Conclusion regarding the peer review of the pesticide risk assessment of the active substance

diflufenican

finalised: 17 December 2007

(version of 11 February 2008 with minor corrections)

SUMMARY

Diflufenican is one of the 79 substances of the third stage Part A of the review programme covered by Commission Regulation (EC) No 1490/2002[1]. This Regulation requires the European Food Safety Authority (EFSA) to organise a peer review of the initial evaluation, i.e. the draft assessment report (DAR), provided by the designated rapporteur Member State and to provide within one year a conclusion on the risk assessment to the EU-Commission.

United Kingdom being the designated rapporteur Member State submitted the DAR on diflufenican in accordance with the provisions of Article 10(1) of the Regulation (EC) No 1490/2002, which was received by the EFSA on 1 August 2005. The peer review was initiated on 3 February 2006 by dispatching the DAR for consultation of the Member States and the applicant Bayer CropScience. Subsequently, the comments received on the DAR were examined by the rapporteur Member State and the need for additional data was agreed on during a written procedure in November 2006. Remaining issues as well as further data made available by the notifier upon request were evaluated in a series of scientific meetings with Member State experts in May – June 2007.

A final discussion of the outcome of the consultation of experts took place with representatives from the Member States on 14 November 2007 leading to the conclusions as laid down in this report.

The conclusion was reached on the basis of the evaluation of the representative uses as pre- and post emergence herbicide as proposed by the main notifier, which comprises spraying applications, up to crop growth stage BBCH 10-13, to control annual broad-leaved weeds and annual grasses in winter wheat, winter barley and winter rye at a single application at a maximum rate of 120 g diflufenican/ha. Full details of the application rates and timings can be found in the attached end points.

The representative formulated product for the evaluation was “Herold SC 600”, an aqueous suspension concentrate (SC), registered under different trade names containing diflufenican and flufenacet. The main notifier submitted two representative uses and formulations, however the RMS and the main notifier agreed to evaluate only “Herold SC 600”.

[1] OJ No L 224, 21.08.2002, p. 25, as last amended by Commission Regulation OJ L 246, 21.9.2007

Adequate methods are available to monitor diflufenican residues in plants, foodstuff of plant and animal origin, soil, water and air. Residues in food of plant and animal origin can be determined with the German multi-residue method DFG S19. For the other matrices only single methods are available to determine residues of diflufenican.
Sufficient analytical methods as well as methods and data relating to physical, chemical and technical properties are available to ensure that quality control measurements of the plant protection product are possible.

Concerning the mammalian toxicology assessment, diflufenican has a low acute toxicity, is not irritant and has no skin sensitisation potential. In repeat dose studies, the main adverse effects were on the body weight gain and in the liver. No concern was raised about the genotoxic properties of diflufenican, and no carcinogenic potential was demonstrated. In the multigeneration study, incidences of dystocia were observed at the high dose but were concomitant with systemic toxicity and did not lead to classification. No teratogenic activity was shown in the developmental studies. The agreed acceptable daily intake (ADI) was 0.2 mg/kg bw/day and the agreed acceptable operator exposure level (AOEL) was 0.11 mg/kg bw/day, both with the use of a safety factor 100. An acute reference dose (ARfD) was not required. The estimated operator exposure is below the AOEL without the use of personal protective equipment (PPE).

The metabolism of diflufenican was investigated in wheat upon pre- and post-emergence application. The application rate and timing used in the plant metabolism study correspond to the notified GAP criteria. In the wheat grains, diflufenican could be detected but an extensive identification of metabolites was difficult due to the low residue levels. In straw, again diflufenican was identified; however the major part of the total residue consisted of different metabolites that, with one exception, were not identified since individually not present above the trigger value of 0.01 mg/kg. The meeting of experts noted that for future cereal uses that deviate from the assessed GAP additional metabolism data may be required in order to refine the residues definition, currently proposed as diflufenican.
The metabolism and distribution of diflufenican in rotational crops was investigated in wheat, cabbage and sugar beet. Two metabolites, AE 0542291[2] and AE B107137[3] could be identified since they presented a substantial part of the total residue in the tested crops. Eventually, the two metabolites were not considered to be of concern for the consumer. The experts concluded that for the particular notified use and GAP it is not expected to get residue levels in rotational crops exceeding the trigger value of 0.01 mg/kg.
A very limited number of residue trials support the notified GAP. In addition, residue trials are available with an increased latest time of application, and it was proposed to use these trials to support the notified GAP. The data allow for an MRL proposal for cereal grains on LOQ level. Based

[2] AE 0542291: 2-[3-(trifluoromethyl)phenoxy]pyridine-3-carboxamide [referenced in the residues section of the DAR as M&B43625]
[3] AE B107137: 2-[3-(trifluoromethyl)phenoxy]pyridine-3-carboxylic acid [referenced in the residues section of the DAR as M&B38181]

on the residue trial data livestock exposure is possible through straw used in animal diet, in particular in ruminant diet. No exposure of poultry is expected. However, the metabolism and distribution in animals was investigated in lactating cows and chickens. As for the assessed representative use it was concluded that no residues of diflufenican above the limit of quantification (LOQ) are likely to occur in edible animal matrices and thus no feeding studies and no MRLs for animal products are considered necessary.
The chronic dietary risk assessment for consumers showed that exposure to residues of diflufenican from the notified use is well below the allocated ADI. As no ARfD was derived an acute risk assessment is not required.

Under dark aerobic conditions at 20 - 22 ºC, diflufenican was moderate to high persistent in soil. Two major soil aerobic metabolites were identified, AE 0542291 and AE B107137 that are moderately persistent in soil. Mineralization was from 3.85 % AR after 120 d to a maximum of 51.2 % AR after 52 d depending on the study and the labelling position. Unextractable residues range from 3.04 % AR after 120 d to 18.5 % AR after 54 d depending on the study and the labelling position.
Diflufenican is medium to very high persistent under anaerobic conditions. Volatile transformation product 2,4-difluroaniline (AE C522392) was identified as a major anaerobic metabolite. Degradation of AE B107137 was also investigated under anaerobic conditions.
Diflufenican is shown to be stable to the photolysis in soil.
Field studies in six German sites and six sites in different European locations (UK, FR, DE, NL, ES and IT) show that diflufenican was high to very high persistent under field conditions. A kinetic analysis of the two field studies to obtain field normalized half lives is also available. In a five years accumulation study conducted at six sites in south-east England (Maycey and Savage, 1991a) a clear tendency to accumulation of diflufenican residues was observed. Since soil concentration derived from the field accumulation study was higher than the obtained from standard calculation this value was used for the ecotoxicological risk assessment and the calculation of the potential maximum concentration of the metabolites.
Diflufenican is slight mobile to immobile in soil, AE B107137 is very highly mobile and AE 0542291 is medium to highly mobile.
Diflufenican and its metabolite AE B107137 were stable to hydrolysis. Diflufenican was also stable to aqueous photolysis and non ready biodegradable.
Degradation of diflufenican in dark water sediment was investigated in a total of four systems. The application rate used in these studies is significantly above of the solubility limit. Diflufenican was medium to very high persistent in these systems and was slowly transformed to the metabolite AE B107137. In all the water sediment systems available mineralization was negligible (< 4 % A R after 120 d). Data from these studies were analyzed in a separated study by multicompartmental kinetic models. Whereas these fitting exercises are able to describe the system as a whole the individual degradation rates for the water phase should be taken with caution. The values obtained from this kinetic analysis were employed in the FOCUS SW modelling presented in the DAR.
In a sediment monitoring study performed in UK winter cereal areas with history of repeated use of diflufenican at rates below 100 g / ha variable results were obtained.

Different FOCUS $PEC_{SW/SED}$ are available in the DAR and in the Addendum, none of them produced with the input parameters agreed by the expert's meeting. However, the expert's meeting decided to retain the $PEC_{SW\ /\ SED}$ values presented in the DAR for the EU risk assessment. Examination of the modelling results and the ecotoxicological risk assessment showed that Step 4 calculation with a 5 m buffer for spray drift only resulted in a complete scenario with acceptable TERs for aquatic risk assessment (D3). After the expert meeting, EFSA identified a data GAP for new FOCUS PEC_{SW} calculations using a plant uptake factor of zero and the input parameters agree for the meeting (mean whole systems half life for SW and 1000 d for sediment, with only spray drift buffer strip mitigation in order to confirm the proposed risk assessment and to make it consistent with the risk assessments performed for other substances of this peer review phase.
Potential ground water contamination by diflufenican and the soil metabolites AE B107137 and AE 0542291 was evaluated by FOCUS PELMO (v.3.3.2). The 80^{th} percentile annual average concentrations in leachates below 1 m were predicted to be less than 0.001 µg / L for all compounds in the nine European scenarios.
Diflufenican may be considered slightly volatile. However, based on the negligible potential for volatilization from plant and soil surface it is considered that exposure to air and therefore long range transport thought air is insignificant for diflufenican. During expert's meeting soil anaerobic metabolite 2,4-difluroaniline was found to be very volatile and may need to be assessed for the air compartment and for transport through air when anaerobic conditions are expected to occur.

The Annex VI triggers were met in the acute and long-term risk assessment for birds and mammals taking into consideration only exposure to diflufenican. However the lead formulation Herold SC 600 contains flufenacet as a second active substance. The toxicity and exposure to the second active substance was not taken into account in the risk assessment. The long-term TER for herbivorous mammals of 5.3 is close to the trigger of 5. It is likely that the TER would be below the trigger if exposure to the second active substance is considered in the risk assessment. A risk assessment taking into consideration also exposure to flufenacet is required before a conclusion can be drawn on the risk to birds and mammals from the representative use of diflufenican formulated as Herold SC 600.

Green algae were the most sensitive organisms driving the aquatic risk assessment. Only the FOCUS step4 part scenario D5 pond reached a TER of >10 including a no-spray buffer zone of 5 metres indicating a high risk to aquatic organisms for the majority of geoclimatic conditions in Europe presented by the FOCUS scenarios. However the risk to aquatic organisms is addressed for the full FOCUS step 4 scenario D3 (ditch) if the approach is followed which was agreed in the meeting of experts on ecotoxicology. It may be possible to identify further scenarios with acceptable risk if recovery is taken into account as suggested in the addendum from April 2007 or if larger no-spray buffer zones are introduced in the PECsw calculations. The RMS stated in the not peer-reviewed addendum from August 2007 that a new risk assessment was submitted by the applicant but the risk assessment was not summarised and evaluated in the addendum. The aquatic risk assessment was based on exposure to diflufenican alone. However tests with the formulation Herold SC 600 suggest lower toxicity to green algae (the most sensitive group of aquatic organisms tested) compared to

technical diflufenican. Therefore it was agreed in the expert meeting that the risk from the formulation would be covered by the risk assessment for diflufenican.

The in-field and off-field HQ values for *Aphidius rhopalosiphi* and *Typhlodromus pyri* were below the trigger of 2 based on studies with formulations different from Herold SC 600. Studies with the formulation Herold SC 600 indicated a high risk to *T. pyri*. No studies with the lead formulation and non-target arthropods other than *T. pyri* were made available. The risk to non-target arthropods was not sufficiently addressed for the suggested representative use. Consequently a data gap was identified by the experts to address the risk to non-target arthropods from the formulation Herold SC 600.

The risk to non-target plants from pre-emergence and post-emergence exposure to diflufenican was assessed as high and risk mitigation measures such as an in-field no-spray buffer zone of 10 meters is required.

The risk to bees, earthworms, other soil non-target macro-organisms, soil non-target micro-organisms and biological methods of sewage treatment was assessed as low.

Key words: Diflufenican, peer review, risk assessment, pesticide, herbicide

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BACKGROUND

Commission Regulation (EC) No 1490/2002 laying down the detailed rules for the implementation of the third stages of the work program referred to in Article 8(2) of Council Directive 91/414/EEC and amending Regulation (EC) No 451/2000, regulates for the European Food Safety Authority (EFSA) the procedure of evaluation of the draft assessment reports provided by the designated rapporteur Member State. Diflufenican is one of the 79 substances of the third stage, part A, covered by the Regulation (EC) No 1490/2002 designating United Kingdom as rapporteur Member State.

In accordance with the provisions of Article 10(1) of the Regulation (EC) No 1490/2002, United Kingdom submitted the report of its initial evaluation of the dossier on diflufenican, hereafter referred to as the draft assessment report, to the EFSA on 1 August 2005. In accordance with Article 11(2) of the Regulation (EC) No 1490/2002 the draft assessment report was distributed for consultation on 3 February 2006 to the Member States and the main applicant Bayer CropScience as identified by the rapporteur Member State. Hermoo Belgium NV and Makhteshim Agan ICC also notified their interest in supporting diflufenican for Annex I inclusion. Hermoo did not make any further submission after the initial notification. The dossier submitted by Makhteshim Agan ICC was found to be substantially incomplete and the RMS has checked only the identity and impurities of the active substance.

The comments received on the draft assessment report were evaluated and addressed by the rapporteur Member State. Based on this evaluation, representatives from Member States identified and agreed during a written procedure in November 2006 on data requirements to be addressed by the notifier as well as issues for further detailed discussion at expert level.

Taking into account the information received from the notifier addressing the request for further data, a scientific discussion of the identified data requirements and/or issues took place in expert meetings in May – June 2007. The reports of these meetings have been made available to the Member States electronically.

A final discussion of the outcome of the consultation of experts took place with representatives from Member States on 14 November 2007 leading to the conclusions as laid down in this report.

During the peer review of the draft assessment report and the consultation of technical experts no critical issues were identified for consultation of the Scientific Panel on Plant Health, Plant Protection Products and their Residues (PPR).

In accordance with Article 11(4) of the Regulation (EC) No 1490/2002, this conclusion summarises the results of the peer review on the active substance and the representative formulation evaluated as finalised at the end of the examination period provided for by the same Article. A list of the relevant end points for the active substance as well as the formulation is provided in appendix 1.

The documentation developed during the peer review was compiled as a **peer review report** comprising of the documents summarising and addressing the comments received on the initial evaluation provided in the rapporteur Member State's draft assessment report:

- the comments received,
- the resulting reporting table (rev. 1-1 of 19 December 2006)

as well as the documents summarising the follow-up of the issues identified as finalised at the end of the commenting period:

- the reports of the scientific expert consultation,
- the evaluation table (rev. 2-1 of date 15 November 2007)

Given the importance of the draft assessment report including its addendum (compiled version of August 2007 containing all individually submitted addenda) and the peer review report with respect to the examination of the active substance, both documents are considered respectively as background documents A and B to this conclusion.

THE ACTIVE SUBSTANCE AND THE FORMULATED PRODUCT

Diflufenican is the ISO common name for 2′,4′-difluoro-2-(α,α,α-trifluoro-*m*-tolyloxy)nicotinanilide.

Diflufenican belongs to the class of anilide herbicides. It acts as a specific inhibitor of phytoene dehydrogenase, a key enzyme of carotenoid biosynthesis. Diflufenican is used for the control of broadleaf weeds and a few annual grasses in winter cereals.

Bayer CropScience and Makhteshim Agan did not conclude an agreement on collective provision of data and because only Bayer CropScience submitted a complete dossier, RMS evaluated only the representative uses submitted by Bayer CropScience.

The representative formulated product for the evaluation was "Herold SC 600", an aqueous suspension concentrate (SC) containing 200 g/L diflufenican and 400 g/L flufenacet, registered under different trade names in Europe. The main notifier submitted two representative uses and formulations, one containing diflufenican and flufenacet and the other diflufenican and isoproturon, however the RMS and the main notifier agreed to evaluate only "Herold SC 600".

The representative uses evaluated comprise pre- and post emergence applications with tractor mounted boom sprayers to control annual broad-leaved weeds and annual grasses (in particular for the control of amaranthaceae, caryophyllaceae, cruciferae, labiatae, malvaceae, polygonaceae, solanaceae, and especially rubiaceae (*Galium aparine*), scrophulariaceae (*Veronica spp.*) and violaceae (*Viola spp.*)) in winter wheat, winter barley and winter rye up to crop growth stage BBCH 10-13, at a single application at a maximum rate of 120 g diflufenican/ha.

SPECIFIC CONCLUSIONS OF THE EVALUATION

1. Identity, physical/chemical/technical properties and methods of analysis

The minimum purity of diflufenican of both sources is 970 g/kg, which is meeting the requirements of the FAO specification AGP:CP/348 (462/TC/S/F (1997)) of minimum 945 g/kg.

According to the equivalence assessment of the two technical materials, the RMS concluded that the Makhteshim Agan source can be considered comparable to the Bayer source, with minor differences in the levels of impurities. The minimum purity of the two sources was identical (Report on the Makhteshim Agan source, July 2005) The RMS stated that the minor differences in impurities which were identified were not considered to be toxicologically significant or were considered to be non-relevant impurities which did not exceed the acceptable maximum increases as defined in the appropriate Guidance Document (Sanco/10597/2003 –rev. 7). However the expert meeting (PRAPeR 21) found the proposed specifications unacceptable with regard to the supporting batch analysis and the experts of PRAPeR 24 considered that further information was required to confirm the toxicological relevance of the impurities in the technical material with respect to the batches tested in toxicology studies.
Following the PRAPeR expert meetings the main data submitter, Bayer CropScience, have provided the information, including a revised technical specification, to address both these points, presented in addendum 4 to Vol. 4 (August 2007), however this has not been evaluated in detail by the RMS nor peer reviewed. The specification of the main data submitter is still open however it is not considered to be a critical area of concern.
Since the specifications for the technical materials are not finalized, it is not possible to conclude on the equivalence of the Makhteshim Agan source and the equivalence has to be determined at MS level.

The assessment of the data package revealed no issues that need to be included as critical areas of concern with respect to the identity, physical, chemical and technical properties of diflufenican or the respective formulation.

The main data regarding the identity of diflufenican and its physical and chemical properties are given in appendix 1.

Adequate analytical methods are available for the determination of diflufenican in the technical material and in the representative formulation as well as for the determination of the respective impurities in the technical material.
Several methods have been developed for the analysis of diflufenican residues in plants based on extraction into acetonitrile followed by determination using GC-ECD. The applicability of the German multi-residue method DFG S19 with both GC-ECD and GC-MS has been demonstrated. For

food and feed of animal origin the applicability of the German multi-residue method DFG S19 with both GC-MS and GC-ECD has been also demonstrated.
Several methods exist for the analysis of diflufenican in soil, based on GC-ECD and newer methods employing GC-MS or LC/MS/MS. Whilst the residue definition for monitoring is defined as diflufenican only, metabolites AE B107137 and AE 0542291 were determined during the soil dissipation study.
For the analysis of diflufenican in water several GC-ECD methods exist, and also an LC/MS/MS method allowing the determination of both diflufenican and the metabolites AE B107137 and AE 0592370[4] in water.
For determination of diflufenican in air one HPLC-UV and an LC/MS/MS method was used.

Adequate methods are available to monitor diflufenican given in the respective residue definition.

Analytical methods for the determination of residue in body fluids and tissues are not required.

2. Mammalian toxicology

Two products were submitted by Bayer as representative uses in the EU dossier: Javelin and Herold SC600. It was agreed between the RMS and Bayer that only Herold SC600 would be evaluated and presented in this DAR.
Diflufenican was discussed by the experts in mammalian toxicology in a PRAPeR meeting in June 2007 (PRAPeR 24, round 5).

