groups of high protein content (dry bean seed) and high acid content (orange fruit) for up to 24 months (flufenacet, FOE-oxalate, FOE-sulfonic acid, FOE-thioglycolate sulfoxide).
In addition, in some samples of supportive trials from two residue studies (12-2001 and 12-2002) the requested temperature of -18°C was exceeded due to problems during the shipment of these samples. In order to address this deviation, a short term storage stability study was conducted. Residues of flufenacet proved to be stable under the experimental conditions tested reflecting the conditions during shipment.
For details please refer to CA 6.1.

Diflufenican
Storage stability studies were conducted with diflufenican in wheat forage, wheat grain and wheat straw. These data were evaluated during the EU review of the active substance (EFSA Scientific Report (2007) 122). The results indicate that diflufenican is stable under frozen conditions in wheat matrices for at least 24 months.

Stability of residues in sample extracts

Flufenacet
The stability of the residues in the sample extracts was checked during the development of the residue analytical methods. For details please refer to CA 4.1.2 and 4.2.

Diflufenican
Relevant information on the stability of diflufenican residues in the final extracts was investigated during development of the residue analytical method.

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.

Supplementary studies on metabolism in plants or livestock

Flufenacet
Metabolism in primary crops
In the EU review process plant metabolism studies with [Fluorophenyl-UL-^{14}C] and [Thiadiazole-2-^{14}C]flufenacet in different crop groups,- *i.e.* cereals (maize), pulses and oilseeds (soybean, cotton) - were evaluated. The table below compiles supplementary metabolism studies submitted in document MCA section 6. For details please refer to CA 6.2.

Table 8- 1: Overview of supplementary plant metabolism studies with ^{14}C-labeled flufenacet in primary crops

Crop	Application scenario	Label	Report	Reported in supplementary dossier Section 6
Potato	Pre- and post-emergence application	[Fluorophenyl-UL-^{14}C	[redacted], E. C.; [redacted], S. L.; 2000; M-020428-01-1	KCA 6.2.1/07
Wheat	Post emergence application	[Fluorophenyl-UL-^{14}C	[redacted], M. E.; [redacted], L. L.; 1997; M-002275-01-1	KCA 6.2.1/05
Corn (maize)	Post emergence application	[Fluorophenyl-UL-^{14}C	[redacted], M. E.; [redacted], L. L.; 1998; M-005755-01-1	KCA 6.2.1/06
Wheat	Post emergence application	[Thiadiazole-5-^{14}C]	[redacted], R.; [redacted], D.; 2013; M-444475-01-1	KCA 6.2.1/09
Potato	Pre-emergence application	[Thiadiazole-5-^{14}C]	[redacted], R; 2012; M-441506-02-1	KCA 6.2.1/08

Metabolism in livestock

The nature of flufenacet resides in hen and goat 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 table below compiles supplementary metabolism studies submitted in MCA section 6. Supplementary studies were conducted using [1-^{14}C] Trifluoroacetic acid (goat and hen) and [Thiadiazole-2-^{14}C] thiadone-N-glucoside (goat) both being main plant metabolites. A bioconcentration study with bluegill sunfish also reporting metabolism data in fish is also submitted. For details please refer to CA 6.2.2, 6.2.3 ad 6.2.5.

Table 8-2: Overview of supplementary livestock metabolism studies with ^{14}C-labeled flufenacet

Animal	Label	Report	Reported in supplementary dossier Section 6
Laying hen	[1-^{14}C] Trifluoroacetic acid	[redacted], J.; et al.; 2013; M-463376-01-1	KCA 6.2.2/04
Lactating goat	[Thiadiazole-2-^{14}C] thiadone-N-glucoside	[redacted], M. E et al.: 2002; M-079251-01-1	KCA 6.2.3/04
Lactating goat	[1-^{14}C] Trifluoroacetic acid	[redacted], J.; et al.; 2013; M-444459-01-1	KCA 6.2.3/05
Fish	[fluorophenyl-UL-^{14}C	[redacted], G. G.; 1994; M-003803-01-1	KCA 6.2.5/01
Fish	[Fluorophenyl-UL-^{14}C	[redacted], W. M.; [redacted], K. S.; 1994; M-003804-01-1	KCA 6.2.5/02

