

European Commission



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FLUFENACET

Volume 3 – B.7 (PPP)

Diflufenican+Flufenacet SC 600 (200+400 g/L)

Rapporteur Member State: Poland

Co-Rapporteur Member State: France

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B.7. RESIDUE DATA

INTRODUCTION

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 Section 2.7 of the Volume 1 and in Volume 3 – B.7 (AS). A 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 originally 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 I 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. Information on the residue definition 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.

B.7.1. STORAGE STABILITY OF RESIDUES

Flufenacet

Please refer to Volume 3, B.7 for the active substance.

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.

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

Conclusion

The studies on storage stability of residues are considered to adequately support the representative uses of the product “Flufenacet + Diflufenican SC 600”.

B.7.2. METABOLISM, DISTRIBUTION AND EXPRESSION OF RESIDUES

Flufenacet

Please refer to Volume 3, B.7 for the active substance.

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 [¹⁴C] 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.

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 [¹⁴C] 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.

Conclusion

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

B.7.3. MAGNITUDE OF RESIDUE TRIALS IN PLANTS

The representative uses of the product “Flufenacet + Diflufenican SC 600” supporting the renewal of approval for flufenacet are summarised in Table 7.3-1.

Table 7.3-1: 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 uses in cereals (wheat, barley, rye, oats) supported with the Annex II dossier and taken into account for Annex I inclusion is summarised in Table 7.3-2. The GAP corresponds to the critical GAP for the northern climatic zone supported for the renewal of approval for flufenacet.

Table 7.3-2: 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) 2 nd 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 7.3-3 summarises the residue trial data (wheat, rye, barley) evaluated in the EU review process.

Table 7.3-3: 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 uses 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 is given in the Table 7.3-4.

Table 7.3-4: 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 Volume 3, B.7 for the active substance.

Diflufenican

Table 7.3-5 summarizes the representative use of the formulation “Flufenacet + Diflufenican SC 600” which was considered for Annex I inclusion of the active substance diflufenican.

Table 7.3-5: 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 uses (see Table 7.3-6). 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 7.3-6: 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 Volume 3, B.7 for the active substance.

Detailed information relative to diflufenican (and flufenacet) can be obtained from appendix of Volume 3, B.7 for the active substance flufenacet, if considered necessary.

Conclusion

The field trials are considered to adequately support the representative uses of the product “Flufenacet + Diflufenican SC 600”.

B.7.4. FEEDING STUDIES

Flufenacet

Please refer to Volume 3, B.7 for the active substance.

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.

Conclusion

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

B.7.5. EFFECTS OF PROCESSING

Flufenacet

Please refer to Volume 3, B.7 for the active substance.

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).

Conclusion

The industrial processing and/or household preparation studies are considered to adequately support the representative uses of the product “Flufenacet + Diflufenican SC 600”.

B.7.6. RESIDUES IN ROTATIONAL CROPS

Flufenacet

Please refer to Volume 3, B.7 for the active substance.

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’.

Conclusion

The studies on residues in rotational crops are considered to adequately support the representative

uses of the product “Flufenacet + Diflufenican SC 600”.

B.7.7. OTHER STUDIES

No other studies were conducted.

B.7.8 MRLs / CONSUMER EXPOSURE CONSIDERATIONS

B.7.8.1 Proposed residue definition

Flufenacet

For commodities of plant and animal origin, a residue definition including all metabolites with the *N*-fluorophenyl-*N*-isopropyl moiety is expected to be the most appropriate (when application is made pre- and early post-emergence) (see Table 7.8.1-1). Consequently the currently binding residue definition for food of plant origin (for monitoring and enforcement purposes) according to Commission Regulation (EU) No 1127/2014 of 20 October 2014 is “**Flufenacet (sum of all compounds containing the *N*-fluorophenyl-*N*-isopropyl moiety expressed as flufenacet)**”. Residue definition for risk assessment purposes is proposed according to the EFSA opinion to be the same. If in the future uses are needed where the application is closer to harvest the metabolism and residue definition would need to be reconsidered.

Table 7.8.1-1: Residue definitions for flufenacet

Matrices	Residue definition		Reference
Food of plant origin	Risk assessment Monitoring	Flufenacet including all metabolites containing the <i>N</i> -fluorophenyl- <i>N</i> -isopropyl moiety, expressed as flufenacet	Report of ECCO 73 Bruno Dujardin, Pesticides Unit, EFSA; 9 th European Pesticide Residue Workshop (Vienna (Austria), 27 June 2012
Food of animal origin	Risk assessment Monitoring	Flufenacet including all metabolites containing the <i>N</i> -fluorophenyl- <i>N</i> -isopropyl moiety, expressed as flufenacet	

For more details, please refer to Volume 3, B.7 for the active substance.