2.1. Absorption, Distribution, Excretion and Metabolism (Toxicokinetics)

The oral absorption of diflufenican was 58% in males and 71% in females based on the biliary excretion. Peak blood concentrations appeared at 0.5 and 12 hours post dose. Distribution occurred preferentially to adipose tissues with some potential for long-term accumulation. Hepatic biotransformation of diflufenican is extensive (up to 22 metabolites, mainly conjugates of hydroxyl derivatives), though unchanged parent was also eliminated in significant amounts in faeces. Excretion is mainly via faeces (87-97%, with 40-50% of biliary excretion), but also via urine (up to 7%). Systematically available fluoride released during metabolism is estimated to be <1% w/w of the administered diflufenican.

2.2. Acute toxicity

Diflufenican has a low toxicity via the oral, dermal, or inhalation routes of exposure (oral LD_{50} >5000 mg/kg bw, dermal LD_{50} >2000 mg/kg bw, inhalation LC_{50} >5.12 mg/L/4h).
The test material is non-irritant to skin and eyes, and has no skin sensitisation potential (Magnusson and Kligman test). No classification for acute toxicity is needed.

[4] AE 0592370: *N*-(2,4-difluorophenyl)-2-oxo-*N*-[3-(trifluoromethyl)phenyl]-1,2-dihydropyridine-3-carboxamide

2.3. SHORT TERM TOXICITY

The short term effects of diflufenican were studied in one 2-week study in rats, two 90-day studies in rats, one 90-day study in mice, one 90-day and one 52-week studies in dogs. An additional 13-week rat study (cfr Addendum to Volume 3, May 2007) provided supportive information.

The target organ was the liver but the critical effect at low doses was a decreased body weight gain. Throughout the studies, inconsistent effects were observed on the body weight gain. Disregarding marginal effects observed in two studies, the experts agreed to set the overall NOAEL at 19.47 mg/kg bw/day based on decreased body weight gain and liver effects in a 13-week rat study (West, 1987a).

No studies were submitted or required with repeated dermal or inhalation exposure.

2.4. GENOTOXICITY

Diflufenican gave negative results in genotoxicity assays *in vitro* (Ames test, cytogenetic assay in human lymphocytes, mammalian cell gene mutation assay, UDS assay in rat hepatocytes). Only one study demonstrated an increased mutation frequency in mouse lymphoma cells, in the absence of metabolic activation. Similarly, *in vivo* studies were unable to demonstrate any potential for diflufenican to cause chromosome aberrations in rat bone marrow.

Nevertheless the Ames test and Mouse Lymphoma Assay had some deficiencies. For classification and labelling purposes, the results of a new Ames test were provided in the addendum (May 2007) and were clearly negative. Similarly, the results of a new Mouse Lymphoma Assay were provided to the RMS after the experts' meeting and not peer-reviewed.

On the overall it was agreed that there was no concern about the genotoxic properties of diflufenican.

2.5. LONG TERM TOXICITY

The carcinogenic potential of diflufenican has been investigated in rats and mice.

The main adverse effects included a dose-dependent decrease in body weight development in both sexes, an increase in relative liver weight and hepatic hypertrophy. Some equivocal effects on reproductive organs were observed at high doses in both rats and mice showing reduced seminal vesicle secretion and histopathological changes of the uterus/cervix (but they were not confirmed in reproductive toxicity studies). Diflufenican did not show any carcinogenic potential in these studies.

The proposed systemic NOAEL is 23.27 mg/kg bw/day from the rat study, based on reduced body weight gain. The proposed NOAEL for carcinogenic effects is equivalent to the highest dose levels tested in both species (614 mg/kg bw/day in rats, and 1618 mg/kg bw/day in mice).

2.6. REPRODUCTIVE TOXICITY

In a multigeneration study with rats, there were several instances of maternal mortality in the perinatal period. At the high dose level, they were attributed to difficult parturition (dystocia) and the single incidence at the mid dose level was considered to be incidental. The potential for endocrine disruption was discussed by the experts and it was agreed that there might be some indications of endocrine disruption at high doses but in view of the potential link with systemic toxicity, no classification for fertility was proposed.

The parental NOAEL was 35.5 mg/kg bw/day based on decreased body weights, organ weights and kidney effects. The offspring NOAEL was 41.9 mg/kg bw/day based on reduced pup weight and litter weight. Based on the above considerations, the NOAEL for the reproductive parameters was 206.1 mg/kg bw/day based on the incidences of dystocia observed at the high dose.
In developmental studies with rats and rabbits, there was no evidence of teratogenic activity in the absence of maternal toxicity. In rats, the NOAEL for maternal toxicity was 50 mg/kg bw/day based on a decreased body weight gain, and the developmental NOAEL was 500 mg/kg bw/day based on an increased incidence in visceral anomalies at 5000 mg/kg bw/day. In rabbits, the NOAEL for maternal and developmental toxicity was 350 mg/kg bw/day based on decreased maternal body weight gain and increased incidence of extra ribs in foetuses at 2500 mg/kg bw/day.

2.7. NEUROTOXICITY

No data submitted. Since diflufenican is not a member of a chemical class associated with delayed neurotoxicity and since there is no evidence of neurotoxic effects in repeat dose studies in rats, mice, dogs or rabbits, neurotoxicity studies were not required.

2.8. FURTHER STUDIES

A mechanistic study with rats showed that the liver hypertrophy/increased liver weights induced by diflufenican treatment was not related to specific induction of cytochrome P450 metabolising enzymes.
Three studies were performed with the major soil metabolite AE B107137. It was found to be of low acute toxicity via the oral and dermal routes (oral LD_{50} >2000 mg/kg bw, dermal LD_{50} >1000 mg/kg bw), and gave a negative result when tested in an Ames test. When tested for the potential to induce chromosome aberrations in human lymphocytes, an equivocal result was obtained (increase at highest concentration). The meeting agreed that there was no genotoxic potential in vitro. Considering that this compound is also a rat metabolite, it was not expected to be more toxic than the parent.

Equivalence of technical materials

Two sources were presented in the DAR. The impurity toluene was not included in the representative source (Bayer) but was present in the second one (Makhteshim). Therefore, the presence of toluene in the technical specification as proposed in the DAR was discussed by the experts.
On one hand, they agreed that toluene was a relevant impurity due to its intrinsic toxic properties. On the other hand, as toluene was not present in the toxicological batches (see volume 4, Bayer), it has not been tested in the toxicological studies and no acceptable level can be set for the technical specification.
The relevance and the acceptability of the levels proposed in the technical specification for the other impurities were also considered (see addendum to Vol.4, May 2007). Some impurities were not analyzed in the toxicological batches, and the major impurity in the technical specification (AE 0592371) was tested at lower levels in the toxicological studies. Some non-GLP screening studies were performed with this impurity (acute oral toxicity, Ames test and in vitro micronucleus assay). The experts agreed that more data were needed to assess the representativeness of the toxicological

batches with regard to the technical specification. A revised specification was provided by the main notifier after the experts meeting to reduce the maximum content proposed for all impurities. This was not evaluated in detail by the RMS and was not peer reviewed (see addendum 4 to Vol.4, August 2007).

2.9. MEDICAL DATA

No adverse health effects were reported from manufacturing, formulation or packing plant workers and no reports of poisoning incidents in man have been identified.

2.11. ACCEPTABLE DAILY INTAKE (ADI), ACCEPTABLE OPERATOR EXPOSURE LEVEL (AOEL) AND ACUTE REFERENCE DOSE (ARFD)

ADI

The agreed ADI was 0.2 mg/kg bw/day based on the NOAEL in the 2-year rat study supported by the NOAELs in the 13-week rat studies and with the use of a safety factor 100. Considering the findings of dystocia in the multigeneration study, a margin of safety of 4440 over the LOAEL (888 mg/kg bw/day) was considered sufficient.

AOEL

The agreed AOEL was 0.11 mg/kg bw/day based on the 13-week rat study with the use of a safety factor 100 and a correction for an enteral absorption rate of 58%.

ARfD

Treatment with diflufenican did not give rise to any obvious acute effects which would justify setting an ARfD.

2.11. DERMAL ABSORPTION

In the DAR, a dermal absorption study with the formulation Javelin SC (containing 62.5 g diflufenican/L) was presented. As the representative formulation Herold SC600 was not used, the validity of the dermal absorption values was questioned. Therefore, a new *in vitro* study with rat and human skin was provided for Herold SC600 (see addendum, May 2007). The values agreed by the experts were 0.15% for the concentrate and 5.0% for the dilution as suggested by the RMS.

2.12. EXPOSURE TO OPERATORS, WORKERS AND BYSTANDERS

The representative plant protection product Herold SC600 is a suspension concentrate (SC) containing 2 active substances: diflufenican (200 g/L) and flufenacet (400 g/L). It will be applied on cereals with tractor-mounted/trailed field crop (boom) sprayer.

EFSA notes that the second active substance contained in Herold SC 600 is flufenacet, included in Annex 1 by the Directive 2003/84/EC. The RMS had provided an assessment of the combined toxicity in the DAR. As there is no harmonized approach on how to perform the risk assessment for a combined product, this has to be considered at MS level.

Operator exposure

According to the intended uses submitted by the applicant the maximum applied dose is 120 g diflufenican/ha and the minimum volume 200 L water/ha. The estimated operator exposure for Herold SC600 is below the AOEL according to both models without the use of PPE (see table beneath).

Estimated exposure presented as % of AOEL (0.11 mg/kg bw/day), according to calculations with the German and UK POEM model. The default for body weight of operator is 70 kg in the German model and 60 kg in the UK-POEM model.

Model	No PPE	With PPE[1]
German	3	3
UK POEM	20	19

PPE[1] (personal protective equipment): gloves during mixing/loading

Worker exposure

The estimations have been performed for crop inspection activities with the use of the EUROPOEM worker re-entry model[5] and the resulting value is 3% of the AOEL for unprotected workers.

Bystander exposure

On the basis of direct measurements performed in a UK study[6], the estimated bystander exposure is 0.1% of the systemic AOEL.

3. Residues

Diflufenican was discussed at the PRAPeR experts' meeting for residues in June 2007 (PRAPeR 25, round 5).

3.1. NATURE AND MAGNITUDE OF RESIDUES IN PLANT

3.1.1. PRIMARY CROPS

The metabolism of diflufenican was investigated in wheat. Pyridine, difluorophenyl and trifluromethylphenyl ring labelled [^{14}C] diflufenican was applied as either a pre-emergence application or a post-emergence foliar application at a rate that corresponds approximately to the notified representative GAP.

At harvest the total radioactive residues (TRR; expressed as diflufenican equivalents) in grain and straw were less than 0.01 mg/kg, with the exception of straw from the pre-and post-emergence pyridine study and the post emergence trifluromethylphenyl study (0.01 mg/kg).

[5] Van Hemmen et al (2002). Post-application exposure of workers to pesticides in agriculture. EUROPOEM II project: FAIR3-CT96-1406US EPA (2000). Policy paper on agricultural transfer coefficients.
[6] Lloyd and Bell, 1983. Hydraulic nozzles: comparative spray drift study.

On characterisation of the extractable radioactivity one major component was identified in the straw at harvest as diflufenican, which accounted for 2-16% of the total radioactivity in the straw for the pre and post-emergence treatments (diflufenican was also identified in the grains but the amount present was not quantified). Extensive identification was difficult due to the low TRR levels in the wheat grains. In the straw, one other metabolite was identified, plus several unknowns which individually did not represent more than 10% (<0.01 mg/kg) of the total radioactivity, with the exception of one unknown polar metabolite, which accounted for up to 70% (<0.01 mg/kg) of the total radioactivity in the straw. The remaining unextractable radioactivity in the straw accounted for less than 0.01 mg/kg.
Based on the plant metabolism data submitted for wheat and in accordance to the notified GAP, residues in cereals should be defined as diflufenican for risk assessment and monitoring purposes.
The meeting highlighted that, if in the future a later time of application is required and residue levels may trigger further identification and quantification of residues, additional plant metabolism data (appropriate to the proposed latest time of application) may be required, in order to refine the residues definition.

The application rate and timing used in the plant metabolism study correspond to GAP criteria. Three supervised residue trials were carried out according to the notified GAP on wheat (1) and barley (2) in Southern Europe and diflufenican was the residue analysed. The plant metabolism study and the three residue trials showed identical results, with residues in grain less than 0.01 mg/kg and residues in straw less than 0.02 mg/kg. In addition, a number of residue trials in wheat and barley in Northern and Southern Europe are available with an increased latest time of application (up to BBCH 30 instead of BBCH 14). Residues in grains were consistently below the LOQ (0.01 mg/kg); however in straw residues occasionally exceeded the LOQ (0.05 mg/kg) and reached up to 0.17 mg/kg (N-EU). For want of a sufficient number of GAP corresponding trials the RMS proposed to use those additional trials to support the notified GAP. Valid storage stability data and validated analytical methods support the residue values found in the selected supervised residue trials. The data support an MRL proposal for wheat, barley and rye grains on LOQ level (refer to 3.4).
No investigation of the behaviour and the level of residues under processing conditions is necessary due to the insignificant level of residues in wheat grain. Straw is usually not processed.

3.1.2 SUCCEEDING AND ROTATIONAL CROPS

The metabolism and distribution of diflufenican in rotational crops was investigated in wheat, cabbage and sugar beet. The crops were grown in soil treated (bare ground application) with pyridine, difluorophenyl and trifluoromethylphenyl ring labelled [^{14}C] diflufenican at a rate of *ca* 3 N. At harvest TRR in the crops were less than 0.06 mg/kg, with the exception of straw (0.08 – 0.17 mg/kg).
On characterisation of the extractable radioactivity three components were identified in the crops at harvest as diflufenican and its metabolites AE 0542291 and AE B107137, free and conjugated. These three components accounted for up to 47% of the TRR in cabbage, for up to 69% of the TRR in sugar beet tops and for up to 88% of the TRR in sugar beet root at harvest. Other residues (of unknown or unextractable nature) were present each with less than 0.01 mg/kg.

For wheat grain the three components reported above accounted for up to 6% of the TRR in the crop at harvest and for wheat straw for up to 13% of the TRR, with the majority of the radioactivity (up to 87% [0.03 mg/kg] in grain and up to 60% [0.08 mg/kg] in straw) being associated with polar material resulting from the fragmentation of the compound in the plant or in the soil prior to uptake. One other unknown metabolite was present at a level of less than 0.01 mg/kg. The remaining unextractable radioactivity in grain accounted for 0.01 mg/kg and in straw for less than 0.07 mg/kg and was probably associated with the fragmentation of the compound and the natural incorporation of these fragments into the plant tissue.

The metabolite AE B107137 was also identified in the rat metabolism studies and is eventually not expected to be more toxic than diflufenican (refer to chapter 2.8). The metabolite AE 0542291 was not found in the rat, but was not considered to be of concern at the levels (<0.01 mg/kg) present in the study.
The highest residue for metabolite AE B107137 found in this study was 0.04 mg/kg in sugar beets after 120 days. Considering the study was at 3N rate, residues >0.01mg/kg may occur in roots. The notifier proposed a waiting period of 150 days before planting root crops. The meeting rejected the proposal. However, the experts concluded that for this particular notified use and according to the intended GAP it is not expected to get residue levels, including metabolite AE B107137, exceeding 0.01 mg/kg considering that the study was overdosed and performed on bare soil. Rotational crop residue trails are currently not necessary.
It is however noted that if uses with higher application rates and/or a later time of application are requested in the future, Member States should pay attention to the residues in rotational crops including crops that may be fed to livestock.

3.2 NATURE AND MAGNITUDE OF RESIDUES IN LIVESTOCK

Residues of up to 0.17 mg/kg in straw from trials with an increased latest time of application were used to estimate the livestock dietary burden because there are insufficient residues trials data available to support the notified representative use. Based on this data livestock exposure, in particular to ruminants, is possible when straw is fed to the animals. It is also noted that based on its log $_{Pow}$ (4.2) diflufenican con be considered fat soluble and thus may accumulate in body tissue upon long term exposure.

The metabolism and distribution in animals was investigated in lactating cows and chickens upon administration of difluorophenyl and pyridine ring labelled [^{14}C] diflufenican for seven consecutive days. As for the representative use no exposure of poultry is expected. However, the study was evaluated in the DAR for future reference.

The doses uses in the submitted ruminant study are exaggerated (up to 500 N) when compared to the estimated maximum exposure (based on the highest residues in cereal grain and straw) for beef and dairy cattle from the representative use. The majority of the administered radioactivity was excreted (70-86%), with less than 0.1% recovered in the milk and less than 0.2% in the tissues.

On characterisation of the extractable radioactivity one major component was identified in the milk as diflufenican, representing 48-52% of the TRR in the milk. Two other metabolites were identified, plus several unknowns, which individually were present at levels of less than 0.01 mg/kg. The remaining unextractable radioactivity, accounted for 22-26% (<0.01 mg/kg) of the TRR in the milk. On characterisation of the extractable radioactivity in the tissues one major component was identified in the fat as diflufenican, representing 82-91% of the TRR in the fat. For liver, several metabolites were tentatively identified as diflufenican, hydroxylated diflufenican and hydroxylated anilines/ defluorinated hydroxylated anilines, however none were present at a quantifiable level, with the exception of AE B107137 (0.02 mg/kg). The remaining unextractable radioactivity, accounted for up to 0.26 mg/kg of the TRR in the liver. For kidney, several metabolites were tentatively identified as hydroxylated anilines/ defluorinated hydroxylated anilines. The remaining unextractable radioactivity accounted for 38% (0.01 mg/kg) of the TRR in the kidney.

It was concluded that, based on the metabolism data submitted residues in products of ruminant origin should be defined as diflufenican for risk assessment and monitoring purposes.

When extrapolating the diflufenican residue levels found in the metabolism study to the levels actually expected upon livestock exposure to cereals (straw and grains) treated according to the notified GAP no residues of diflufenican above the limit of quantification (LOQ) are likely to occur in edible animal matrices.

Therefore, at the moment no feeding studies and no MRLs for animal products are considered necessary.

However, the experts noted the following: Livestock feeding studies might be required, if in the future uses with more critical application rates or timings or with other feed items including cereal forage are requested. Particular consideration should also be given to residue levels in rotational crops.

3.3. CONSUMER RISK ASSESSMENT

The chronic dietary risk assessment for consumers is based on the proposed MRL of 0.01* mg/kg and on consumption data from the WHO/GEMS Food European diet and UK consumption data, respectively.

The TMDI and total NEDIs from the consumption of wheat, barley, rye and oats for adults, infants, toddlers, children, vegetarians and the elderly are all significantly below (< 1%) the allocated ADI of 0.2 mg/kg bw/day.

As no ARfD was allocated an acute risk assessment is not required.

The consumer risk assessment cannot be concluded on with regard to the second active substance, flufenacet, in the notified formulation.

3.4. PROPOSED MRLS

Wheat, barley, rye	0.01* mg/kg
	* LOQ

4. Environmental fate and behaviour

Diflufenican was discussed at the PRAPeR experts' meeting for fate and behaviour in the environment (PRAPeR 23) in April 2007.

4.1. FATE AND BEHAVIOUR IN SOIL

4.1.1. ROUTE OF DEGRADATION IN SOIL

The route of degradation of diflufenican in soil under dark aerobic conditions was investigated in two studies with three soils (pH 6.5 – 7.6; OM 2.9 – 3.6 %; clay 15.1 – 34 %) at 22 ºC (two soils) and 20 ºC (one soil) with the pyridine ^{14}C labelled diflufenican. No transformation products above 5 % AR were identified in the first study that only lasted for 52 d. In the second study, AE 0542291, max. 15.7 % AR after 286 d) and AE B107137 (max. 8.79 % AR after 286 d) were identified as major metabolites. Mineralization amounted to a maximum of 51.2 % AR after 52 d in the first study but only up to 3.85 % AR after 120 d in the second study. Unextractable residues reached the 18.5 % AR after 54 d in the first study and 3.04 % AR after 120 d in the second study.