Diflufenican

Metabolism in primary crops

Metabolism data on wheat were evaluated during the EU review of the active substance and in the EFSA Reasoned Opinion on existing MRLs (2013). Pyridine, difluorophenyl and trifluoromethylphenyl ring labelled [^{14}C] diflufenican was applied as either a pre-emergence application or a post-emergence foliar application (at growth stage BBCH 13/14) with an application rate of 187.5 to 400 g as/ha. The relevant residue in plants was defined as parent diflufenican.
The wheat metabolism studies for post-emergence application of diflufenican which were evaluated during the EU review are considered to adequately support the intended uses of 'Flufenacet + Diflufenican SC 600' which involve application rates up to 120 g diflufenican/ha.

Metabolism in livestock

The metabolism and distribution of residues was investigated in lactating cow and laying hen upon administration of difluorophenyl and pyridine ring labelled [^{14}C] diflufenican.
The cow and hen metabolism studies were both reviewed in the Draft Assessment Report and considered acceptable by the Rapporteur Member State. In the EFSA Conclusions on the evaluation of diflufenican (EFSA Scientific Report (2007) 122) the hen metabolism study was mentioned but not assessed since the anticipated exposure of poultry to diflufenican residues was estimated to be negligible. Based on the cow metabolism study the relevant residue in livestock commodities was defined as parent diflufenican.

The metabolism studies on plants and livestock are considered to adequately support the representative uses of the product 'Flufenacet + Diflufenican SC 600'.

Supplementary residue trials (supervised field trials)

Cereals

The representative uses of the product 'Flufenacet + Diflufenican SC 600' supporting the renewal of approval for flufenacet are summarised in Table 8-3.

Table 8-3: Summary of the representative uses of 'Flufenacet+Diflufenican SC 600' supporting the renewal of approval for flufenacet

Crop	Region*	Maximum Number of Applications	Growth stage at application	Maximum Rate flufenacet (g a.s./ha)	Maximum Rate diflufenican (g a.s./ha)	Minimum PHI (days)
Cereals (winter wheat, winter barley, winter rye)	EU-N	1	Early post-emergence BBCH 10-13 (autumn use)	240	120	n.a.
Cereals (winter wheat, winter barley, winter rye)	EU-N	1	Pre-emergence; early post-emergence BBCH 00-22	120	60	n.a.
Cereals (wheat, barley)	EU-S	1	Early post-emergence BBCH 11-13	240	120	n.a.
Cereals (wheat, barley)	EU-S	1	Early post-emergence BBCH 11-13	160	80	n.a.

* EU-N northern Europe EU-S southern Europe
n.a. not applicable, the PHI is covered by the vegetation period of the crop from treatment to harvest.

Flufenacet

The GAP of the representative use in cereals (wheat, barley, rye, oats) supported with the Annex II dossier and taken into account for Annex I inclusion is summarised in Table 8-4. The GAP corresponds to the critical GAP for the northern climatic zone supported for the renewal of approval for flufenacet.

Table 8-4: Summary of the representative use of 'Flufenacet WG 60' considered for Annex I inclusion of the active substance flufenacet

Crop	Region *	Maximum Number of Applications	Growth stage	Maximum Rate (g as/ha)	Minimum PHI (days)
Winter wheat Winter barley Winter rye	EU-N	1	pre-emergence to early post emergence (autumn) 2nd leaf stage of weeds	240	n.a.

*EU-N: northern Europe
n.a. : not applicable. The pre-harvest interval covers the vegetation period of the crop until harvest.

In total 18 trials on wheat, barley and rye, conducted in the northern European climatic zone were evaluated for Annex I inclusion (one trial providing data only on plant green material). The residue trials considered to grant Annex I inclusion of flufenacet support application of flufenacet to cereals at the rate of 240 g as/ha at pre- or early post emergence growth stages up to mid of tillering (BBCH 11 to 25). The trials were considered suitable to support the product Flufenacet WG 60. No residues were determined in cereal grain (< 0.05 mg/kg) or straw (< 0.1 mg/kg) at harvest.
Table 8-5 summarises the residue trial data (wheat, rye, barley) evaluated in the EU review process.