Diflufenican

The residue definitions set in the EFSA Conclusions on the evaluation of diflufenican are shown in Table 7.8.1-2. The residue definitions were confirmed for cereal commodities in the EFSA Reasoned Opinion on existing MRLs.

Table 7.8.1-2: 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	

B.7.8.2 Proposed Maximum Residue Levels (MRLs)Flufenacet

The EU MRLs for flufenacet in all types of small grain cereals (wheat, rye, triticale, barley, oats) were established in Commission Regulation (EU) No 1127/2014 of 20 October 2014 as recommended in the EFSA Reasoned Opinion on the review of existing MRLs according to Article 12 of Regulation (EC) No 396/2005 (EFSA Journal 2012;10(4):2689 (see Table 7.8.2-1).

According to animal metabolism and livestock feeding studies residues in animal matrices, milk and eggs are unlikely to occur. The representative uses supported correspond to the frame which was evaluated by EFSA when reviewing the MRLs. MRLs for animal commodities have been set up in Commission Regulation (EU) No 1127/2014 of 20 October 2014 at LOQ for the individual matrices. It is considered to be appropriate for the representative uses of flufenacet and MRLs do not need to be modified (see Table 7.8.2-1).

Table 7.8.2-1: Existing EU MRLs for flufenacet in cereal grains and products of animal origin(mg/kg)

Crop/animal commodities	Commission Regulation (EU) No 1127/2014 of 20 October 2014
Wheat, barley	0.1
Rye, oats	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 lower limit of analytical determination

For more details, please refer to Volume 1 for the active substance.

Diflufenican

Table 7.8.2-2 summarises the existing EU MRLs of diflufenican in grain cereals (barley, wheat, rye, oat) and animal commodities as laid down in the Commission Regulation (EU) No 2015/603 of 13 April 2015 based on the EFSA reasoned opinion on existing MRLs according to Art. 12 of Regulation (EC) No 396/2005 (EFSA Journal 2013;11(6):3281).

Table 7.8.2-2: Existing EU MRLs for diflufenican in cereal grains and products of animal origin (mg/kg)

Crop/animal commodities	Commission Regulation (EU) No 2015/603 of 13 April 2015
Wheat, barley, rye, oats	0.02
Products of animal origin	Meat: 0.02* Fat: 0.02* Liver: 0.02* Kidney: 0.02* Milk: 0.01* Eggs: 0.02*

* indicates lower limit of analytical determination

Conclusion

The intended uses of “Flufenacet + Diflufenican SC 600” are compatible with both the currently binding EU MRLs as recommended by EFSA in its recent reasoned opinions for both active substances.

B.7.8.3 Estimation of Exposure Through Diet and Other Means

The toxicological reference values (ADI, ARfD) for flufenacet as published in the Review Report (7469/VI/98-Final – 3rd July 2003) are summarised in Table 7.8.3-1.

Table 7.8.3-1: 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 – 3 rd July 2003)
Acute Reference Dose (ARfD)	0.017	90 day, 1 year dog study	100	

The toxicological reference values for diflufenican as set in the EFSA Scientific Report are summarised in the Table 7.8.3-2.

Table 7.8.3-2: 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 Theoretical Maximum Daily Intake (TMDI) was calculated using the EFSA PRIMo rev. 2 and compared with the toxicological reference value. TMDI is based on the MRLs as established in Regulation (EU) 1127/2014 limited to the representative uses (wheat, rye, barley). Additionally MRLs for products of animal origin (swine, bovine, sheep, goat, poultry commodities, milk and birds eggs) established at the respective LOQ levels were considered. The total calculated intake values accounted up to 21.9 % of the ADI (WHO Cluster diet B). For more details, please refer to Volume 1 for the active substance.

Diflufenican

The calculation of the TMDI for diflufenican was performed based on the current EU MRLs for diflufenican laid down in Regulation (EU) No 2015/603. The highest TMDI was calculated for the Dutch children diet (0.3 % 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%).

For more details, please refer to Volume 1 for the active substance.

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 3.5% of ARfD for adults due to consumption of poultry meat. It is concluded that the herein supported uses in cereals do not result in unacceptable health risks to European consumers.

For more details, please refer to Volume 1 for the active substance.

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.

Conclusion

Residues arising from the supported uses of “Flufenacet + Diflufenican SC 600” in cereals (wheat, barley, rye), following application consistent with good plant protection practice, do not result in unacceptable health risks to European consumer.

B.7.8.4 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.

Conclusion

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.