A separated study was performed with diflufenican ^{14}C labelled at the rings 2,4-difluorophenyl and 3-trifluoromethylphenyl in one soil (pH 6.5, OM 3.1 %, clay 23.75 %) under dark aerobic conditions at 20 ºC. Only AE B107137 (max 11.3 % AR after 60 d) was detected as a major metabolite in the 3-trifluoromethyl ring labelled sample. No major metabolites were identified in the 2,4-difluorophenyl ring labelled sample. The fractionation of unextracted residues from the 269 d samples showed that unextracted radioactivity from 2,4-difluorophenyl ring labelled diflufenican treated soil (unextracted max. 15.5 % AR after 119 d) was mostly associated with the humin and humic acid fractions whereas that from 3-trifluromethylphenyl ring labelled diflufenican treated soil (unextracted max. 21,6 % AR after 269 d) was more evenly distributed across the fractions. CO_2 amounted to 25.9 – 23.15 % AR after 269 d in 2,4-difluorophenyl ring labelled diflufenican and 3-trifluromethylphenyl ring labelled diflufenican respectively. In the aerobic rate of degradation study (see next section) both metabolites AE 0542291 (max. 26.26 % AR after 320 d) and AE B107137 (max. 14 % AR after 120 d) appeared as major metabolites in at least one of the three soils tested.

Two degradation studies under dark anaerobic conditions were performed with 2,4-difluorophenyl and 3-trifluorophenyl labelled diflufenican (one soil: pH 6.5, OM 3.1 %, clay 23.75 %) and with pyridine labelled diflufenican (one soil: pH 7.7, OM 3.6 %, clay 15.1 %). Transformation product 2,4-difluroaniline (max. 34.35 % AR after 272 d) was identified as a major anaerobic metabolite that had not been previously found in the aerobic studies and show to be very volatile.

In the available soil photolysis study, diflufenican is shown to be stable to the photolysis in soil.

4.1.2. PERSISTENCE OF THE ACTIVE SUBSTANCE AND THEIR METABOLITES, DEGRADATION OR REACTION PRODUCTS

Rate of degradation of diflufenican in soil under aerobic conditions at 20 ºC was investigated in a study with three soils (pH 5.5 – 7.5, OM 3.4 – 5.5 %, clay 9.7 – 32.7 %) and was calculated from the results of the route studies. Diflufenican was moderate to high persistent in soil ($DT_{50\ lab}$ = 44.3 –

248.5 d). Degradation was seen to be relatively slower at 10 ºC ($DT_{50\ lab\ 10\ ºC}$ = 204.4 – 875 d) and under anaerobic conditions ($DT_{50\ anaerobic}$ = 87.7 d – 400 d). A multicompartmental kinetic analysis of the data of rate study (Mahay and Burr, 2001 a) was performed with the modelling program TopFit 2.0. In principle, this exercise was used by the notifier only to derive the formation fractions of the metabolites AE B107137 and AE 0542291. However, RMS observed that the degradation rates derived from these studies are much slower than the ones observed in other studies (AE B107137: DT_{50} = 67 d; AE 0542291: DT_{50} = 273 d). RMS attributed these longer half lives to an artefact due to the fact that the degradation phase of the metabolites occurred in the latter stages of the parent study when the microbial activity of the soil may have decreased.

The rate of degradation of metabolites AE B107137 and AE 0542291 were investigated under dark aerobic conditions at 20 ºC in three soils (pH 6.2 – 7.3, OC 0.82 – 2.75 %, clay 11.1 – 29.4 %). These metabolites are moderate persistent in soil (AE B107137: $DT_{50\ lab\ 20\ ºC}$ = 9.1 – 17. 9 d; AE 0542291: $DT_{50\ lab\ 20\ ºC}$ = 13.6 – 58.7 d). For metabolite AE 0542291 the RMS considered that there may be some evidence of pH dependence on the degradation rate of this metabolite since the longest half life was observed for the only acidic soil tested.

Degradation of AE B107137 was also investigated under anaerobic conditions. It was shown to be very high persistent under these conditions ($DT_{50\ anaerobic}$ = 413 d).

A field study in six German sites is available (Maycey and Savage, 1990b). However, the study was considered by the RMS to provide only supporting information since samples were analyzed to a depth of only 5 cm and only metabolite AE B107137 was analyzed in two sites. Diflufenican was shown to be high persistent in this study (DT_{50} = 214 – 245 d).

Another field study (Duncan, Doran and Livinstone, 2004a) was conducted under GLP in six European locations (Dunbar, UK; Santilly, France; Goch, Germany; Limburg, Netherlands; Lérida, Spain; Lodi, Italy). Soil layers were analyzed down to 90 cm for diflufenican and the two major soil metabolites. Diflufenican was detected in the 0-30 cm soil layer, mainly in the top 0-10 cm layer. The two metabolites AE B107137 and AE 0542291 were not observed practically at any time point in any of the trials above the LOQ (LOQ = 0.002 mg/kg). Diflufenican show to be high to very high persistent (DT_{50} = 224 d – >241 d) in these trials.

A kinetic analysis of the two field studies to obtain field normalized half lives is also available. Excluding the values from the not fully reliable dissipation rates of the firs field study (Maycey and Savage, 1990b) normalised half lives are in the rank of 103–282 d (Geometric mean half life=156 d).

A four years accumulation study in two Italian sites (Roma and Bologna) is available. In this study a combined formulation of diflufenican and trifluralin was applied to wheat. Minimal risk for accumulation was identified by the RMS in this study. However, the agronomic practices undertaken (i.e. ploughing to 40 cm) may not make the study representative of uses with minimum tillage. Additionally, the varying sampling depth in the Rome site does not allow reaching conclusive results from this site.

Also a five years accumulation study conducted at six sites in south-east England is available (Maycey and Savage, 1991a). In this study a clear tendency to accumulation of diflufenican residues is observed. After five years of successive applications, plateau of diflufenican residues had not been reached for three of the six sites. The need for further or longer accumulation studies was discussed

by the expert's meeting. The meeting agreed that even the plateau has not been actually reached the level at the end of the study was close enough to assess the potential accumulation of diflufenican. The highest average accumulation factor calculated from the studies give almost the same plateau PEC as the empirical values selected by the RMS. The applicant's proposal to exclude soils with high OM content was found unjustified by the meeting. Also the selection of data sampling depth to represent till and no-till situations was disregarded by the meeting as a non justified approach.

PEC soil were initially calculated by the RMS assuming a single pre-emergence application of 120 g a.s. / ha to winter wheat with no interception and the worst case field half life (DT_{50} = 245 d) from the study not considered fully reliable by the RMS. PEC soil has been calculated for 100 d and after repeated yearly application. Maximum peak PEC soil for the metabolites AE B107137 and AE 0542291 were calculated based on maximum amount observed in the laboratory degradation studies and the max peak PEC soil calculated for the parent compound in the accumulation PEC soil calculation. However, since soil concentration derived from the field accumulation study was higher than the obtained from this calculation this late value was used for the ecotoxicological risk assessment and the calculation of the potential maximum concentration of the metabolites. This later approach was considered acceptable by the experts' meeting.

4.1.3. MOBILITY IN SOIL OF THE ACTIVE SUBSTANCE AND THEIR METABOLITES, DEGRADATION OR REACTION PRODUCTS

Batch adsorption desorption studies were performed with diflufenican in four soils (pH 6.6 – 7.7; OC 0.75 – 2.25 %; clay 3.1 – 34 %), with AE B107137 in four soils (pH 5.7 – 7.0; OC 1.6 – 4.7 %; clay 6 – 27.6 %) and with AE 0542291 in other four soils (pH 4.5. – 6.9; OC 0.8 – 3.9 %; clay 6.8 – 68.8 %). Diflufenican is slight to low mobile in soil (K_{foc} = 1622 – 2369 mL / g), AE B107137 is very highly mobile (K_{foc} = 7 – 23 mL / g) and AE 0542291 is medium to high mobile (K_{foc} = 103 – 160 mL / g).

After the DAR was finalized the applicant submitted an additional batch adsorption desorption study that was evaluated and summarized in the Addendum by the RMS. Adsorption desorption of diflufenican was investigated in six additional soils (pH 4.1 – 7.7; OC 0.9 – 3.6 %; clay 18 – 38 %). In this study diflufenican was shown to be immobile to slight mobile in soil ((K_{foc} = 3066 – 7431 mL / g). The applicant proposed that results from this study should replace the results from previous one. This was found unjustifiable by the experts' meeting since the first study has already been assessed as acceptable by the RMS and MS's experts. The meeting of experts agreed that all 10 values and its arithmetic mean should be collected in the list off end points (new mean Koc = 3417 mL / g).

After the DAR was finalized, the applicant also presented a time dependent sorption study in four soils that was summarized by the RMS in the addendum. Although the study design appeared appropriate, the way in which results had been used in the revised exposure assessment in the addendum were not accepted by the experts meeting. The experts' meeting realized that the study actually measures a decreased desorption not an increasing adsorption. It is not clear if the effect observed is due to a real ageing effect or to a decreasing range of concentrations effect. With the

current assessment, the meeting considered that this study does not allow supporting higher tier assessment of diflufenican fate.

A two years lysimeter study was provided by the applicant in the dossier. RMS considered it to provide only additional evidence since the soil employed does not represents a realistic worst cased for leaching.

4.2. FATE AND BEHAVIOUR IN WATER

4.2.1. SURFACE WATER AND SEDIMENT

Diflufenican and its metabolite AE B107137 were stable to hydrolysis in aqueous buffer solutions (pH 5, 7 and 9) at 22, 50 and 70 ºC. Photolysis of diflufenican and its metabolite AE B107137 was investigated in sterile aqueous solutions. Minimal degradation of diflufenican was observed in the irradiated samples with respect to the dark ones (DT_{50} ≈ 139 d). No degradation was observed for the metabolite AE B107137. Therefore aqueous photolysis is not expected to be a major route of degradation of diflufenican in the aqueous environment.

Diflufenican was not readily biodegradable according the available study.

Degradation of diflufenican was investigated in one study with two water / sediment systems ($pH_{sediment}$ = 7.5 – 7.8; pH_{water} = 8.2) under dark aerobic conditions at 20 ºC and with the compound ^{14}C labelled at the pyridine ring. The product was applied at a rate of 83 µg / L (equivalent to an overspray of 250 g / ha on a 30 cm depth water body). This application rate is significantly above of the solubility in the range of pHs of the study (solubility pH 9 = 6 µg / L; solubility pH 7 = 50 µg / L). Initially diflufenican partitioned to the sediment. This effect was likely enhanced by the fact that the substance was tested above the water solubility limit. Diflufenican was medium high persistent in these systems (DT_{50} = 85 – 181 d) and was slowly transformed to the metabolite AE B107137 (max. 32.6 % AR in the sediment and max. 13.3 % AR in the water after 30 d). Data from this study were analyzed in a separated study by a multicompartmental kinetic model using modelling program TopFit 2.0. Separated rate constant for all the processes (degradation and partitioning) were calculated for parent diflufenican and metabolite AE B107137. Rate constant are likely to be strongly correlated in this multicompartmental system. Whereas they are able to describe the system as a whole the individual degradation rates for the water phase should be taken with caution (Diflufenican $DT_{50water}$ = 95.3 -104 d; AE B107137 $DT_{50water}$ = 54.6 – 97.8 d). The values obtained from this kinetic analysis were employed in the FOCUS SW modelling presented in the DAR.

Degradation of diflufenican was also investigated in one study with two water / sediment systems ($pH_{sediment}$ = 5.2 – 5.9; pH_{water} = 6.75 – 7.84) under dark aerobic conditions at 20 ºC and with the compound ^{14}C labelled at the 2,4-difluorophenyl ring. The product was applied at a rate of 160 µg / L and 220 µg / L for each of the systems (equivalent to an overspray of 187.5 g a.s. / ha). This application rates are significantly above of the solubility in the range of pHs of the study (solubility pH 4.5 = 5 µg / L; solubility pH 7 = 50 µg / L). Initially diflufenican partitioned to the sediment. This effect was likely enhanced by the fact that the substance was tested above the water solubility limit. Degradation of diflufenican in these systems was slower than in the previous study. However, no whole system half lives are reported in the DAR for this study. The only metabolite identified was 2,4-difluroaniline (max 8.2 % AR in the whole system after 30 d, 1.6 % AR of it bounded to

sediment). Data from this study were analyzed in a separated study by a multicompartmental kinetic model using modelling program ModelMaker. The model proposed included two compartments for the parent in the sediment phase (precipitated and true adsorbed). There is not separated experimental data on the precipitated and the true adsorbed diflufenican. Therefore, the modelling of the sediment in two separated compartments (precipitated and adsorbed) improves the fitting by artificially increasing the number of free parameters, not necessarily giving more reliable degradation parameters. Dissipation parameters from the water phase (DT_{50} = 20.1 – 36.1 d) and the sediment (DT_{50} = 277 – 877 d) were calculated by the RMS on basis of the kinetic parameters estimated in this study.
In all the water sediment systems available mineralization was negligible (< 4 % A R after 120 d).

No water sediment study is available with diflufenican labelled at the 3-trifluoromethylphenyl ring. In soil studies the same metabolites that for the diflufenican labelled at the other rings are identified. Therefore, the RMS considered that the route of degradation in water sediment systems was adequately addressed by the submitted information. Experts' meeting agreed with RMS view.
A sediment monitoring study performed between March and July 1996 on heavily drained winter cereal areas in UK with history of repeated use of diflufenican at rates below 100 g / ha is available. Variable results with concentrations of diflufenican ranging from < 5 to 44 µg / Kg were obtained.
Summary of run-off mitigations studies has been provided by the applicant and reproduced by the RMS in its integrity. Raw studies were required to consider the results with respect to EU risk assessment. Published results of these studies seem to have been used in the draft FOCUS landscape and Mitigation Factors and in the opinion of the RMS results are in agreement with the proposals of this draft document with respect to the mitigation effect of vegetative buffer zones on run off loadings to surface water.
Kinetic parameters estimated in the multicompartmental fitting exercises are based on data from systems where diflufenican was applied above the solubility limit. In this way the dissipation from the water phase to the sediment is enhanced by the precipitation. These, parameters have been used in FOCUS even when the surface water concentration is well below the solubility limit. Kinetic parameters from water sediment systems where diflufenican is applied below its solubility limit would be needed to derive reliable FOCUS PEC_{SW}.
FOCUS Step 1 and Step 2 $PEC_{SW/SED}$ calculation were performed for diflufenican and the metabolites AE B107137 and AE 0542291. The values obtained in these lower tier estimations were sufficient to address the risk presented by the metabolites for the EU representative uses. FOCUS Step 3 calculations were presented by the notifier for the parent diflufenican. Plant uptake of 0.5 was assumed in FOCUS step 3 calculations. This plant uptake factor was not considered fully justified by the RMS, since diflufenican is a borderline systemic product. RMS repeated the Step 3 calculation assuming no uptake from plants. Since the concentrations obtained were not dramatically different than the resulting form the applicant calculation the later ones were used in the risk assessment by the RMS. Step 4 calculations were proposed by the applicant taking into consideration spray drift buffer zones and vegetative filter strips of 5 m. The run off mitigation figures proposed by the applicant were based on a study where effectiveness of vegetative filter strips on diflufenican run off was

actually tested. However, the actual report of the study was not found in the dossier and a data gap was identified. The study was however finally found under a different authors name (Schaefer 2003). In the Addendum, RMS assesses and summarizes the new FOCUS $PEC_{SW / SED}$ calculations provided by the applicant using direct whole system degradation half life ($DT_{50\ whole\ system}$ = 214 d) applied to the water phase and a simple worst case default half life (DT_{50} = 1000 d) for the sediment phase. The whole system half life used in modelling was derived from the arithmetic mean of the four whole systems half lives calculated with "best fit" kinetics. Experts' meeting agreed on this approach but using SFO instead of best fit kinetics. It was agreed that SFO values should be in the list of end points for future use by MS's, however the repetition of the calculation was not required since the best fit values are a more worst case in this specific case. Since whole system values are used the issue of the possible precipitation during the experiment was considered superseded, since any possible precipitation would result in longer whole system half lives. New calculations were performed assuming time dependent adsorption, that was not considered demonstrated by the experts' meeting. Numerical values for max PEC_{SW} and PEC_{SED} obtained with the two approaches available to the meeting (DAR and Addendum) were in the same range indicating that the models and scenarios calculated were relatively insensitive to water and sediment half lives.

In conclusion, the expert's meeting decided to retain the $PEC_{SW / SED}$ values presented in the DAR for the EU risk assessment. It was noted that the Kfoc used from the DAR (1989 as opposed to the new mean value of 3417) was conservative but it was decided not to redo the risk assessment because an acceptable scenario for aquatic risk assessment was identified in the DAR. It was questioned whether the mitigation effect of vegetative buffer strips assumed in the Step 4 calculations may be considered acceptable according the panel opinion of FOCUS Landscape and mitigation.[7] Examination of the modelling results and the ecotoxicological risk assessment showed that Step 4 calculation with a 5 m buffer for spray drift only resulted in one scenario with acceptable TERs for aquatic risk assessment (D5 pond), which the experts' meeting considered not to be affected by the run off mitigation. However if the same approach is applied as was agreed in the expert meeting than the risk to aquatic organisms is addressed also for the full scenario D3 (ditch). Therefore, it was considered that in this case the consideration of the run off mitigation had no effect on the outcome of the final risk assessment for this scenario. This should not be understood as that the meeting agreed on the run off figures proposed by the applicant since these were not discussed by the meeting. After the expert meeting, EFSA identified a data GAP for new FOCUS PEC_{SW} calculations using a plant uptake factor of zero and the input parameters agree for the meeting (mean whole systems half life for SW and 1000 d for sediment, with only spray drift buffer strip mitigation) in order to confirm the proposed risk assessment and to make it consistent with the risk assessments performed for other substances of this peer review phase.

PEC_{SED} derived from FOCUS Step 3 calculations were slightly lower than concentrations measured in the sediment in the UK monitoring studies. (Max FOCUS Step 3 PEC_{SED} = 30.4 µg / kg, max.

[7] Opinion of the Scientific Panel on Plant protection products and their residues (PPR) related on the Final Report of the FOCUS Working Group on Landscape and Mitigation Factors in Ecological Risk Assessment. The EFSA Journal (2006) 437, 1-30.

monitored $[diflufenican]_{SED}$ = 44 µg / kg). The experts' meeting considered difficult to compare monitoring with modelling results. The expert's meeting considered that the monitoring studies do no motivate the need to deviate form FOCUS guidance.

4.2.2. POTENTIAL FOR GROUND WATER CONTAMINATION OF THE ACTIVE SUBSTANCE THEIR METABOLITES, DEGRADATION OR REACTION PRODUCTS

Potential ground water contamination by diflufenican and the soil metabolites AE B107137 and AE 0542291 was evaluated by FOCUS PELMO (v.3.3.2). The 80th percentile annual average concentrations in leachates below 1 m were predicted to be less than 0.001 µg / L for all compounds in the nine European scenarios.