Table 8-5: Summary of flufenacet residue data supporting the representative use considered for Annex I inclusion of the active substance flufenacet

Application	Sample material	n	Residue level (mg/kg)		
			Min.	Max.	Median
Northern Europe					
240 (186-260) g as/ha	Grain	17	< 0.05	< 0.05	< 0.05
	Straw	17	< 0.1	< 0.1	< 0.1
	Green material (BBCH 51)	18	< 0.05	< 0.05	< 0.05

Since WG and SC formulations are known to produce comparable residues – particularly when applied early during the crop development - ,the residue trials reviewed in the Annex II dossier of flufenacet are considered to adequately support the representative use of 'Flufenacet + Diflufenican SC 600' in northern Europe.

An overview on the supplementary residue data for the northern zone using mixed formulations with diflufenican and for the southern climatic zone which are reported in the MCA document, section 6.3 is given in the table below.

Table 8-6: Summary of supplementary residue data on cereals supporting the representative GAPs for renewal of approval of flufenacet

Application rate flufenacet (g as/ha)	Region	Formulation	Crop	Sample material	n	Residue level (mg/kg) flufenacet		
						Min.	Max.	STMR
240	EU-N	FFA+DFF WG 60 FFA+DFF SC 600	wheat, barley	grain	6	<0.05	<0.05	<0.05
				straw	6	<0.10	<0.10	<0.10
110-120	EU-N	FFA+FLT+DFF SC 360	Wheat, barley	grain	8	<0.01	0.022	<0.01
				straw	8	<0.05	<0.05	<0.05
220-254	EU-S	FFA+DFF SC 600	Wheat, barley	grain	9	<0.01	0.05	<0.01
				straw	9	<0.05	0.11	0.06
120-126	EU-S	FFA+FLT+DFF SC 360 FFA+DFF WG 70	Wheat, barley	grain	12	<0.01 <0.05	0.035/ <0.05	0.022
				straw	12	<0.05	0.069	<0.05

EU-N northern Europe EU-S southern Europe n: number of trials
FFA+DFF WG 60 containing 40% flufenacet and 20% diflufenican
FFA+ DFF SC600 containing 400 g/L flufenacet and 200 g/L diflufenican
FFA+FLT+DFF SC 360 containing 120 g/L flufenacet, 120 g/L flurtamone and 120 g/L diflufenican
FFA+DFF WG 70 containing 35% flufenacet and 35% diflufenican

For further details please refer to CA 6.3.1

<u>Diflufenican</u>

Table 8-7 summarises the representative use of the formulation 'Flufenacet + Diflufenican SC 600' which was considered for Annex I inclusion of the active substance diflufenican.

Table 8-7: Summary of representative use of 'Flufenacet + Diflufenican SC 600' considered for Annex I inclusion of the active substance diflufenican

Crop	Region *	Maximum Number of Applications	Latest Growth stage	Maximum Rate (g as/ha)	Minimum PHI (days)
Winter wheat Winter barley Winter rye	EU-N EU-S	1	BBCH 13 (application in autumn)	120	n.a.

* EU-N: Northern Europe; EU-S: Southern Europe
n.a. : not applicable. The pre-harvest interval covers the vegetation period of the crop until harvest.

In the EFSA Scientific Report (2007) 20 trials on wheat and barley (9 trials from the northern zone and 11 trials from the southern zone) were deemed acceptable to support the representative use. The residue trials considered to grant Annex I inclusion of diflufenican actually support application of diflufenican to cereals during tillering in spring at the rate of 150 g as/ha. Therefore, the representative uses of 'Flufenacet + Diflufenican SC 600' are covered by the evaluation and risk assessment conducted during the EU review of diflufenican and, in principle, no supplementary residue trials are necessary to support this GAP.

Table 8-8: Summary of diflufenican residue data supporting the representative use considered for Annex I inclusion of the active substance diflufenican

Application	Sample material	n	Residue level (mg/kg)		
			Min.	Max.	Median
Northern Europe					
150 g as/ha at latest BBCH 30 (application in spring)	Grain	9	<0.01	<0.01	<0.01
	Straw	9	<0.05	0.17	<0.05
Southern Europe					
150 g as/ha at latest BBCH 30 (application in spring)	Grain	8	<0.01	<0.01	<0.01
	Straw	8	<0.05	0.07	<0.05
126 g as/ha at latest BBCH 13 (application in autumn)	Grain	3	<0.01	<0.01	<0.01
	Straw	3	<0.02	<0.02	<0.02

Supplementary residue data were generated for diflufenican using combination products with flufenacet. The studies are reviewed in document MCA section 6.3 relative to flufenacet.
Detailed information relative to diflufenican (and flufenacet) can be obtained from the Tier 1 summary forms ([redacted], M, 2014; M-478066-01-1) if considered necessary.