Only one FOCUS model has been used to assess the potential ground water contamination by diflufenican and its metabolites. In principle, at least results of two models are needed to complete the risk assessment to take into account the disparity of results observed among the available models.[8] However, since the results are three orders of magnitude below the trigger of 0.1 µg / L it not expected that the trigger will be breached when the calculation is performed with other model. Additionally the results were obtained with the K_{OC} obtained from the study presented in the original DAR. This is a worst case when new data available is considered. The values reported in the DAR are the ones resulting from the notifier calculation only. A recalculation by the RMS using worst case plant uptake factor of 0 and a more conservative formation fraction of 1 for each metabolite did not alter the PEC_{GW} values derived using the FOCUS PELMO model, hence only the Applicant values are reported.

4.3. FATE AND BEHAVIOUR IN AIR

Diflufenican has a vapour pressure of 4.25 10^{-6} Pa at 25 ºC and a Henry's Law constant of > 1.18 10^{-2} Pa m^3/mol at 20 ºC and could be considered slightly volatile. Volatilization of diflufenican from plant surface and soil was negligible (plants: 0.3 AR % after 24 h, soil: 0.0 – 0.005 % AR after 24 h). A theoretical calculation of the potential for photo-oxidation resulted in a half life of 3.3 d based on an OH radical concentration of 1.5 10^6 cm^{-3} on a 12 h day basis. Based on the negligible potential for volatilization form plant and soil surface it is considered that exposure to air and therefore long range transport thought air is insignificant for diflufenican. However, during expert's meeting soil anaerobic metabolite 2,4-difluroaniline was found to be very volatile and may need to be assessed for the air compartment and for transport through air when prolonged anaerobic conditions are expected to occur in soil. The meeting agreed that at any case exposure is expected to be "very low".

5. Ecotoxicology

Diflufenican was discussed at the PRAPeR experts' meeting for ecotoxicology (PRAPeR 23) in April 2007. A data requirement was set for the applicant to submit a full specification of the material used

[8] Opinion of the Scientific Panel on Plant Health, Plant Protection Products and their Residues on a request of EFSA related to FOCUS groundwater models. The EFSA Journal (2004) 93, 1-20.

in the ecotox studies including an assessment of the compliance with the specification of the technical material. This was submitted by the applicant and considered as addressed by the RMS. The experts agreed to the assessment of the RMS. It should be noted that the technical specification was not agreed by section 1 and the modified specification presented after the meeting was not peer-reviewed.

5.1. RISK TO TERRESTRIAL VERTEBRATES

The representative use of diflufenican evaluated is as an herbicide in winter cereals formulated with flufenacet as a second active substance. The formulation Herold 600 SC contains 206.2 g diflufenican/L and 421.1 g flufenacet/L. The risk assessment as presented below is based on exposure to diflufenican alone.

No short-term study with birds was submitted. However the short-term risk from diflufenican was considered to be addressed by the long-term study and the acute NOEL is 4000 mg diflufenican/kg bw.

The acute and long-term TER values for herbivorous and insectivorous birds and herbivorous mammals exceeded the Annex VI trigger values. The risk to birds and mammals from uptake of contaminated earthworms and fish was assessed as low as well as the acute risk from uptake of contaminated drinking water.

Since the BCF in fish was > 1000 and the DT_{90} in sediment was >100 days the risk of bioaccumulation in terrestrial food chains was assessed. The BAF (bioaccumulation factor) was calculated as 0.77. Since the BAF is <1 the risk of bioaccumulation is considered to be low.

Exposure to the second active substance (flufenacet) was neither taken into account in the toxicity endpoints nor in the exposure estimates. It should be noted that the long-term TER for herbivorous mammals of 5.3 is close to the trigger of 5 based on exposure to diflufenican alone. It is likely that a risk assessment based on combined exposure to both active substances would lead to a TER value below the trigger of 5. No conclusion can be drawn on the risk to birds and mammals from the representative use of diflufenican formulated with flufenacet as suggested in the GAP table.

5.2. RISK TO AQUATIC ORGANISMS

Green algae were the most sensitive organisms tested driving the aquatic risk assessment. For all other organisms the Annex VI trigger was met based on maximum PECsw from the worst case FOCUS step 3 scenario (0.000835 mg diflufenican/L).

A no-spray buffer zone of 5 metres was included in the FOCUS step4 calculations. Only in the part scenario D5 pond the TER was 10.9. The RMS presented also a calculation with a vegetated filter strip which resulted in a TER >10 for the part scenario R1 pond. However, no full FOCUS scenario resulted in a TER >10. To include a vegetated filter strip in the FOCUS step 4 calculations was not agreed in the experts meeting on fate and behaviour. A new aquatic risk assessment including new

PECsw calculations was presented in the addendum from April 2007. The risk to algae was refined by using data on recovery. In a test it was shown that *Scenedesmus subspicatus* which was the most sensitive algae species tested can recover within 3 days when transferred to fresh growing media after 3 days of exposure to 4.2 µg diflufenican/L. In order to cover effects on less sensitive but slower reproducing algal species the safety factor of 10 was maintained in the risk assessment. The exposure pattern of the FOCUS scenarios were analysed and the risk was considered acceptable provided that the peak exposure is below 0.42 µg diflufenican/L and that this exposure does not last longer than 3 days. In order to cover the overall NOEC of 0.1 µg diflufenican/L no other peak exposure should exceed the NOEC of 0.1 µg diflufenican/L. (observed in a test with the algae *Pseudokirchnerialla subcapitata* which was the second most sensitive species) the peak PECsw values were compared to the NOEC of 0.1 µg diflufenican/L which was lower than the exposure level at which recovery was observed for *S. subspicatus*). Based on this assumptions the risk was considered as addressed for the following FOCUS step 4 scenarios (including a 5m no spray buffer zone): D1 (stream), D3 (ditch), D4 (pond), D4 (stream), D5 (pond), D5 (stream), D6 (ditch) and R1 (pond). The risk was not sufficiently addressed for the scenarios D1 (ditch), D2 (ditch), D2 (stream), R1 (stream), R3 (stream) and R4 (stream). The suggested approach was agreed by the experts in the meeting on ecotoxicology. However the experts on fate and behaviour rejected some of the input parameters applied in the FOCUS step 4 calculations as presented in the addendum (see point 4.2.1). It was agreed in the fate meeting that the PECsw values from the DAR should be used in the risk assessment. In the final addendum of August 2007 the RMS referred to the original risk assessment in the DAR. The RMS stated that a new risk assessment was submitted by the applicant but that this was not assessed and has not been summarised in the addendum. In the original DAR only one part scenario D5(pond) but no full FOCUS step 4 scenario (with a 5 m no-spray buffer zone) resulted in TERs >10. However if the same approach is applied as was agreed in the expert meeting than the risk to aquatic organisms is addressed also for the full scenario D3 (ditch). It may be possible to identify some full FOCUS step 4 scenarios for which the risk to aquatic organisms is acceptable if the same approach is used as suggested in the addendum of April 2007 or if larger no spray-buffer zones than 5 metres would have been used as a risk mitigation measure in the FOCUS step 4 calculations.

The BCF of 1596 for the whole fish indicates a potential risk of bioaccumulation. The depuration in fish is rapid with 50 % elimination from the whole fish within 2.4 – 3.3 days (97% of AR after 14 days). The product is applied only once per year and the DT_{50} in water is 31.4 days. The long-term TER to fish of 18 was above the trigger of 10. Therefore the risk from bioconcentration in fish is considered to be low. However some uncertainty remains regarding uptake of diflufenican via contaminated sediment dwelling prey. Sediment dwelling organisms could carry a high load of diflufenican because of the high log P_{ow} of diflufenican of 4.2 and its persistence in sediment (mean DT_{50} of 338.7 days). In the expert meeting it was decided that there is no further assessment required since guidance is lacking and no agreed way to assess the risk to fish from this exposure route currently exists.

The risk from the major water metabolite AE B107137 and the major soil metabolite AE 0542291 to aquatic organisms was assessed as low based on FOCUS step 2 PECsw values. AE C522392 (2,4-difluroaniline) is a major soil metabolite formed under anaerobic soil conditions. Entry into water is possible via drainage. AE C522392 was tested with algae and *Chironomus riparius*. AE C522392 is more than 3 orders of magnitude less toxic to the most sensitive group of aquatic organisms (algae) compared to diflufenican.

In the aquatic risk assessment only exposure to diflufenican was taken into account. However a lower toxicity of diflufenican was observed in comparison to technical diflufenican in the studies with aquatic organisms. Herold SC 600 was tested with green algae (the group of the most sensitive organisms). The endpoint of formulation (attributing all the toxicity to diflufenican) was about 2 times higher than for technical diflufenican. Therefore it was decided in the meeting of experts that the risk from the formulation Herold SC 600 would be covered by the risk assessment for diflufenican.

5.3. RISK TO BEES

Studies with technical and formulated diflufenican were conducted with honeybees. The LD_{50}s for oral and contact toxicity for technical a.s. were >112.3 µg/L and >100 µg/L. The LD_{50}s for oral and contact exposure to the formulation Herold SC 600 were determined as >198 µg product/L and >200 µg product/L, respectively. The corresponding HQ values were in the range of <1.1 to <3.8. Since the HQ values are markedly below the HQ trigger of 50 the risk to bees is considered to be low for the representative use of diflufenican.

5.4. RISK TO OTHER ARTHROPOD SPECIES

Studies with formulated diflufenican were conducted with *Aphidius rhopalosiphi* and *Typhlodromus pyri* on glass plates and in addition extended laboratory studies were made available with *A. rhopalosiphi, Aleochara bilineata* and *Poecilus cupreus*. The HQ value for the risk to *A. rhopalosiphi* and *T. pyri* were calculated as <0.64 and <0.02 for the in-field and off field risk, respectively. In the addendum from April 2007 studies with *T. pyri* and a formulation with a similar composition as the lead formulation Herold SC 600 indicated a high risk to predatory mites. No studies with other non-target arthropods were submitted. Consequently a data gap was identified in the expert meeting to address the risk to non-target arthropods from exposure to the lead formulation Herold SC 600.

5.5. RISK TO EARTHWORMS

Diflufenican and its soil metabolites AE B107137 and AE 0542291 are of low toxicity to earthworms. The TER value of >1235, >10000 and >6250 indicate a low acute risk to earthworms from diflufenican and its metabolites AE B107137 and AE 0542291. Diflufenican is persistent in soil. No effects on reproduction or other sublethal effects were observed in a chronic test within 8 weeks up to the highest tested dose of 1000 mg diflufenican/kg soil. The long-term TER was calculated with the accumulated PECsoil of 0.405 mg a.s./kg soil to be 1235. The DT_{90} of the metabolite AE B107137 is

<100 days and therefore a chronic risk assessment is not triggered. The mean DT_{90} of AE 0542291 was 117 for 3 different soils. However the acute TER for this metabolite was higher than the TER for the parent and no sublethal effects were observed in the acute test. Therefore it is assumed that the long term risk from this metabolite posed to earthworms is low. Overall it is concluded that the risk to earthworms from the representative use is low. A new risk assessment based on new PECsoil values was presented in the addendum from April 2007. The new PECsoil values were rejected and the original PECsoil values (as presented in the DAR) were considered appropriate for risk assessment by the fate experts (see point 4.1.2). No studies with the lead formulation Herold SC 600 and earthworms were submitted. Considering the large margin of safety (the acute and long-term TERs for technical diflufenican exceed the trigger by more than 3 orders of magnitude) the risk from the formulation is likely to be covered from the risk assessment for technical diflufenican.

2,4-difluroaniline is a major soil metabolite formed under anaerobic soil conditions. No information on the toxicity to soil dwelling organisms is available for this metabolite. The risk to earthworms from metabolite 2,4-difluroaniline should be addressed in Member States where prolonged anaerobic conditions are likely to occur during the period of application.

5.6. RISK TO OTHER SOIL NON-TARGET MACRO-ORGANISMS

A litterbag study was submitted. Accelerated organic matter breakdown and a decrease in abundance of three different collembola species were observed until the end of the study after 5 months. A laboratory study with *Hypoaspis aculeifer* and the lead formulation "Herold SC 600" was conducted. The TER value was calculated as 24 based on the accumulated PECsoil of 0.405 diflufenican/kg soil indicating a low risk to soil dwelling mites.
However the litterbag study provided some indication that diflufenican affects soil functioning and community structure of soil dwelling organisms at concentrations of 0.141 and 0.423 diflufenican/kg soil. A new assessment of the available litterbag study and a study with the lead formulation "Herold SC 600" and collembola (*Folsomia candida*) were summarised in the addendum from April 2007. The TER value for collembola was calculated as 1521 based on a PECsoil of 0.288 mg diflufenican/kg soil. Also with the accumulated PECsoil of 0.405 mg diflufenican/kg soil the TER would be significantly above the long-term trigger of 5. The effects on community structure endpoints observed in the litterbag study were due to pronounced growth of one collembolan species (*Isotoma sp.*) in the controls. However no adverse effects were observed on biodiversity indices (Shannon index, evenness). Therefore the experts in the meeting agreed that the risk to soil dwelling non-target macro organisms and organic matter breakdown is sufficiently addressed.

5.7. RISK TO SOIL NON-TARGET MICRO-ORGANISMS

Studies with the technical diflufenican conducted at concentrations of 0.25 and 1.25 mg diflufenican/kg resulted in effects of less than ± 25% on soil respiration and nitrification. No effects of greater than ± 25% on soil respiration and nitrification were observed in tests with the soil metabolites AE B107137 and AE 0542291 at a concentration of 0.36 mg/kg which is in excess of the PECs of 0.05 mg/kg and 0.08 mg/kg. New studies with the lead formulation were submitted by the

applicant and assessed by the RMS in the addendum from April 2007. No effects of >25% were observed on soil respiration and nitrification at tested concentrations of up to 4 mg product/kg soil (equivalent to 3 kg product/ha, about 5 times the suggested field rate). The effects on nitrification were erroneously not reported in the addendum from April 2007 and therefore included later in the addendum from August 2007. Overall it is concluded that the risk to soil non-target micro-organisms is low for the representative use evaluated.

2,4-difluroaniline is a major soil metabolite formed under anaerobic soil conditions. No information on the toxicity to soil micro-organisms is available for this metabolite. The risk to soil non-target micro-organisms from metabolite 2,4-difluroaniline should be addressed in Member States where prolonged anaerobic conditions are likely to occur during the period of application.

5.8. RISK TO OTHER NON-TARGET-ORGANISMS (FLORA AND FAUNA)

Pre- and post emergence phytotoxicity was tested with formulated diflufenican (Herold 600 SC and Quarz) and 5 dicotyledone and 2 monocotyledone plant species. Since diflufenican is persistent in soil a risk assessment was conducted for exposure of seeds. The lowest endpoint for pre-emergence (fresh weight) was observed for *Lolium perenne* (EC_{50} = 171.8 mg a.s./ha, formulation = Quarz). The PECsoil at 1 m distance was calculated as 0.0112 mg a.s./kg (drift rate 2.77%). A soil concentration equivalent to the EC_{50} rate of 171.8 mg a.s./ha would be 0.229 mg a.s./kg soil. The TER values for pre-emergence toxicity were calculated as 20.4 indicating a low risk. The lowest endpoint for post emergence effects (fresh weight) was observed with *Brassica napus* (EC_{50} = 2.88 g a.s./ha). The TER for the post-emergence toxicity was calculated as 0.86 for a distance of 1m. A no spray buffer zone of 10 m would be required to achieve a TER of 8.28 which is above the trigger of 5. The EC_{50} values (endpoint fresh weight) observed for the lead formulation Herold 600 SC were 190.43 g a.s./ha pre-emergence treatment and 27.75 mg a.s./ha post-emergence treatment. The TER values were calculated as 18.76 and 2.73 for 1 m distance from the treated field. A no spray buffer zone of 5 m would be required to achieve a TER of 13.28 for post-emergence treatment. Two new studies with diflufenican formulations containing only diflufenican were submitted and assessed in the addendum from April 2007. However since these formulations differ from the representative formulation the outcome of the original risk assessment remains unchanged. For seedling-emergence a new risk assessment with updated PECsoil values was presented in the final addendum from August 2007. The risk assessment shows the need of risk mitigation comparable to a 5 metre non-spray buffer zone for pre-emergence exposure. However to achieve TERs >5 for post-emergence exposure a no-spray buffer zone of 10 metres is required and covers the risk from pre-emergence as well.

5.9. RISK TO BIOLOGICAL METHODS OF SEWAGE TREATMENT

No inhibition of respiration of activated sewage sludge of >10 % was observed up to the highest tested concentration of 1000 mg diflufenican/L. The EC_{50} is therefore >1000 mg diflufenican/L. It is not expected that diflufenican reaches biological sewage treatment plants at higher concentrations. Therefore the risk to biological methods of sewage treatment is expected to be low from the representative use.

6. Residue definitions

Soil

Definitions for risk assessment: diflufenican, AE B107137 and AE 0542291. Metabolite 2,4-difluroaniline also needs to be assessed for soil when prolonged anaerobic conditions are prevalent.

Definitions for monitoring: diflufenican

Water

Ground water

Definitions for exposure assessment: diflufenican, AE B107137, AE 0542291 and 2,4-difluoroaniline (anaerobic soil metabolite needs to be addressed when prolonged anaerobic conditions are prevalent).

Definitions for monitoring: diflufenican

Surface water

Definitions for risk assessment: diflufenican, AE B107137, AE 0542291 (via soil) and 2,4-difluoroaniline (anaerobic soil metabolite needs to be addressed when prolonged anaerobic conditions are prevalent)

Definitions for monitoring: diflufenican

Air

Definitions for risk assessment: diflufenican and 2,4-difluroaniline (volatile in an anaerobic soil degradation study)
Definitions for monitoring: diflufenican

Food of plant origin

Definitions for risk assessment: diflufenican (restricted to assessed GAP in cereals)
Definitions for monitoring: diflufenican (applicable to cereals only)

Food of animal origin

Definitions for risk assessment: diflufenican [9]
Definitions for monitoring: diflufenican (however no MRLs are currently proposed)

[9] currently only relevant for ruminants

Overview of the risk assessment of compounds listed in residue definitions for the environmental compartments

Soil

Compound (name and/or code)	**Persistence**	**Ecotoxicology**
Diflufenican	Highly to very highly persistent (DT_{50lab} = 44.4 – 248.5 d; $DT_{50field}$ = 214 – >241* d)	Low toxicity and risk to earthworms, low risk to other soil non-target macro- and micro-organisms
2-[3-(trifluoromethyl)phenoxy]pyridine-3-carboxylic acid (AE B107137)	Low to moderately persistent (DT_{50lab} = 9.1 – 17.9 d)	Low toxicity and low risk to earthworms, low risk to soil micro-organisms
2-[3-(trifluoromethyl)phenoxy]pyridine-3-carboxamide (AE 0542291)	Moderately persistent (DT_{50lab} = 13.6 – 58.7 d)	Low toxicity and low risk to earthworms, low risk to soil micro-organisms
2,4-difluroaniline (AE C522392), major metabolite under anaerobic conditions, behaviour in the environment is potentially pH dependent.	No data available. Data gap identified to address situations when prolonged anaerobic conditions are prevalent.	No data available Data gap identified to address situations when prolonged anaerobic conditions are prevalent.

* At least two longer half lives were calculated for two sites in the GLP field dissipation study; however, goodness of fit is statistically inappropriate for risk assessment. Nevertheless, soil risk assessment is based on the field accumulation study results which demonstrated that realistic worst case half life is longer than the longest reliable value obtained in the field dissipation studies.

Ground water

Compound (name and/or code)	Mobility in soil	0.1 µg / L 1m depth for the representative uses (at least one FOCUS scenario or relevant lysimeter)	Pesticidal activity	Toxicological relevance	Ecotoxicological relevance
Diflufenican	Low to immobile (K_{foc} = 1622 – 7431 mL / g)	No	Yes	Yes	Very toxic to aquatic organisms.
2-[3-(trifluoromethyl)phenoxy]pyridine-3-carboxylic acid (AE B107137)	Very high (K_{foc} = 7 – 23 mL / g)	No	~~No data available~~ Screening studies submitted No data required	oral LD_{50} >2000 mg/kg bw dermal LD_{50} >1000 mg/kg bw no genotoxic potential in vitro	Harmful to aquatic organisms
2-[3-(trifluoromethyl)phenoxy]pyridine-3-carboxamide (AE 0542291)	High to medium (K_{foc} = 103 – 160 mL / g)	No	~~No data available~~ Screening studies submitted No data required	No data available No data required	Harmful to aquatic organisms
2,4-difluroaniline (AE C522392), major metabolite under anaerobic conditions.	No data available Data gap identified to address situations when prolonged anaerobic conditions are prevalent.	No data available Data gap identified to address situations when prolonged anaerobic conditions are prevalent.	No data available Data gap identified to address situations when prolonged anaerobic conditions are prevalent.	No data available Data gap identified to address situations where anaerobic conditions are prevalent.	Toxic to aquatic organisms

Surface water and sediment

Compound (name and/or code)	**Ecotoxicology**
Diflufenican (water and sediment)	Very toxic to aquatic organisms, the risk assessment indicated a high risk to aquatic organisms
2-[3-(trifluoromethyl)phenoxy]pyridine-3-carboxylic acid (AE B107137) (water and sediment)	Harmful to aquatic organisms, the risk to aquatic organisms was assessed as low.
2-[3-(trifluoromethyl)phenoxy]pyridine-3-carboxamide (AE 0542291) (potential surface water trough run off / drainage	Harmful to aquatic organisms, the risk to aquatic organisms was assessed as low.
2,4-difluroaniline (AE C522392), (major metabolite under anaerobic conditions, potential surface water trough run off / drainage).	Toxic to aquatic organisms. No risk assessment was conducted but on the basis of the available information the risk to aquatic organisms is assumed to be low.

Air

Compound (name and/or code)	**Toxicology**
Diflufenican	Not acutely toxic by inhalation (rat LC_{50} > 5.12 mg/L/4h)
2,4-difluroaniline (AE C522392), major volatile metabolite under anaerobic conditions in soil.	No data available. PRAPeR 23 meeting (fate and behaviour in the environment) agreed that at any case exposure is expected to be "very low".

LIST OF STUDIES TO BE GENERATED, STILL ONGOING OR AVAILABLE BUT NOT PEER REVIEWED

- A data gap was identified by the expert meeting for a new technical specification (BCS) (relevant for all representative uses evaluated; already submitted, presented in addendum 4 to Vol.4, not peer reviewed, refer to chapter 1).
- A mouse lymphoma assay with diflufenican, with counting of both small and large colonies (relevant for all representative uses; provided by the applicant to the RMS after the experts meeting but not evaluated or peer-reviewed; refer to point 2.4).
- After the expert meeting, EFSA identified a data GAP for new FOCUS PEC_{SW} calculations using a plant uptake factor of zero and the input parameters agree for the meeting (mean whole systems half life for SW and 1000 d for sediment, with only spray drift buffer strip mitigation in order to confirm the proposed risk assessment and to make it consistent with the risk assessments performed for other substances of this peer review phase (relevant for all representative uses; data gap identified by EFSA after the experts meeting, new calculations have been provided to the RMS by the applicant but there are not evaluated or peer reviewed; refer to point 4.2.1).
- After the expert meeting, EFSA identified a data gap for the information necessary to address the major anaerobic metabolite 2,4-difluroaniline in the different environmental compartments including the biological activity and ecotoxicological relevance to address situations were prolonged anaerobic conditions are prevalent (relevant for all representative uses when prolonged anaerobic conditions are expected; data gap identified by EFSA after the experts meeting, no date of submission has been proposed by the notifier; refer to chapters 4 and possibly to 2 and 5).
- A risk assessment for birds and mammals for the representative use of the formulation Herold SC 600 (relevant for the representative use evaluated; data gap identified in the meeting of experts (PRAPeR 23 in April 2007); no submission date proposed by the notifier; refer to point 5.1).
- The risk assessment for aquatic organisms needs further refinement (relevant for the representative use evaluated; data gap identified in the meeting of experts (PRAPeR 23 in April 2007); a new aquatic risk assessment was submitted by the applicant in August 2007 but not included by the RMS in the addendum from August 2007; refer to point 5.2).
- The risk to non-target arthropods need to be addressed for the representative use of Herold SC 600 (relevant for the representative uses evaluated; data gap identified in the meeting of experts (PRAPeR 23 in April 2007); so submission date proposed by the applicant; refer to point 5.4).

Data gaps identified for the assessment of the identity and the impurities of the dossier provided by the applicant Makhteshim Agan:

- the source of the starting materials,
- a justification for the maximum content of impurity 6,
- a new technical specification where toluene has been removed as its presence is not justified.

CONCLUSIONS AND RECOMMENDATIONS

Overall conclusions

The conclusion was reached on the basis of the evaluation of the representative uses as proposed by the applicant which comprise pre- and post emergence applications with tractor mounted boom sprayers to control annual broad-leaved weeds and annual grasses (in particular for the control of amaranthaceae, caryophyllaceae, cruciferae, labiatae, malvaceae, polygonaceae, solanaceae, and especially rubiaceae (*Galium aparine*), scrophulariaceae (*Veronica spp.*) and violaceae (*Viola spp.*)) in winter wheat, winter barley and winter rye up to crop growth stage BBCH 10-13, at a single application at a maximum rate of 120 g diflufenican/ha.

The representative formulated product for the evaluation was "Herold SC 600", an aqueous suspension concentrate (SC) containing 200 g/L diflufenican and 400 g/L flufenacet, registered under different trade names in Europe.

Adequate analytical methods are available for the determination of diflufenican residues in food of plant and animal origin, soil, water and air.

Sufficient analytical methods as well as methods relating to physical, chemical and technical properties are available to ensure that quality control measurements of the plant protection products are possible.

The compliance of the toxicological batches with the technical specification could not be concluded since the final specification was not agreed (see section 1), and more data were needed to assess the relevance of the impurities. It should be noted that a revised specification has been provided to the RMS but not peer reviewed.

With regard to the mammalian toxicology, diflufenican has a low acute toxicity, is not irritant and has no skin sensitisation potential. In repeat dose studies, the main adverse effects were on the body weight gain and in the liver. No concern was raised about the genotoxic properties of diflufenican, and no carcinogenic potential was demonstrated. In the multigeneration study, incidences of dystocia were observed at the high dose but were concomitant with systemic toxicity and did not lead to classification. Furthermore the margin of safety between the dose where dystocia is observed and the reference values was considered sufficient. No teratogenic activity was shown in the developmental studies.

Taking into account the available data and the fact that the metabolite AE B107137 is also a rat metabolite, the experts agreed that it is unlikely to be more toxic than the parent.

The agreed acceptable daily intake (ADI) was 0.2 mg/kg bw/day with the use of a safety factor 100. The agreed acceptable operator exposure level (AOEL) was 0.11 mg/kg bw/day, with a correction for oral absorption (58%) and the use of a safety factor 100. An acute reference dose (ARfD) was not required. The estimated operator exposure is below the AOEL without the use of personal protective equipment (PPE).

The metabolism of diflufenican was investigated in wheat upon pre- and post-emergence application. The application rate and timing used in the plant metabolism study correspond to the notified GAP criteria. In the wheat grains, diflufenican could be detected but an extensive identification of metabolites was difficult due to the low residue levels. In straw, again diflufenican was identified; however the major part of the total residue consisted of different metabolites that, with one exception, were not identified since individually not present above the trigger value of 0.01 mg/kg. The meeting of experts noted that for future cereal uses that deviate from the assessed GAP additional metabolism data may be required in order to refine the residues definition, currently proposed as diflufenican.

The metabolism and distribution of diflufenican in rotational crops was investigated in wheat, cabbage and sugar beet. Two metabolites, AE 0542291[10] and AE B107137[11] could be identified since they presented a substantial part of the total residue in the tested crops. Eventually, the two metabolites were not considered to be of concern for the consumer. The experts concluded that for the particular notified use and GAP it is not expected to get residue levels in rotational crops exceeding the trigger value of 0.01 mg/kg.

A very limited number of residue trials support the notified GAP. In addition, residue trials are available with an increased latest time of application, and it was proposed to use these trials to support the notified GAP. The data allow for an MRL proposal for cereal grains on LOQ level. Based on the residue trial data livestock exposure is possible through straw used in animal diet, in particular in ruminant diet. No exposure of poultry is expected. However, the metabolism and distribution in animals was investigated in lactating cows and chickens. As for the assessed representative use it was concluded that no residues of diflufenican above the limit of quantification (LOQ) are likely to occur in edible animal matrices and thus no feeding studies and no MRLs for animal products are considered necessary.

The chronic dietary risk assessment for consumers showed that exposure to residues of diflufenican from the notified use is well below the allocated ADI. As no ARfD was derived an acute risk assessment is not required.

Under dark aerobic conditions at 20 – 22 ºC, diflufenican was moderate to high persistent in soil ($DT_{50\ lab}$ = 44.3 – 248.5 d). Two major soil aerobic metabolites were identified, AE 0542291 (max. 26.26 % AR after 320 d) and AE B107137 (AE B107137, max. 14 % AR after 120 d). These metabolites are moderately persistent in soil (AE B107137: $DT_{50\ lab\ 20\ ºC}$ = 9.1 – 17. 9 d; AE 0542291: $DT_{50\ lab\ 20\ ºC}$ = 13.6 – 58.7 d). Mineralization varied from 3.85 % AR after 120 d to a maximum of 51.2 % AR after 52 d depending on the study and the labelling position. Unextractable residues range from 3.04 % AR after 120 d to 18.5 % AR after 54 d depending on the study and the labelling position.

Diflufenican is medium to very high persistent under anaerobic conditions ($DT_{50\ anaerobic}$ = 87.7 d – 400 d). Volatile transformation product 2,4-difluroaniline (max. 34.35 % AR after 272 d) was

[10] AE 0542291: 2-[3-(trifluoromethyl)phenoxy]pyridine-3-carboxamide [referenced in the residues section of the DAR as M&B43625]

[11] AE B107137: 2-[3-(trifluoromethyl)phenoxy]pyridine-3-carboxylic acid [referenced in the residues section of the DAR as M&B38181]

identified as a major anaerobic metabolite that had not been previously found in the aerobic studies. Degradation AE B107137 was also investigated under anaerobic conditions ($DT_{50\ anaerobic}$ = 413 d).
Diflufenican is shown to be stable to the photolysis in soil.
Field studies in six German sites and six sites in different European locations (UK, FR, DE, NL, ES and IT) show that diflufenican was high to very high persistent (DT_{50} = 214 d – 621 d) under field conditions.
A kinetic analysis of the two field studies to obtain field normalized half lives is also available. Excluding the values from the not fully reliable dissipation rates of the firs field study (Maycey and Savage, 1990b) normalised half lives are in the rank of 103–282 d (Geometric mean half life=156 d).
In a five years accumulation study conducted at six sites in south-east England (Maycey and Savage, 1991a) a clear tendency to accumulation of diflufenican residues is observed. Since soil concentration derived from the field accumulation study was higher than the obtained from standard calculation this value was used for the ecotoxicological risk assessment and the calculation of the potential maximum concentration of the metabolites.
Diflufenican is slightly mobile to immobile in soil (K_{foc} = 1622 – 7431 mL / g), AE B107137 is very highly mobile (K_{foc} = 7 – 23 mL / g) and AE 0542291 is medium to highly mobile (K_{foc} = 103 – 160 mL / g).
Diflufenican and its metabolite AE B107137 were stable to hydrolysis. Diflufenican was also stable to aqueous photolysis and non ready biodegradable.
Degradation of diflufenican in dark water sediment systems was investigated in two studies with a total of four systems. The application rate used in these studies is significantly above of the solubility limit. Diflufenican was medium to very high persistent in these systems ($DT_{50\ whole\ system}$ = 90 – 345 d; geometric mean $DT_{50\ whole\ system}$ = 175 d) and was slowly transformed to the metabolite AE B107137 (max. 32.6 % AR in the sediment and max. 13.3 % AR in the water after 30 d). Data from these studies were analyzed in a separated study by multicompartmental kinetic models. Whereas these fitting exercises are able to describe the system as a whole the individual degradation rates for the water phase should be taken with caution (Diflufenican $DT_{50water}$ = 20.1 – 48.1 d, DT_{50sed} = 95 – 877 d; AE B107137 $DT_{50water}$ = 54.6 – 97.8 d). The values obtained from this kinetic analysis were employed in the FOCUS SW modelling presented in the DAR. In all the water sediment systems available mineralization was negligible (< 4 % A R after 120 d).
A sediment monitoring study performed in UK winter cereal areas with history of repeated use of diflufenican at rates below 100 g / ha is available. Variable results with concentrations of diflufenican ranging from < 5 to 44 µg / Kg were obtained.
Different FOCUS $PEC_{SW/SED}$ are available in the DAR and in the addendum, none of them produced with the input parameters agreed by the expert's meeting. However, the expert's meeting decided to retain the $PEC_{SW\ /\ SED}$ values presented in the DAR for the EU risk assessment. It was noted that the Koc used from the DAR (1989 as opposed to the new mean value of 3417) was conservative but it was decided not to redo the risk assessment because an acceptable scenario for aquatic risk assessment was identified in the DAR. Examination of the modelling results and the ecotoxicological risk assessment showed that Step 4 calculation with a 5 m buffer for spray drift only resulted in a complete scenario with acceptable TERs for aquatic risk assessment (D3). This should not be

understood as that run off figures proposed by the applicant were agreed by the meeting, since these were not discussed. After the expert meeting, EFSA identified a data GAP for new FOCUS PEC_{SW} calculations using a plant uptake factor of zero and the input parameters agree for the meeting (mean whole systems half life for SW and 1000 d for sediment, with only spray drift buffer strip mitigation in order to confirm the proposed risk assessment and to make it consistent with the risk assessments performed for other substances of this peer review phase.

Potential ground water contamination by diflufenican and the soil metabolites AE B107137 and AE 0542291 was evaluated by FOCUS PELMO (v.3.3.2). The 80^{th} percentile annual average concentrations in leachates below 1 m were predicted to be less than 0.001 µg / L for all compounds in the nine European scenarios.

Diflufenican may be considered slightly volatile. Volatilization of diflufenican from plant surface and soil was negligible (plants: 0.3 AR % after 24 h, soil: 0.0 – 0.005 % AR after 24 h). A theoretical calculation of the potential for photo-oxidation resulted in a half life of 3.3 d. Based on the negligible potential for volatilization from plant and soil surface it is considered that exposure to air and therefore long range transport thought air is insignificant for diflufenican. However, during expert's meeting soil anaerobic metabolite 2,4-difluroaniline was found to be very volatile and may need to be assessed for the air compartment and for transport through air when anaerobic conditions are expected to occur.

The Annex VI triggers were met in the acute and long-term risk assessment for birds and mammals taking into consideration only exposure to diflufenican. However the lead formulation Herold SC 600 contains flufenacet as a second active substance. The toxicity and exposure to the second active substance was not taken into account in the risk assessment. The long-term TER for herbivorous mammals of 5.3 is close to the trigger of 5. It is likely that the TER would be below the trigger if exposure to the second active substance is considered in the risk assessment. A risk assessment taking into consideration also exposure to flufenacet is required before a conclusion can be drawn on the risk to birds and mammals from the representative use of diflufenican formulated as Herold SC 600. Green algae were the most sensitive organisms driving the aquatic risk assessment. Only the FOCUS step4 part scenario D5 pond reached a TER of >10 but no full FOCUS step 4 scenario reached the trigger of 10 including a no-spray buffer zone of 5 metres indicating a high risk to aquatic organisms for the majority of geoclimatic conditions in Europe presented by the FOCUS scenarios. However if the same approach is applied as was agreed in the expert meeting than the risk to aquatic organisms is addressed also for the full scenario D3 (ditch). It may be possible to identify further scenarios with acceptable risk if recovery is taken into account as suggested in the addendum from April 2007 or if larger no-spray buffer zones are introduced in the PECsw calculations. The RMS stated in the not peer-reviewed addendum from August 2007 that a new risk assessment was submitted by the applicant but the risk assessment was not summarised and evaluated in the addendum. The aquatic risk assessment was based on exposure to diflufenican alone. However tests with the formulation Herold SC 600 suggest lower toxicity to green algae (the most sensitive group of aquatic organisms tested) compared to technical diflufenican. Therefore it was agreed in the expert meeting that the risk from the formulation would be covered by the risk assessment for diflufenican. The in-field and off-

field HQ values for *Aphidius rhopalosiphi* and *Typhlodromus pyri* were below the trigger of 2 based on studies with formulations different from Herold SC 600. Studies with the formulation Herold SC 600 indicated a high risk to *T. pyri*. No studies with the lead formulation and non-target arthropods other than *T. pyri* were made available. The risk to non-target arthropods was not sufficiently addressed for the suggested representative use. Consequently a data gap was identified by the experts to address the risk to non-target arthropods from the formulation Herold SC 600. The risk to non-target plants from pre-emergence and post-emergence exposure to diflufenican was assessed as high and risk mitigation measures such as an in-field no-spray buffer zone of 10 meters is required. The risk to bees, earthworms, other soil non-target macro-organisms, soil non-target micro-organisms and biological methods of sewage treatment was assessed as low.

Particular conditions proposed to be taken into account to manage the risk(s) identified

- Based on a no-spray buffer zone of 5 metres only one part scenario (D5 pond) resulted in a TER above the Annex VI trigger. If the same approach is applied as was agreed in the expert meeting than the risk to aquatic organisms is addressed also for the full FOCUS step4 scenario D3 (ditch) with a buffer zone of 5 metres. Possibly larger no-spray buffer zones would result in more FOCUS scenarios with a TER above the Annex VI trigger.
- Risk mitigation comparable to a 10 meter in-field no spray buffer zone is required to achieve a TER of >5 for non-target plants in the off-field area.

Critical areas of concern

- The risk assessment of the formulation (containing diflufenican and flufenacet) for the operator/worker/bystander and consumer could not be concluded and has to be considered at MS level.
- No conclusion can be drawn on the risk from the lead formulation Herold SC 600 to birds and mammals
- A high risk to non-target arthropods was indicated by the available studies with Herold SC 600.