Supplementary Livestock Feeding Studies

Flufenacet

During the EU peer review process and recently in the EFSA Reasoned Opinion on existing MRLs (2012) it was concluded that on the basis of the animal metabolism studies, after exposure to the maximum dietary burden (about 200 times lower than the dose level in the metabolism studies)

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 and MRLs and risk assessment values for the relevant commodities in ruminants, pigs and poultry can be established at the LOQ level .The representative uses on cereals supported in the present dossier are shown not to produce higher residues than those previously evaluated.
Taking into account the findings from the ruminant feeding study with the main plant metabolite EOE oxalate which was conducted for the US it was concluded that no detectable residues of EOE oxalate are to be expected in products of animal origin.
For details please refer to CA 6.4.

Diflufenican
In the EFSA Scientific Report (2007) 122 it was concluded that for the representative use supported during the EU evaluation of diflufenican, no feeding studies and no MRLs for animal products were necessary.

Supplementary Studies on Industrial Processing and/or Household Preparation

Flufenacet
The relevant residues of flufenacet in raw agricultural commodities are determined by means of a common moiety method capturing the parent substance and all metabolites that contain the N-fluorophenyl-N-isopropyl functional group according to the residue definition in plants. This residue analytical method for risk assessment and enforcement involves a hydrolysis at conditions that are much harsher than those used to investigate the nature of processed residues. Therefore, a study on the nature of processed residues (high temperature hydrolysis according to OECD GL 507) can be omitted.
Supplementary processing data are reported in document MCA section 6 for wheat and barley. For wheat, the processed fractions resulting from milling, baking, production of wheat germs and starch were investigated. For barley, processed fractions from pearl barley processing and preparation of alcoholic beverages (malting, brewing, distillation) were investigated for flufenacet residues. Concentration of residues was observed in some by-products, germs and bran.
For details please refer to CA 6.5.

Diflufenican
As residues of diflufenican exceeding 0.1 mg/kg are not expected in the treated cereal grain, and since the chronic exposure does not exceed 10 % of the ADI, there is no need to investigate the effect of industrial and/or household processing. This was considered acceptable during the EU review of diflufenican (EFSA Scientific Report (2007) 122).

Supplementary Studies for Residues in Representative Succeeding Crops

Flufenacet
Metabolism in rotational crops was found to be very similar to primary crop metabolism. In the EU review process rotational crop metabolism studies using [fluorophenyl-UL-^{14}C] and [thiadiazole-2-^{14}C]flufenacet were evaluated. In the Monograph and in the EFSA reasoned opinion on existing

MRLs it was concluded that flufenacet residue levels in rotational crop commodities are not expected to exceed 0.01 mg/kg, provided flufenacet is applied in compliance with the GAPs that involve application rates ranging from 150 – 600 g as/ha.

In the supplementary dossier, a rotational crop metabolism study is reported using [thiadiazole-5-^{14}C]flufenacet enabling the detection of a new major metabolite trifluoroacetic acid (M45, TFA) taken up by plants from soil.

Although according to the evaluation in the Monograph and by EFSA, no field rotational crop trials were deemed necessary four field rotational crop studies are reported in the supplementary dossier. The study design covers a scenario where the maximum registered rates are applied to potatoes as preceding crop followed by application on winter cereals. No flufenacet residues were determined in grain or straw of the succeeding crop.

For further details please refer to CA 6.6.

Diflufenican

Data on metabolism of diflufenican in succeeding crops were evaluated during the EU review of the substance (EFSA Scientific Report (2007) 122).

In the EFSA Reasoned Opinion (2013), further investigation of residue levels of diflufenican and its metabolite AE B107137 is only recommended for application rates exceeding the one evaluated during the EU review (*i.e.* 120 g as/ha).

The maximum application rate of diflufenican using the formulation 'Flufenacet + Diflufenican SC 600' is the same (*i.e.* 120 g as/ha) as evaluated during the EU Review and, therefore, field rotational crop trials with diflufenican are not deemed necessary to support the representative uses of 'Flufenacet + Diflufenican SC 600'.