APPENDIX 1 – LIST OF ENDPOINTS FOR THE ACTIVE SUBSTANCE AND THE REPRESENTATIVE FORMULATION

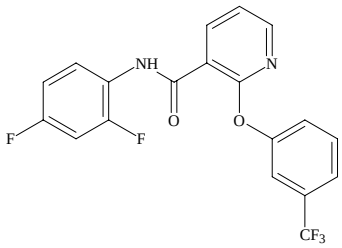
(Abbreviations used in this list are explained in appendix 2)

Appendix 1.1: Identity, Physical and Chemical Properties, Details of Uses, Further Information

Active substance (ISO Common Name) ‡	Diflufenican
Function (e.g. fungicide)	Herbicide

Rapporteur Member State	UK
Co-rapporteur Member State	None

Identity (Annex IIA, point 1)

Chemical name (IUPAC) ‡	2′,4′-difluoro-2-(*α*,*α*,*α*-trifluoro-*m*-tolyloxy)nicotinanilide
Chemical name (CA) ‡	N-(2,4-difluorophenyl)-2-[3-(trifluoromethyl)phenoxy]-3-pyridinecarboxamide
CIPAC No ‡	462
CAS No ‡	83164-33-4
EC No (EINECS or ELINCS) ‡	Not available
FAO Specification (including year of publication) ‡	462/TC/S/F (1997) min 945 g/kg active substance
Minimum purity of the active substance as manufactured ‡	970 g/kg (on a dry weight basis)
Identity of relevant impurities (of toxicological, ecotoxicological and/or environmental concern) in the active substance as manufactured	None
Molecular formula ‡	$C_{19}H_{11}F_5N_2O_2$
Molecular mass ‡	394 g/mol
Structural formula ‡	

‡ Endpoints identified by EU-Commission as relevant for Member States when applying the Uniform Principles

Physical and chemical properties (Annex IIA, point 2)

Melting point (state purity) ‡	159.5 °C (995 g/kg)
Boiling point (state purity) ‡	compound decomposed before boiling at 304 °C
Temperature of decomposition (state purity)	304.6 °C (995 g/kg)
Appearance (state purity) ‡	White crystalline solid (998 g/kg)
Vapour pressure (state temperature, state purity) ‡	4.25×10^{-6} Pa at 25°C (997 g/kg)
Henry's law constant ‡	> 1.18 $\times^{-2}$ Pa m^3 mol^{-1}
Solubility in water (state temperature, state purity and pH) ‡	<0.05 mg/L at 20°C (pH 6.89) (995 g/kg) solubility is not pH dependent
Solubility in organic solvents ‡ (state temperature, state purity)	Solubility at 20 °C in g/L (981 g/kg) Acetone (72.2); ethyl acetate (65.3); methanol (4.7); acetonitrile (17.6); dichloromethane (114.0); n-heptane (0.75); toluene (35.7); n-octanol (1.9)
Surface tension ‡ (state concentration and temperature, state purity)	71.46 mN/m at °C (0.045 mg/L)(981 g/kg)
Partition co-efficient ‡ (state temperature, pH and purity)	log PO/W = 4.2 at 20 °C no pH dependence of solubility (998 g/kg)
Dissociation constant (state purity) ‡	Due to the poor solubility of the molecule in water it was not possible to determine a dissociation constant.
UV/VIS absorption (max.) incl. ε ‡ (state purity, pH)	solution: neutral media λ_{max} (nm); ε ($L.mol^{-1}.cm^{-1}$) 205.5 35616 282.5 11155 292.5 9402
Flammability ‡ (state purity)	Not classified as flammable (981 g/kg)
Explosive properties ‡ (state purity)	Not classified as explosive (981 g/kg)
Oxidising properties ‡ (state purity)	Not classified as oxidising (981 g/kg)

‡ Endpoints identified by EU-Commission as relevant for Member States when applying the Uniform Principles

Summary of representative uses evaluated *

Crop and/ or situation (a)	Member State or Country	Product name	F G or I (b)	Pests or Group of pests controlled I	Preparation		Application				Application rate per treatment			PHI (days) (m)	Remarks
					Type (d-f)	Conc. Of as (i)	method kind (f-h)	growth stage & season (j)	number min/ max (k)	interval between applications (min)	g as/hL min – max (l)	water L/ha min – max	g as/ha min – max (l)		
Winter wheat Winter barley Winter rye	EU	Herold SC 600	F	Annual dicot weeds, ALOMY, APESV, POAAN	SC	1. 200 g/L 2. 400 g/L	Tractor mounted boom spraying	Pre-emergence; Post-emergence BBCH 10-13	1		1. 0.06 – 0.03 2. 0.12 – 0.06	200 – 400	1. 0.12 2. 0.24	#	0.6 L / ha product; Autumn use only

1 – active substance diflufenican, 2 – active substance flufenacet

* For uses where the column "Remarks" is marked in grey further consideration is necessary. Uses should be crossed out when the notifier no longer supports this use(s).
(a) For crops, the EU and Codex classifications (both) should be taken into account; where relevant, the use situation should be described (e.g. fumigation of a structure)
(b) Outdoor or field use (F), greenhouse application (G) or indoor application (I)
I *e.g.* biting and suckling insects, soil born insects, foliar fungi, weeds
(d) *e.g.* wettable powder (WP), emulsifiable concentrate (EC), granule (GR)
(e) GCPF Codes – GIFAP Technical Monograph No 2, 1989
(f) All abbreviations used must be explained
(g) Method, e.g. high volume spraying, low volume spraying, spreading, dusting, drench
(h) Kind, *e.g.* overall, broadcast, aerial spraying, row, individual plant, between the plant- type of equipment used must be indicated
(i) g/kg or g/L. Normally the rate should be given for the active substance (according to ISO) and not for the variant in order to compare the rate for same active substances used in different variants (e.g. fluoroxypyr). **In certain cases, where only one variant is synthesised, it is more appropriate to give the rate for the variant (e.g. benthiavalicarb-isopropyl).**
(j) Growth stage at last treatment (BBCH Monograph, Growth Stages of Plants, 1997, Blackwell, ISBN 3-8263-3152-4), including where relevant, information on season at time of application
(k) Indicate the minimum and maximum number of application possible under practical conditions of use
(l) The values should be given in g or kg whatever gives the more manageable number (e.g. 200 kg/ha instead of 200 000 g/ha or 12.5 g/ha instead of 0.0125 kg/ha
(m) PHI – minimum pre-harvest interval

‡ Endpoints identified by EU-Commission as relevant for Member States when applying the Uniform Principles

Appendix 1.2: Methods of Analysis

Analytical methods for the active substance (Annex IIA, point 4.1)

Technical as (analytical technique)	Reversed phase HPLC with UV detection at 220 nm
Impurities in technical as (analytical technique)	Reversed phase HPLC with UV detection at 220 nm
Plant protection product (analytical technique)	Reversed phase HPLC with UV detection at 230 nm

Analytical methods for residues (Annex IIA, point 4.2)

Residue definitions for monitoring purposes

Food of plant origin		Diflufenican
Food of animal origin		Diflufenican
Soil		Diflufenican
Water	surface	Diflufenican
	drinking/ground	Diflufenican
Air		Diflufenican

Monitoring/Enforcement methods

Food/feed of plant origin (analytical technique and LOQ for methods for monitoring purposes)	DFG S19 Multi-residue method. GC-ECD with GC-MS for confirmation. LOQ grain 0.01 mg/kg.
Food/feed of animal origin (analytical technique and LOQ for methods for monitoring purposes)	DFG S19 Multi-residue method. GC-MS with GC-ECD for confirmation. LOQ milk 0.01 mg/kg, tissue 0.02 mg/kg
Soil (analytical technique and LOQ)	LC-MS-MS LOQ: 0.002 mg/kg Diflufenican, metabolites AE B107137 & AE 0542291: GC-MS LOQ: 0.002 mg/kg
Water (analytical technique and LOQ)	LC-MS-MS LOQ: 0.05 µg/L
Air (analytical technique and LOQ)	LC-MS-MS LOQ: 0.4 µg/m^3
Body fluids and tissues (analytical technique and LOQ)	Not required as material not classified as toxic

Classification and proposed labelling with regard to physical and chemical data (Annex IIA, point 10)

	RMS/peer review proposal
Active substance	None

‡ Endpoints identified by EU-Commission as relevant for Member States when applying the Uniform Principles

Appendix 1.3: Impact on Human and Animal Health

Absorption, distribution, excretion and metabolism (toxicokinetics) (Annex IIA, point 5.1)

Rate and extent of oral absorption ‡	58% (males) / 71% (females), based on urinary and biliary excretion within 48 h. Lower absorption at high dose levels. Moderate rate of absorption (max. blood concentration t_{max} ≈6 h)
Distribution ‡	Preferential distribution to fat, residues in fat increase with time over 2.5-32 h
Potential for accumulation ‡	Long whole body elimination half-life (50-60 h). Residues in fat increase with time.
Rate and extent of excretion ‡	Approximately 90% elimination over several days (62-76% within 48 h, 77-89% within 72 h, 82-92% within 96 h), mainly via faeces (≈5% via urine, 40-50% in bile within 48 h).
Metabolism in animals ‡	Extensively metabolised, predominantly by hydroxylation of difluorophenyl ring (with or without conjugation).
Toxicologically relevant compounds ‡ (animals and plants)	Diflufenican
Toxicologically relevant compounds ‡ (environment)	Diflufenican

Acute toxicity (Annex IIA, point 5.2)

Rat LD_{50} oral ‡	> 5000 mg/kg bw	-
Rat LD_{50} dermal ‡	> 2000 mg/kg bw	-
Rat LC_{50} inhalation ‡	>5.12 mg /L/4 h (whole body)	-
Skin irritation ‡	Non-irritant	-
Eye irritation ‡	Slightly irritating (no classification proposed)	-
Skin sensitisation ‡	Non-sensitiser (M & K)	-

Short term toxicity (Annex IIA, point 5.3)

Target / critical effect ‡	Reduced bodyweight gain, liver (hepatocyte hypertrophy)	
Relevant oral NOAEL ‡	13 week rat: 19.47 mg/kg bw/day 1 year dog: 100 mg/kg bw/day	
Relevant dermal NOAEL ‡	No data – not required	
Relevant inhalation NOAEL ‡	No data – not required	

‡ Endpoints identified by EU-Commission as relevant for Member States when applying the Uniform Principles

Genotoxicity ‡ (Annex IIA, point 5.4)

……..	No outstanding genotoxicity concerns.	

Long term toxicity and carcinogenicity (Annex IIA, point 5.5)

Target/critical effect ‡	Reduced bodyweight gain, increased liver weight	
Relevant NOAEL ‡	2 year rat: 23.27 mg/kg bw/day 2 year mouse: 62.2 mg/kg bw/day	
Carcinogenicity ‡	No carcinogenic potential.	

Reproductive toxicity (Annex IIA, point 5.6)

Reproduction toxicity

Reproduction target / critical effect ‡	Reduced pup and litter weight at maternally toxic doses (which are reduced bw gains > 10%, organ weight changes). Dystocia and reduced pup viability at the highest dose.	
Relevant parental NOAEL ‡	35.5 mg/kg bw/day – male	
Relevant reproductive NOAEL ‡	206.1 mg/kg bw/day – female	
Relevant offspring NOAEL ‡	41.9 mg/kg bw/day – female	

Developmental toxicity

Developmental target / critical effect ‡	Developmental toxicity (reduced litter size & litter weights in rats, increased extra ribs in rabbits) at maternally toxic doses (reduced bodyweight gains). No teratogenic effects.	
Relevant maternal NOAEL ‡	Rat: 50 mg/kg bw/day Rabbit: 350 mg/kg bw/day	
Relevant developmental NOAEL ‡	Rat: 500 mg/kg bw/day Rabbit: 350 mg/kg bw/day	

Neurotoxicity (Annex IIA, point 5.7)

Acute neurotoxicity ‡	No data – not required.	
Repeated neurotoxicity ‡	No data – not required.	
Delayed neurotoxicity ‡	No data – not required.	

‡ Endpoints identified by EU-Commission as relevant for Member States when applying the Uniform Principles

Other toxicological studies (Annex IIA, point 5.8)

Mechanism studies ‡	No specific induction of cytochrome P450 enzymes by diflufenican.
Studies performed on metabolites or impurities ‡	AE B107137 (M&B 38181): oral LD_{50} >2000 mg/kg bw (rat), dermal LD_{50} >1000 mg/kg bw (rat), Ames test: negative, *in vitro* cytogenetic assay (metaphase analysis in human lymphocytes): equivocal. Overall, no genotoxic potential *in vitro*.

Medical data ‡ (Annex IIA, point 5.9)

……..	No evidence of toxicological concern from medical surveillance of manufacturing plant personnel. No cases of poisoning.

Summary (Annex IIA, point 5.10)

	Value	Study	Safety factor
ADI ‡	0.2 mg/kg bw/d	2-year rat study (supported by 13 week rat)	100
AOEL ‡	0.11 mg/kg bw/d	rat, 13 week	100 (58%*)
ArfD ‡	Not allocated – not necessary	Not allocated – not necessary	Not allocated – not necessary

Dermal absorption ‡ (Annex IIIA, point 7.3)

For '*Herold SC600*' (aqueous suspension concentrate (SC) containing ≈200 g /L diflufenican)	Concentrate: 0.15% Spray dilutions: 5% Based on *in vitro* human/rat skin study.

Exposure scenarios (Annex IIIA, point 7.2)

Operator	Application in cereals	
	POEM	% of AOEL
	(tractor, 0.12 kg a.s./ha, without PPE)	19.7%
	(tractor, 0.12 kg a.s./ha, PPE = gloves during mixing/loading)	19.5%

‡ Endpoints identified by EU-Commission as relevant for Member States when applying the Uniform Principles

	BBA (tractor, 0.12 kg a.s./ha, without PPE) 3.3% (tractor, 0.12 kg a.s./ha, PPE = gloves during mixing/loading) 3.2%
Workers	According to van Hemmen et al, 2002 and using EUROPOEM dislodgeable foliar residue and transfer coefficient values : 3 % of AOEL (no PPE)
Bystanders	According to Lloyd and Bell, 1983: 0.1% of AOEL

Classification and proposed labelling with regard to toxicological data (Annex IIA, point 10)

	RMS/peer review proposal
Substance	No classification is proposed.

‡ Endpoints identified by EU-Commission as relevant for Member States when applying the Uniform Principles

Appendix 1.4: Residues

Metabolism in plants (Annex IIA, point 6.1 and 6.7, Annex IIIA, point 8.1 and 8.6)

Plant groups covered	Wheat I[12]
Rotational crops	Cabbage (L), Wheat I and Sugar beet (R/T)
Metabolism in rotational crops similar to metabolism in primary crops?	Yes
Processed commodities	No data were submitted or required as residues in cereal grain were less than 0.01 mg/kg.
Residue pattern in processed commodities similar to residue pattern in raw commodities?	No data were submitted or required as residues in cereal grain were less than 0.01 mg/kg.
Plant residue definition for monitoring	Diflufenican
Plant residue definition for risk assessment	Diflufenican[13]
Conversion factor (monitoring to risk assessment)	None

Metabolism in livestock (Annex IIA, point 6.2 and 6.7, Annex IIIA, point 8.1 and 8.6)

Animals covered	Dairy cattle and hens
Time needed to reach a plateau concentration in milk and eggs	Milk = 3 days Egg = 8 days
Animal residue definition for monitoring	Diflufenican
Animal residue definition for risk assessment	Diflufenican
Conversion factor (monitoring to risk assessment)	None
Metabolism in rat and ruminant similar (yes/no)	Yes
Fat soluble residue: (yes/no)	Yes

Residues in succeeding crops (Annex IIA, point 6.6, Annex IIIA, point 8.5)

……..	Rotational crop metabolism study indicates that a cold rotational crop study is not required [14]

[12] For future cereal uses that deviate from the assessed GAP additional metabolism data may be required in order to refine the proposed residues definition.
[13] Notified use only. For future cereal uses that deviate from the assessed GAP additional metabolism data may be required in order to refine the proposed residues definition.
[14] If uses with higher application rates and/or a later time of application are requested in the future, Member States should pay attention to the residues in rotational crops including crops that may be fed to livestock.

‡ Endpoints identified by EU-Commission as relevant for Member States when applying the Uniform Principles

Stability of residues (Annex IIA, point 6 introduction, Annex IIIA, point 8 Introduction)

……..	Freezer storage stability study indicated that residues of diflufenican are stable for up to 24 months in wheat forage, wheat grain and wheat straw.

Residues from livestock feeding studies (Annex IIA, point 6.4, Annex IIIA, point 8.3)

	Ruminant: yes	Poultry: no	Pig: no
	Conditions of requirement of feeding studies		
Expected intakes by livestock ≥ 0.1 mg/kg diet (dry weight basis) (yes/no – If yes, specify the level) ('As Received'):15	no	no	no
Potential for accumulation (yes/no):	not assessed	not assessed	not assessed
Metabolism studies indicate potential level of residues ≥ 0.01 mg/kg in edible tissues (yes/no)	no	no	not applicable
	Feeding studies Residue levels in matrices : Mean (max) mg/kg		
Muscle	n/a	n/a	n/a
Liver	n/a	n/a	n/a
Kidney	n/a	n/a	n/a
Fat	n/a	n/a	n/a
Milk	n/a		
Eggs		n/a	

[15] Cereal forage not considered

‡ Endpoints identified by EU-Commission as relevant for Member States when applying the Uniform Principles

Summary of residues data according to the representative uses on raw agricultural commodities and feedingstuffs (Annex IIA, point 6.3, Annex IIIA, point 8.2)

Crop	Northern or Mediterranean Region, field or glasshouse, and any other useful information	Trials results relevant to the representative uses (a)	Recommendation/comments	MRL estimated from trials according to the representative use	HR I	STMR (b)
Wheat, barley	S	Grain: 3 x <0.01 Straw: 3 x <0.02	Data set for the notified GAP (0.12 kg as/ha up to BBCH 13) incomplete			
Wheat, barley Grain Straw	 N S N S	 9 x <0.01 8 x <0.01 7 x <0.05, 0.14, 0.17 6 x <0.05, 0.06, 0.07	Insufficient residue trials data available to support the notified GAP. Sufficient residues trials data were available with an increased latest time of application of up to BBCH 30. The trials can be used to support the proposed use due to residues in the grain being below LOQ (0.01 mg/kg) and the residues in straw not leading to the setting of positive EU MRLs for animal products (intakes by animals did not exceed the trigger value for animal studies of 0.1 mg/kg diet 'As Received').	 0.01* Wheat, barley and rye[16] 	 0.01 0.17	 0.01 0.05

(a) Numbers of trials in which particular residue levels were reported e.g. 3 x <0.01, 1 x 0.01, 6 x 0.02, 1 x 0.04, 1 x 0.08, 2 x 0.1, 2 x 0.15, 1 x 0.17
(b) Supervised Trials Median Residue i.e. the median residue level estimated on the basis of supervised trials relating to the representative use
I Highest residue

[16] by extrapolation

‡ Endpoints identified by EU-Commission as relevant for Member States when applying the Uniform Principles

Consumer risk assessment (Annex IIA, point 6.9, Annex IIIA, point 8.8)

ADI	0.2
TMDI (% ADI) according to WHO European diet	0.000051 (<1%)
TMDI (% ADI) according to national (to be specified) diets	Not assessed
IEDI (WHO European Diet) (% ADI)	Not applicable
NEDI (specify diet) (% ADI)	UK diet: The individual and total NEDIs for adults, children, toddlers, infants, vegetarians and the elderly are all less than 1%.
Factors included in IEDI and NEDI	None
ARfD	An ARfD was not set.
IESTI (% ARfD)	Not applicable
NESTI (% ARfD) according to national (to be specified) large portion consumption data	Not applicable
Factors included in IESTI and NESTI	Not applicable

Processing factors (Annex IIA, point 6.5, Annex IIIA, point 8.4)

Crop/ process/ processed product	Number of studies	Processing factors		Amount transferred (%) (Optional)
		Transfer factor	Yield factor	
None, residues in cereal grains were less than 0.01 mg/kg	not applicable	not applicable	not applicable	not applicable

Proposed MRLs (Annex IIA, point 6.7, Annex IIIA, point 8.6)

Wheat, barley and rye	0.01* mg/kg

* LOQ

‡ Endpoints identified by EU-Commission as relevant for Member States when applying the Uniform Principles

Appendix 1.5: Fate and Behaviour in the Environment

Route of degradation (aerobic) in soil (Annex IIA, point 7.1.1.1.1)

Mineralization after 100 days ‡	18.3 % after 119 d, [^{14}C-2,4-difluorophenyl]-label (n=1) 8.1-43.6 % after 120 d, [^{14}C-3-trifluoromethylphenyl]-label (n=4) 3.0-18.9 % after 112 d, [^{14}C-2-pyridyl]-label (n=3)
Non-extractable residues after 100 days ‡	15.5 % after 119 d, [^{14}C-2,4-difluorophenyl]-label (n=1) 11.2-31.0 % after 120 d, [^{14}C-3-trifluoromethylphenyl]-label (n=4) 3.9-18.9 % after 112 d, [^{14}C-2-pyridyl]-label (n=3)
Metabolites requiring further consideration ‡ - name and/or code, % of applied (range and maximum)	AE B107137[17] – 16.8 % at 180 d at 10°C, [^{14}C-3-trifluoromethylphenyl] label (n=6) AE 0542291[18] - 26.3 % at 320 d at 20°C (pH 5.5) [^{14}C-3-trifluoromethylphenyl] label (n=1), in soils pH >6.5 15.7 % at 286 d at 20°C [^{14}C-2-pyridyl]-label (n=5)

Route of degradation in soil – Supplemental studies (Annex IIA, point 7.1.1.1.2)

Anaerobic degradation ‡

Mineralization after 100 days	Not available for [^{14}C-2,4-difluorophenyl]-label Not available for [^{14}C-3-trifluoromethylphenyl]-label 4.0 % after 112 d, [^{14}C-2-pyridyl]-label (n=1)
Non-extractable residues after 100 days	16.6 % after 120 d, [^{14}C-2,4-difluorophenyl]-label (n=1) 11.2 % after 120 d, [^{14}C-3-trifluoromethylphenyl]-label (n=1) 4.0 % after 112 d, [^{14}C-2-pyridyl]-label (n=1)
Metabolites that may require further consideration for risk assessment – name and/or code, % of applied (range and maximum)	AE C522392[19] – 10.7 % at 90 d [^{14}C-2,4-difluorophenyl]-label (n=1) AE B107137 – 48.5 % at 272 d [^{14}C-3-trifluoromethylphenyl]-label (n=2)

Soil photolysis ‡

Metabolites that may require further consideration for risk assessment – name and/or code, % of applied (range and maximum)	None. Diflufenican was stable during the 31 d study.

[17] AE B107137 = 2-(3-trifluoromethylphenoxy)nicotinic acid
[18] AE 0542291 = 2-(3-trifluoromethylphenoxy)-nicotinamide
[19] AE C522392 = 2,4-difluoroaniline

‡ Endpoints identified by EU-Commission as relevant for Member States when applying the Uniform Principles

Rate of degradation in soil (Annex IIA, point 7.1.1.2, Annex IIIA, point 9.1.1)

Laboratory studies ‡

Diflufenican	Aerobic conditions						
Soil type	X[20]	pH ($CaCl_2$)	t. °C / % MWHC	DT_{50} /DT_{90} (d)	DT_{50} (d) 20 °C pF2/10kPa	St. (r^2)	Method of calculation
Sandy loam		7.7 [(a)]	22°C/ 75 % of 0.33 bar	248.5/825.5	237.9	0.9980	SFO
Clay loam		6.6 [(a)]	22°C/ 75 % of 0.33 bar	139.5/463.4	119.9	0.9967	SFO
Clay loam		6.5	20°C/45 %	232.6/772.7	193.5	0.9954	SFO
Clay loam		6.5	20°C/45 %	206.0/684.3	172.1	0.9975	SFO
Clay loam		6.5	20°C/45 %	176.3/585.8	147.3	0.9967	SFO
Silty clay loam		7.5	20°C/45 %	44.3/147.2	44.3	0.9819	SFO
Sandy loam 1		5.5	20°C/45 %	129.3/429.5	129.3	0.9836	SFO
Sandy loam 2		6.9	20°C/45 %	89.8/298.3	89.8	0.9890	SFO
Sandy loam 2		6.9	10°C/45 %	204.4/679.0 [(b)]			SFO
Geometric mean/median					128 / 138.3		
Arithmetric mean					141.8		

AE B107137	Aerobic conditions							
Soil type	X[1]	pH ($CaCl_2$)	t. °C / % MWHC	DT_{50}/ DT_{90} (d)	f. f. k_{dp}/k_f [(c)]	DT_{50} (d) 20 °C pF2/10kPa	St. (r^2)	Method of calculation
Silt loam 1		7.0	20 °C/45 %	9.1/30.2	1	7.5	0.9919	SFO
Sandy loam		6.2	20 °C/45 %	17.9/59.5	1	13.9	0.9868	SFO
Silt loam 2		7.4	20 °C/45 %	14.5/48.1	1	10.4	0.9959	SFO
Geometric mean/median						10.3 / 10.4		
Arithmetric mean						10.6		

AE 0542291	Aerobic conditions							
Soil type	X[1]	pH ($CaCl_2$)	t. °C / % MWHC	DT_{50}/ DT_{90} (d)	f. f. k_{dp}/k_f [(c)]	DT_{50} (d) 20 °C pF2/10kPa	St. (r^2)	Method of calculation
Silt loam 1		7.0	20 °C/45 %	13.6/45.2	1	11.1	0.987	SFO
Sandy loam		6.2	20 °C/45 %	58.7/194.9	1	45.7[d]	0.999	SFO

[20] X This column is reserved for any other property that is considered to have a particular impact on the degradation rate.

‡ Endpoints identified by EU-Commission as relevant for Member States when applying the Uniform Principles

AE 0542291	Aerobic conditions							
Soil type	X[1]	pH ($CaCl_2$)	t. °C / % MWHC	DT_{50}/ DT_{90} (d)	f. f. k_{dp}/k_f [(c)]	DT_{50} (d) 20 °C pF2/10kPa	St. (r^2)	Method of calculation
Silt loam 2		7.4	20 °C/45 %	33.2/110.2	1	23.8	0.991	SFO
Geometric mean/median						22.9 / 23.8		
Arithmetric mean						26.9		

[a] pH calculation method not stated
[b] Calculated by the Rapporteur
[c] The Rapporteur could not verify the lower formation fractions of 33 and 37% provided by Notifier for AE B107137 and AE 0542291 respectively and therefore a formation fraction of 1 (i.e. 100%) was additionally assumed as a worst case in FOCUS groundwater modeling
[d] Since the longest DT_{50} occurred in the only acidic soil, the Rapporteur considered there may be some evidence of an influence of pH on degradation. The longest DT_{50} was additionally used for FOCUSgw modeling.

Field studies ‡

Diflufenican	Aerobic conditions								
Soil type (indicate if bare or cropped soil was used).	Location (country or USA state).	X[1]	pH	Depth (cm)	DT_{50} (d) actual	DT_{90}(d) actual	St. (r^2)	DT_{50} (d) 20°C / pF2	Method of calculation
Loamy sand (b)	UK		5.8	30	621	2063	0.493	282.0	SFO
Sandy silt loam I	France		7.1	30	241	801	0.796	130.0	SFO
Sandy loam (b)	Netherlands		6.3	30	389	1292	0.495	199.5	SFO
Clay (b)	Spain		7.6	30	236	784	0.728	122.2	SFO
Clay loam (b)	Italy		6.9	30	224	744	0.748	103.4	SFO
Geometric mean/median					315/241			156/130*	

*Note a Q10 of 2.2 was assumed during the normalization.

pH dependence ‡ (yes / no) (if yes type of dependence)	No
Soil accumulation and plateau concentration ‡	Maximum soil accumulation concentration of 0.405 mg/kg over top 5cm soil layer. Plateau concentration (i.e. the maximum amount of diflufenican remaining immediately prior to the following years application) would be 0.245 mg/kg. Maximum accumulation factor = 2.53

‡ Endpoints identified by EU-Commission as relevant for Member States when applying the Uniform Principles

Soil adsorption/desorption (Annex IIA, point 7.1.2)

Diflufenican ‡								
Soil Type	OC %	Soil pH	Kd (mL/g)	Koc (mL/g)	Kf (mL/g)	Kfoc (mL/g)	1/n	R^2
Sandy loam	2.09	7.7			33.9	1622	0.875	>0.988
Loamy sand	0.75	6.6			13.5	1800	0.917	>0.988
Clay loam	1.68	6.6			39.8	2369	0.934	>0.988
Silty clay loam	2.26	6.8			48.9	2164	0.923	>0.988
Clay loam (Shelley Field)	2.4	6.2			98.82	4118	0.901	0.998
Silt loam (Kissendorf)	1.4	6.7			46.28	3306	0.897	1.000
Sandy loam (Manningtree)	3.6	5.3			267.51	7431	0.991	0.998
Loam (Santilly)	0.9	7.0			39.86	4428	0.940	0.999
Clay loam (Lleida)	2.9	8.0			88.91	3066	0.917	0.999
Clay loam (Chazay)	1.9	6.6			73.49	3868	0.879	0.998
Arithmetic mean					75.1	3417	0.917	-
Median					47.6	3186	0.917	
pH dependence, Yes or No			No					

AE B107137 ‡							
Soil Type	OC %	Soil pH	Kd (mL/g)	Koc (mL/g)	Kf (mL/g)	Kfoc (mL/g)	1/n
Clay loam	1.9	7.0			0.22	12	0.72
Sand	1.6	5.8			0.11	7	0.99
Clay loam	4.7	7.6			0.38	8	0.54
Sandy loam	1.8	6.0			0.42	23	0.68
Arithmetic mean/median						13/10	0.73/0.70
pH dependence (yes or no)			No				

AE 0542291							
Soil Type	OC %	Soil pH	Kd (mL/g)	Koc (mL/g)	Kf (mL/g)	Kfoc (mL/g)	1/n
Sandy loam	0.8	6.0			1.3	160	0.80
Sandy loam	1.2	5.3			1.5	127	0.84
Clay loam	2.6	7.0			3.6	137	0.77
Clay	3.9	6.0[(a)]			4.0	103	0.85
Arithmetic mean/median						132/132	0.81/0.82

‡ Endpoints identified by EU-Commission as relevant for Member States when applying the Uniform Principles

pH dependence (yes or no)	No

[a] pH in CaCl2

Mobility in soil (Annex IIA, point 7.1.3, Annex IIIA, point 9.1.2)

Column leaching ‡	None submitted, none required
Aged residues leaching ‡	None submitted, none required

Lysimeter/ field leaching studies ‡	Location: Germany (Bruhl, Schwemmlob) Study type (e.g. lysimeter, field): lysimeter Soil properties: pH = 7.2, OC= 1.05 Dates of application: 3rd December 1990 Crop: 1st year winter wheat, 2nd year winter barley, final green mustard Interception estimated: None (application pre-emergent) Number of applications: lysimeter 219 1 application each year, lysimeter 220 1 application 1st year Duration: 2 years Application rate: 185 g a.s./ha/year (nominal) Average annual rainfall and irrigation (mm): 853 mm Average annual leachate volume (mm): 325 mm %radioactivity in leachate (maximum/year): 0.014 % AR 1st year, 0.117 % AR 2nd year Individual annual average concentrations: 1st year 0.003 µg /L and 2nd year <0.003 µg /L active substance, <0.003 µg /L metabolites AE B107137 and AE 0542291. Unidentified radioactivity: total max 0.01 µg /L parent equivalents.

PEC (soil) (Annex IIIA, point 9.1.3)

$PEC_{(s)}$ derived from UK field soil accumulation studies

Parent Method of calculation	Maximum soil accumulation concentration of 0.405 mg/kg over top 5cm soil layer. Plateau concentration (i.e. the maximum amount of diflufenican remaining immediately prior to the following years application) would be 0.245 mg/kg. Maximum accumulation factor = 2.53.

‡ Endpoints identified by EU-Commission as relevant for Member States when applying the Uniform Principles

Metabolite AE B107137	Molecular weight relative to the parent: 283 g/mol, 394 g/mol diflufenican
Method of calculation	DT_{50} (d): 10.6 days Kinetics: SFO Field or Lab: Arithmetic mean from laboratory studies
Application data	Application rate assumed: 120 g as/ha (assumed AE B107137 is formed at a maximum of 16.8 % of the applied dose)
PEC(s) (mg/kg)	Single application Actual
Maximum predicted from a single application	0.02
Peak concentration	0.05 mg/kg based on accumulated residues of diflufenican in the field

Metabolite AE 0542291	Molecular weight relative to the parent: 282 g/mol, 394 g/mol diflufenican
Method of calculation	DT_{50} (d): 26.9 days Kinetics: SFO Field or Lab: Arithmetic mean from laboratory studies
Application data	Application rate assumed: 120 g as/ha (assumed AE 0542291 is formed at a maximum of 26.3 % of the applied dose)
PEC(s) (mg/kg)	Single application Actual
Maximum predicted from a single application	0.03
Peak concentration	0.08 mg/kg based on accumulated residues of diflufenican in the field

Route and rate of degradation in water (Annex IIA, point 7.2.1)

Hydrolytic degradation of the active substance and metabolites > 10 % ‡	Diflufenican is stable to hydrolysis at pH 5, 7 and 9 over 30 days and the only radioactive component was diflufenican. Metabolite AE B107137 was also stable at pH 5, 7 and 9.
Photolytic degradation of active substance and metabolites above 10 % ‡	DT_{50} : 133 d (equivalent to 259 d of 50°N UK summer sunlight). AE B107137stable in 14 d study (irradiation equivalent to 26 d summer sunlight at 50°N in the UK 12:12 light:dark basis).
Quantum yield of direct phototransformation in water at Σ > 290 nm	2.75×10^{-5}

‡ Endpoints identified by EU-Commission as relevant for Member States when applying the Uniform Principles

Readily biodegradable ‡ (yes/no)	No. Only 5.2 % biodegradation occurred over 28 d.

Degradation in water / sediment

Diflufenican	Distribution (Max. in sed 74.4 % after 14 d)									
Water / sediment system	pH water phase	pH sed	t. °C	DT_{50}-DT_{90} whole sys.	St. (r^2)	DT_{50}-DT_{90} water	St. (r^2)	DT_{50}- DT_{90} sed	St. (r^2)	Method of calculation
Unter Widdersheim	8.2	7.5	20	90	0.76	n.a.	n.a.	n.a.		SFO
Bickenbach	8.2	7.8	20	154	0.77	n.a.	n.a.	n.a.		SFO
Clay, UK	7.8	6.3	20	345	0.82	n.a.	n.a.	n.a.		SFO
Sand, UK	6.8	5.4	20	195	0.96	n.a.	n.a.	n.a.		SFO
Arithmetic mean (DT_{50})				196		n.a.		n.a.		
Geometric mean				175		n.a.		n.a.		

n.a. no reliable value available.

AE B107137	Distribution (max in water 32.6 % after 30 d, max in sed 13.3 % after 30 d)
AE C522392	Distribution (max in water 6.1 % after 30 d, max in sed 1.0 % after 59 d)

Mineralization and non extractable residues					
Water / sediment system	pH water phase	pH sed	Mineralization x % after n d. (end of the study).	Non-extractable residues in sed. Max x % after n d	Non-extractable residues in sed. Max x % after n d (end of the study)
Unter Widdersheim	8.2	7.5	0.6 % after 121 d	11.1 % after 121 d	11.1 % after 121 d
Bickenbach	8.2	7.8	0.2 % after 121 d	9.0 after 61 d	8.6 % after 121 d
Clay, UK	7.8	6.3	0.8 % after 365 d	35.2 % after 365 d	35.2 % after 365 d
Sand, UK	6.8	5.4	6.8 % after 365 d	27.4 % after 212 d	22.7 % after 365 d

PEC (surface water) and PEC sediment (Annex IIIA, point 9.2.3)

Parent Parameters used in FOCUSsw step 1 and 2	Molecular weight (g/mol): 394 Water solubility (mg/L): 0.05 Koc (L/kg): 1989 (arithmetic mean of data available in original DAR)* DT_{50} soil (d): 141.8 days (Arithmetic mean lab. In accordance with FOCUS SFO)* DT_{50} water/sediment system (d): 214 (Arithmetic mean of four systems – 2 non-first order values included but

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	overall mean more worse case than SFO values only) DT_{50} water (d): 31.7 (arithmetic mean of SFO values)* DT_{50} sediment (d): 338.7 (arithmetic mean of SFO values)* Crop interception (%): 0
Parameters used in FOCUSsw step 3 (if performed)	Vapour pressure: 0.425 x 10^{-5} Pa Koc: 1989 (mean of data available in original DAR)* 1/n: 0.91 Plant uptake factor: 0.5
Application rate	Crop: wheat Crop interception: 0 Number of applications: 1 Application rate(s): 120 g as/ha Application window: 2 weeks prior and 2 weeks post emergence dates

* These input parameters were not agreed for future use by MSs. However, experts' meeting agreed that the available calculation could be used for the EU risk assessment since the input parameters used are either worst case or do not have a high influence on the result.