Proposed residue definition and maximum residue levels

Proposed residue definition

Flufenacet

The Review Report for flufenacet (7469/VI/98-Final – 3rd July 2003) does not contain information on the residue definition. The relevant information can be taken from the Complete List of Endpoints, Report of ECCO 73, Annex 2, 5 Residue Section.

Table 8-9: Residue definitions for flufenacet

Matrices	Residue definition		Reference
Food of plant origin	Risk assessment Monitoring	Flufenacet including all metabolites containing the N-fluorophenyl-N-isopropyl moiety, expressed as flufenacet	Report of ECCO 73, Complete list of endpoints, Annex 2, 5 Residue section:
Food of animal origin	Risk assessment Monitoring	Flufenacet including all metabolites containing the N-fluorophenyl-N-isopropyl moiety, expressed as flufenacet	

In the EFSA reasoned opinion on existing MRLs (EFSA Journal 2012;10(4):2689), EFSA considered

that the 'common moiety residue definition' might not be the most adequate for enforcement purposes for plants and therefore proposed to investigate the option to include six individual metabolites in a multi-residue method. In chapter CA 4.2 a justification is provided where it is concluded that the established residue definition is still adequate and shall be maintained.
For further details please refer to CA 6.7.1 and CA 4.2.

Diflufenican

The residue definitions set in the EFSA Conclusions on the evaluation of diflufenican are shown in the table below. The residue definitions were confirmed for cereal commodities in the EFSA Reasoned Opinion on existing MRLs.

Table 8-10: Residue definitions for diflufenican

Matrices	Residue definition		Reference
Food of plant origin	Risk assessment Monitoring	Diflufenican	EFSA Scientific Report (2007) 122
Food of animal origin	Risk assessment Monitoring	Diflufenican	

Proposed maximum residue levels (MRLs)

Flufenacet

Table 8-11 summarises the existing EU MRLs of flufenacet in grain cereals (barley, wheat, rye, oat) and animal commodities as laid down in Regulation (EU) No 149/2008 as well as the MRLs proposed in the EFSA reasoned opinion on existing MRLs according to Art 12 of Regulation (EC) No 396/2005 (EFSA Journal 2012;10(4):2689).

Table 8-11: Existing and anticipated EU MRLs for flufenacet

Crop/animal commodities	Existing EU MRL (mg/kg) Regulation (EC) No. 149/2008, (Annex II)	EU MRL proposed by EFSA (mg/kg) (EFSA Journal 2012; 10(4):2689)
Wheat, barley	0.05*	0.1
Rye, oats [a)]	0.05*	0.05*
Products of animal origin		Meat: 0.05* Fat: 0.05* Liver: 0.02* Kidney (excl. poultry): 0.05* milk: 0.01* Eggs: 0.05*

* indicates that the MRL is set at the LOQ

[a)] Uses in rye and oats were only reported for the northern region and thus included in EFSA's evaluation in the framework of the MRL review according to Art. 12 of (EC) 396/2005. Thus, MRLs for rye and oats were derived from the northern European data set by means of extrapolation from wheat and barley.

Diflufenican

Table 8-12 summarises the existing EU MRLs of diflufenican in grain cereals (barley, wheat, rye, oat) and animal commodities as laid down in Regulation (EU) No 897/2012 as well as the MRLs proposed in the EFSA reasoned opinion on existing MRLs according to Art. 12 of Regulation (EC) No 396/2005 (EFSA Journal 2013;11(6):3281).

Table 8-12: Existing and anticipated EU MRLs for diflufenican

Crop/animal commodities	Existing EU MRL (mg/kg) Regulation (EC) No. 897/2012	EU MRL proposed by EFSA (mg/kg) EFSA Journal 2013;11(6):3281
Barley, rye, wheat	0.05*	0.02
Meat, fat, liver & kidney of cattle, sheep & goat	0.05*	0.02*
Milk	0.05*	0.01*

* indicates that the MRL is set at the LOQ of the method

The intended uses of 'Flufenacet + Diflufenican SC 600' are compatible with both the existing EU MRLs and the EU MRLs recommended by EFSA in its recent reasoned opinions for both active substances.

Proposed Pre-Harvest Intervals, Re-Entry or Withholding Periods

It is not necessary to define a pre-harvest interval for 'Flufenacet + Diflufenican SC 600'. The pre-harvest interval is given by the growing period between the growth stage at treatment and harvest.

It is not relevant to define a re-entry period for livestock, since these crops are not intended to be grazed by livestock.

Flufenacet + Diflufenican SC 600 is used on cereals at early growth stages, when there is no need to enter crops shortly after spraying. It is, therefore, not necessary to define particular re-entry times for workers.

Handling of treated cereals is generally not required before harvest, which is always done mechanically. Therefore there is no need to define a waiting period between application and handling of treated products.

The use of Flufenacet + Diflufenican SC 600 in cereals is not likely to result in significant uptake of residues by succeeding crops. Thus, it is not necessary to set a waiting period between last application and sowing or planting succeeding crops beyond those relevant to agricultural practice.

Estimation of Exposure Through Diet and Other Means

Flufenacet

The toxicological reference values (ADI, ARfD) as published in the Review Report (7469/VI/98-Final – 3rd July 2003) are summarised in the table below.

Table 8-13: Toxicological endpoints for flufenacet

Endpoint	Value (mg/kg bw/day)	Study	Safety factor	Reference
Acceptable Daily Intake (ADI)	0.005	2 year rat study (LOEL)	250	Review Report (7469/VI/98-Final – 3rd July 2003)
Acute Reference Dose (ARfD)	0.017	90 day, 1 year dog study	100	

Diflufenican

The toxicological endpoints for diflufenican as set in the EFSA Scientific Report are summarised in the table below.

Table 8-14: Toxicological endpoints for diflufenican

Endpoint	Value (mg/kg bw/day)	Study	Safety factor	Reference
Acceptable Daily Intake (ADI)	0.2	2 year rat study	100	EFSA Scientific Report (2007) 122
Acute Reference Dose (ARfD)	Not allocated/not necessary			

TMDI calculation

In order to evaluate the potential chronic exposure through the diet, the Theoretical Maximum Dietary Intakes (TMDI) are estimated using the EFSA PRIMo model (revision 2).

Flufenacet

The highest TMDI calculated for flufenacet represented about 59% of the ADI taking into account the the current EU MRLs laid down in Regulation (EU) No 149/2008 and the proposed MRLs for wheat and barley as well as the MRLs for products of animal origin (EFSA, 2012). For details please refer to CA 6.9.

Diflufenican

The calculation of the TMDI for diflufenican was performed based on the current EU MRLs for diflufenican laid down in Regulation (EU) No 897/2012. The highest TMDI was calculated for the Dutch children diet (1.7% ADI).

Based on these results, chronic exposure to flufenacet or diflufenican residues is unlikely to cause any unacceptable risk to consumers.

NEDI calculation

Flufenacet

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 using revision 2 of the EFSA PRIMo. No long-term consumer intake concerns were identified for any of the European diets. The total calculated intake values accounted up to 24.7 % of the ADI (WHO cluster diet B). A modified calculation taking into account a limited number of crops which will be supported in the future results in a slightly lower usage of the ADI (21.2%).

Diflufenican

A NEDI calculation that takes into account all the existing uses of diflufenican in Europe is presented in the EFSA reasoned opinion on the review of the existing maximum residue levels (MRLs) (EFSA Journal 2013;11(6):3281. The highest NEDI was calculated for the Dutch children diet, representing 0.3% of ADI. These results confirm that chronic exposure to diflufenican residues is unlikely to cause harm to consumers.

NESTI calculation

Flufenacet

In the EFSA Reasoned Opinion (2012) the acute consumer exposure to flufenacet was calculated for all types of cereals (wheat, rye, barley and oats) using the highest residue level found in cereal grain (0.05 mg/kg). Taking into account the ARfD of 0.017 mg/kg, the highest NESTI was estimated at 7.3% of ARfD for children due to consumption of milk and 2.3% of ARfD for adults due to consumption of wheat. It is concluded that the herein supported uses in cereals do not result in unacceptable health risks to European consumers.

Diflufenican

Diflufenican is characterised by low acute toxicity and it was not deemed necessary to set or propose an ARfD for this compound. It is, therefore, not relevant to perform a NESTI calculation