FOCUS STEP 1 Scenario	Day after overall maximum	PEC_{SW} (µg/L)		PEC_{SED} (µg/kg)	
		Actual	TWA	Actual	TWA
	0 h	12.06		217.85	
	24 h	11.22	11.64	223.41	220.50
	2 d	11.18	11.42	222.42	221.64
	4 d	11.11	11.28	220.98	221.67
	7 d	11.00	11.19	218.85	220.92
	14 d	10.76	11.03	213.94	218.65
	21 d	10.52	10.90	209.14	216.28
	28 d	10.28	10.77	204.45	213.91
	42 d	9.82	10.53	195.39	209.23
	50d	9.57	10.40	190.39	206.62
	100d	8.14	9.62	161.93	191.20

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FOCUS STEP 2 Scenario	Day after overall maximum	PEC_{SW} (µg/L)		PEC_{SED} (µg/kg)	
		Actual	TWA	Actual	TWA
Northern EU	0 h	5.75		112.36	
	24 h	5.54	5.64	111.53	111.94
	2 d	5.50	5.58	110.70	111.53
	4 d	5.42	5.52	109.07	110.71
	7 d	5.30	5.45	106.66	109.49
	14 d	5.03	5.31	101.25	106.71
	21 d	4.77	5.17	96.12	104.03
	28 d	4.53	5.04	91.24	101.44
	42 d	4.08	4.79	82.22	96.51
	50d	3.85	4.66	77.48	93.84
	100d	2.65	3.94	53.42	79.27
Southern EU	Maximum	4.68			

Total load PECsw for use in sediment dweller risk assessments: Step 1 = 41.1µg /L; Step 2 = 20.7µg /L

FOCUS STEP 3 Scenario	Water body	Day after overall maximum	PEC_{SW} (µg/L)	PEC_{SED} (µg/kg)
			Actual	Actual
D1	Ditch	0	0.784	6.964
D1	Stream	0	0.672	3.695
D2	Ditch	0	0.835	3.703
D2	Stream	0	0.707	2.563
D3	Ditch	0	0.755	0.349
D4	Pond	0	0.038	0.450
D4	Stream	0	0.656	0.192
D5	Pond	0	0.026	0.220
D5	Stream	0	0.708	0.194
D6	Ditch	0	0.763	1.346
R1	Pond	0	0.076	0.658
R1	Stream	0	0.499	0.675
R3	Stream	0	0.693	30.369
R4	Stream	0	0.680	0.540

Note: all peak surface water concentrations occurred on day of application (indicating a significant contribution from spray drift) with the exception of D4 pond (peak on 22 December) and R4 stream (peak on 21 December)

‡ Endpoints identified by EU-Commission as relevant for Member States when applying the Uniform Principles

FOCUS STEP 4 Scenario	Water body	Day after overall maximum	PEC_{SW} (µg/L)	PEC_{SED} (µg/kg)
			Actual	Actual
Assuming a no spray buffer zone of 5 m for all scenarios				
D1	Ditch	0	0.393	6.453
D1	Stream	0	0.246	3.678
D2	Ditch	0	0.420	3.223
D2	Stream	0	0.272	1.842
D3	Ditch	0	0.206	0.097
D4	Pond	0	0.038	0.438
D4	Stream	0	0.239	0.182
D5	Pond	0	0.023	0.205
D5	Stream	0	0.258	0.073
D6	Ditch	0	0.410	0.416
R1	Pond	0	0.075	0.640
R1	Stream	0	0.482	0.668
R3	Stream	0	0.587	30.348
R4	Stream	0	0.680	0.532

Metabolite AE 0542291 Parameters used in FOCUSsw step 1 and 2	Molecular weight: 282 g/mol Water solubility (mg /L): 100 mg /L Soil or water metabolite: soil Koc (L/kg): 131.9 DT_{50} soil (d): 26.9 days (Mean from normalised laboratory studies, in accordance with FOCUS SFO) DT_{50} water/sediment system (d): 730 (worst case assumption) DT_{50} water (d): 730 (worst case assumption) DT_{50} sediment (d): 730 (worst case assumption) Crop interception (%): 0 Maximum occurrence observed (% molar basis with respect to the parent) Soil: 26.3% Water and sediment: 0.01 % (metabolite was not found in water/sediment studies)
Parameters used in FOCUSsw step 3 (if performed)	Not performed

‡ Endpoints identified by EU-Commission as relevant for Member States when applying the Uniform Principles

Application rate	Crop: winter wheat Number of applications: 1 Application rate(s): 120 g as/ha Application window: 2 weeks prior and 2 weeks post emergence dates
Main routes of entry	2.759 % drift from 1 meter 10% runoff/drainage (at FOCUSsw Step 1) 5% runoff/drainage (at FOCUSsw Step 2 NE) 4% runoff/drainage (at FOCUSsw Step 2 SE)

AE 0542291 Steps 1 & 2 (Northern and Southern Europe scenario)

FOCUS STEP 1 Scenario	Day after overall maximum	PEC_{SW} (µg/L)		PEC_{SED} (µg/kg)	
		Actual	TWA	Actual	TWA
	0h	6.40		8.45	
	24h	6.40	6.40	8.44	8.44
	2d	6.39	6.40	8.43	8.44
	4d	6.38	6.39	8.41	8.43
	7d	6.36	6.38	8.39	8.42
	14d	6.32	6.36	8.33	8.39
	21d	6.28	6.34	8.28	8.36
	28d	6.24	6.32	8.22	8.33
	42d	6.15	6.28	8.12	8.28
	50d	6.11	6.25	8.05	8.25
	100d	5.82	6.11	7.68	8.06

FOCUS STEP 2 Scenario	Day after overall maximum	PEC_{SW} (µg/L)		PEC_{SED} (µg/kg)	
		Actual	TWA	Actual	TWA
Northern EU	0 h	2.89		3.81	
	24 h	2.89	2.89	3.81	3.81
	2 d	2.88	2.89	3.80	3.81
	4 d	2.88	2.88	3.80	3.80
	7 d	2.87	2.88	3.78	3.80
	14 d	2.85	2.87	3.76	3.78
	21 d	2.83	2.86	3.73	3.77
	28 d	2.81	2.85	3.71	3.76

‡ Endpoints identified by EU-Commission as relevant for Member States when applying the Uniform Principles

FOCUS STEP 2 Scenario	Day after overall maximum	PEC_{SW} (µg/L)		PEC_{SED} (µg/kg)	
		Actual	TWA	Actual	TWA
	42 d	2.78	2.83	3.66	3.73
	50d	2.75	2.82	3.63	3.72
	100d	2.63	2.76	3.46	3.63
Southern EU	Maximum	2.31			

Metabolite AE B107137	
Parameters used in FOCUSsw step 1 and 2	Molecular weight: 283 g/mol Water solubility (mg /L): 410 mg /L Soil or water metabolite: soil and water Koc (L/kg): 13 DT_{50} soil (d): 10.6 days (Mean normalised laboratory studies. In accordance with FOCUS SFO) DT_{50} water/sediment system (d): 730 (worst case assumption) DT_{50} water (d): 76.2 (mean of two systems) DT_{50} sediment (d): 730 (worst case assumption) Crop interception (%): 0 Maximum occurrence observed (% molar basis with respect to the parent) Soil: 16.8 % Water/sediment: 35.7 %
Parameters used in FOCUSsw step 3 (if performed)	Not performed
Application rate	Crop: winter wheat Number of applications: 1 Application rate(s): 120 g as/ha Application window: 2 weeks prior and 2 weeks post emergence dates
Main routes of entry	2.759 % drift from 1 meter 10% runoff/drainage (at FOCUSsw Step 1) 5% runoff/drainage (at FOCUSsw Step 2 NE) 4% runoff/drainage (at FOCUSsw Step 2 SE)

AE B107137 Steps 1 & 2 (Northern and Southern Europe scenario)

FOCUS STEP 1 Scenario	Day after overall maximum	PEC_{SW} (µg/L)		PEC_{SED} (µg/kg)	
		Actual	TWA	Actual	TWA
	0h	5.02		0.62	
	24h	5.01	5.02	0.65	0.63
	2d	5.01	5.01	0.65	0.64

‡ Endpoints identified by EU-Commission as relevant for Member States when applying the Uniform Principles

FOCUS STEP 1 Scenario	Day after overall maximum	PEC_{SW} (µg/L)		PEC_{SED} (µg/kg)	
		Actual	TWA	Actual	TWA
	4d	5.00	5.01	0.65	0.65
	7d	4.98	5.00	0.65	0.65
	14d	4.95	4.98	0.64	0.65
	21d	4.92	4.97	0.64	0.64
	28d	4.89	4.95	0.64	0.64
	42d	4.82	4.92	0.63	0.64
	50d	4.78	4.90	0.62	0.64
	100d	4.56	4.79	0.59	0.62

FOCUS STEP 2 Scenario	Day after overall maximum	PEC_{SW} (µg/L)		PEC_{SED} (µg/kg)	
		Actual	TWA	Actual	TWA
Northern EU	0 h	2.09		0.27	
	24 h	2.07	2.08	0.27	0.27
	2 d	2.06	2.07	0.27	0.27
	4 d	2.02	2.06	0.26	0.27
	7 d	1.97	2.03	0.26	0.26
	14 d	1.85	1.97	0.24	0.26
	21 d	1.73	1.91	0.23	0.25
	28 d	1.63	1.85	0.21	0.24
	42 d	1.44	1.74	0.19	0.23
	50d	1.34	1.69	0.17	0.22
	100d	0.85	1.38	0.11	0.18
Southern EU	Maximum	1.73			

PEC (ground water) (Annex IIIA, point 9.2.1)

Method of calculation and type of study (e.g. modelling, field leaching, lysimeter)	For FOCUS gw modeling, values used – Modeling using FOCUS model(s), with appropriate FOCUS gw scenarios, according to FOCUS guidance. Model(s) used: FOCUSPELMO 3.3.2 Scenarios (list of names): Châteaudun, Hamburg, Jokioinen, Kremsmünster, Okehampton, Piacenza, Porto, Sevilla, Thiva Crop: winter wheat Arithmetic mean parent DT_{50lab} 141.8 d (normalisation to

‡ Endpoints identified by EU-Commission as relevant for Member States when applying the Uniform Principles

	10kPa or pF2, 20°C with Q10 of 2.2). K_{foc}: parent, arithmetic mean 1989, $^1/_n$= 0.91 (mean of data available in original DAR). Arithmetic mean AE B107137 DT_{50lab} 10.6 d K_{foc}: AE B107137, arithmetic mean 13, $^1/_n$= 0.73 Arithmetic mean AE 0542291 DT_{50lab} 26.9 d (additionally longest DT_{50lab} 45.7 d to account for possible pH effect on degradation) K_{foc}: AE 0542291, arithmetic mean 132, $^1/_n$= 0.81 (mean)
Application rate	Application rate: 187.5 g as/ha. No. of applications: 1/year Time of application (month or season): autumn

PEC(gw) – FOCUS modelling results (80th percentile annual average concentration at 1m)

	Scenario	Parent (µg/L)	Metabolite (µg/L)		
			AE B107137	AE 0542291	3
PELMO / winter wheat	Chateaudun	<0.001	<0.001	<0.001	
	Hamburg	<0.001	<0.001	<0.001	
	Jokioinen	<0.001	<0.001	<0.001	
	Kremsmünster	<0.001	<0.001	<0.001	
	Okehampton	<0.001	<0.001	<0.001	
	Piacenza	<0.001	0.001	<0.001	
	Porto	<0.001	<0.001	<0.001	
	Sevilla	<0.001	<0.001	<0.001	
	Thiva	<0.001	<0.001	<0.001	

NB: The groundwater exposure assessment presented here was based on an earlier parent Koc of 1989 ml/g (compared with the new mean value of 3417 ml/g derived from a modern GLP compliant study). Since the groundwater modelling gave acceptable results for all scenarios with a lower (and therefore more conservative) Koc, the assessment is considered acceptable.

$PEC_{(gw)}$ From lysimeter / field studies

Diflufenican	1st year	2nd year	3rd year
Annual average (µg/L), Lysimeter 1	0.003	<0.003	
Annual average (µg/L), Lysimeter 2	<0.003	<0.003	

‡ Endpoints identified by EU-Commission as relevant for Member States when applying the Uniform Principles

Metabolite AE B107137	1st year	2nd year	3rd year
Annual average (µg/L), Lysimeter 1	<0.003	<0.003	
Annual average (µg/L), Lysimeter 2	<0.003	<0.003	

Metabolite AE 0542291	1st year	2nd year	3rd year
Annual average (µg/L), Lysimeter 1	<0.003	<0.003	
Annual average (µg/L), Lysimeter 2	<0.003	<0.003	

Fate and behaviour in air (Annex IIA, point 7.2.2, Annex III, point 9.3)

Direct photolysis in air ‡	Not studied – no data requested
Quantum yield of direct phototransformation	Not studied – no data requested
Photochemical oxidative degradation in air ‡	DT_{50} of 5.0 d (EU), 3.3 d (USA) derived by the Atkinson method of calculation
Volatilisation ‡	From plant surfaces (BBA guideline): negligible (max. 0.3 %) after 24 hours
	from soil (BBA guideline): negligible (<0.01 %) after 24 hours
Metabolites	Metabolite AE C522392 was found to be volatile in an anaerobic soil degradation study (peak of 28.11% AR in volatile traps). However because its DT_{50} in air is 10.5 hours (via Atkinson calculation), it is unlikely to persist in the troposphere or be subject to long range transport.

PEC (air)

Method of calculation	Expert judgment, based on vapour pressure, dimensionless Henry's Law Constant and information on volatilisation from plants and soil.

$PEC_{(a)}$

Maximum concentration	Negligible for parent and AE C522392

‡ Endpoints identified by EU-Commission as relevant for Member States when applying the Uniform Principles

Residues requiring further assessment

Environmental occurring metabolite requiring further assessment by other disciplines (toxicology and ecotoxicology).	**Soil**: Diflufenican, AE B107137 (2-(3-trifluoromethylphenoxy) nicotinic acid) and AE 0542291 (2-(3-trifluoromethylphenoxy)-nicotinamide). Under prolonged anaerobic conditions metabolite AE C522392 (2,4-difluroaniline) was formed at >10% in soil **Surface Water**: Diflufenican, AE B107137, AE 0542291 (via soil) and 2,4-difluoroaniline (anaerobic soil metabolite only needs to be addressed when prolonged anaerobic conditions are prevalent) **Sediment**: Diflufenican, AE B107137, AE 0542291 **Ground water**:Diflufenican, AE B107137, AE 0542291 and 2,4-difluoroaniline (anaerobic soil metabolite only needs to be addressed when prolonged anaerobic conditions are prevalent) **Air**: Diflufenican and AE C522392 (volatile in an anaerobic soil degradation study)

Monitoring data, if available (Annex IIA, point 7.4)

Soil (indicate location and type of study)	UK, monitoring of drainage sediments, results variable (<5-44 µg/kg dw, mean 8 µg/kg)
Surface water (indicate location and type of study)	No data provided – none requested
Ground water (indicate location and type of study)	No data provided – none requested
Air (indicate location and type of study)	No data provided – none requested

Points pertinent to the classification and proposed labelling with regard to fate and behaviour data

Not readily biodegradable. Candidate for R53

‡ Endpoints identified by EU-Commission as relevant for Member States when applying the Uniform Principles

Appendix 1.6: Effects on non-target Species

Effects on terrestrial vertebrates (Annex IIA, point 8.1, Annex IIIA, points 10.1 and 10.3)

Acute toxicity to mammals ‡	> 5000 mg/kg bw
Long term reproductive toxicity to mammals	35.5 mg/kg bw (parental effects)
Acute toxicity to birds ‡	> 2150 mg /kg bw
Dietary toxicity to birds ‡	Not available
Reproductive toxicity to birds ‡	91.84 mg/kg bw

At the PRAPeR expert meeting in July 2007 it was agreed that the lower NOED of 35.5 mg/Kg bw for long term effects in mammals is the appropriate endpoint.

Toxicity/exposure ratios for terrestrial vertebrates (Annex IIIA, points 10.1 and 10.3)

Application rate (kg as/ha)	Crop	Category (*e.g.* insectivorous bird)	Time-scale	TER	Annex VI Trigger
120	Winter wheat/winter barley	Large herbivorous bird	Acute	>287	10
120	Winter wheat/winter barley	Small insectivorous bird	Acute	>331	10
120	Winter wheat/winter barley	Large herbivorous bird	Long term	43.12	5
120	Winter wheat/winter barley	Small insectivorous bird	Long term	25.37	5
120	Winter wheat/winter barley	Earth worm-eating bird	Long term	82.46	5
120	Winter wheat/winter barley	Fish-eating bird	Long term	22.85	5
120	Winter wheat/winter barley	Drinking water	Acute	> 66.4	10
120	Winter wheat/winter barley	Herbivorous mammal	Acute	> 211.01	10
120	Winter wheat/winter barley	Insectivorous mammal	Acute	> 4717	10
120	Winter wheat/winter barley	Herbivorous mammal	Long term	5.3	5
120	Winter wheat/winter barley	Insectivorous mammal	Long term	91.0	5
120	Winter wheat/winter barley	Earth-worm eating mammal	Long term	25.04	5

‡ Endpoints identified by EU-Commission as relevant for Member States when applying the Uniform Principles

Application rate (kg as/ha)	Crop	Category (*e.g.* insectivorous bird)	Time-scale	TER	Annex VI Trigger
120	Winter wheat/winter barley	Fish- eating mammal	Long term	14.3	5

Toxicity data for aquatic species (most sensitive species of each group) (Annex IIA, point 8.2, Annex IIIA, point 10.2)

Group	Test substance	Time-scale (Test type)	End point	Toxicity (mg/L)
Laboratory tests ‡				
Fish				
(*C carpio*)	Diflufenican	96 h	LC_{50}	> 0.0985*
(*Onchorhynchus mykiss*)	Diflufenican	35 d	NOEC	0.015
(*Onchorhynchus mykiss*)	AE B107137	96 h	LC_{50}	> 17.3*
(*Oncorhynchus mykiss*)	FOE 5043 and diflufenican WG 60 (39.6% flufenacet, 18.8% diflufenican)	96 h	LC_{50}	12.3
Aquatic invertebrate				
(*Daphnia magna*)	Diflufenican	48 h	EC_{50}	> 0.24*
(*Daphnia magna*)	Diflufenican	21 d	NOEC	0.052
(*Daphnia magna*)	AE B107137	48 h	EC_{50}	> 20.4*
(*Daphnia magna*)	AE 0542291	48 h	EC_{50}	> 10
(*Daphnia magna*)	FOE 5043 and diflufenican WG 60 (39.6% flufenacet, 18.8% diflufenican)	48 h	EC_{50}	>100
Sediment dwelling organisms				
(*Chironomus riparius*) spiked water	Diflufenican	28 d	NOEC	0.10
(*Chironomus riparius*) spiked sediment	Diflufenican	28 d	NOEC	2.0 mg/kg sediment
(*Chironomus riparius*)	AE C522392	28 d	NOEC	1 mg/kg sediment

‡ Endpoints identified by EU-Commission as relevant for Member States when applying the Uniform Principles

Group	Test substance	Time-scale (Test type)	End point	Toxicity (mg/L)
Algae				
(*Scenedesmus subspicatus*) Without sediment	Diflufenican	72 h	E_bC_{50} E_rC_{50} NOEC	0.00025 0.00045 0.0001
(*Scenedesmus subspicatus*) With sediment	Diflufenican	72 h	E_bC_{50} E_rC_{50} NOEC	0.0024 0.0047 0.00076
(*Scenedesmus subspicatus*) Without sediment	Diflufenican	72 h	E_bC_{50} E_rC_{50} Maximum concn. from which recovery possible NOEC	0.00046 0.00122 0.0042 0.00015
(*Scenedesmus subspicatus*) Without sediment	AE B107137	72 h	E_bC_{50} E_rC_{50}	> 20.4* > 20.4*
(*Scenedesmus subspicatus*) Without sediment	AE 0542291	72 h	E_bC_{50} E_rC_{50}	36.0 66.0
(*Pseudokirchneriella subcapitata*)	AE 592370	72 h	E_bC_{50} E_rC_{50}	39.0 58.0
(*Pseudokirchneriella subcapitata)*	AE C522392	72 h	E_bC_{50} E_rC_{50}	3.4 16.0
(*Selenastrum capricornutum*)	FOE 5043 and diflufenican SC 600 (401.5g flufenacet/L, 217.0g diflufenican/L) i.e. 'Herold SC'	72 h	E_bC_{50} E_rC_{50}	0.0024 0.0063
Higher plant				
(*Lemna gibba*)	Diflufenican	14 d	E_bC_{50} EC_{50} frond density	0.056 0.039

‡ Endpoints identified by EU-Commission as relevant for Member States when applying the Uniform Principles

Group	Test substance	Time-scale (Test type)	End point	Toxicity (mg/L)
(*Lemna gibba* G3)	FOE 5043 and diflufenican SC 600 (401.5g flufenacet/L, 217.0g diflufenican/L) i.e. 'Herold SC'	7 days	E_bC_{50} based on dry weight E_rC_{50} based on frond counts	0.258 0.307
Microcosm or mesocosm tests				
None submitted.				

*above the visual limit of solubility
In a study in which *Scenedesmus subspicatus* was exposed to diflufenican for 72 h at concentrations up to 0.0042 mg/L growth recovered within 72 h after transfer to untreated growth medium

Toxicity/exposure ratios for the most sensitive aquatic organisms (Annex IIIA, point 10.2)

FOCUS Step1

Exposure resulting from application at 120 g diflufenican/ha to winter wheat, winter barley and winter rye.

Test substance	Organism	LC/EC_{50}/NOEC mg/L	Time scale	PEC_i At 1 m mg/L	PEC_{twa}	TER	Annex VI Trigger
	Fish (*Onchorhynchus mykiss*)	> 0.0985	96 h	0.012		**>8.2**	100
	Inverterbrate (*Daphnia magna*)	> 0.24	48 h	0.012		**>20**	100
	Algae (*Scenedesmus subspicatus*)	0.00025	72 h	0.012		**0.021**	10
	Aquatic higher plant (*Lemna gibba*)	0.039	14 d	0.012		**3.25**	10
	Fish (*Onchorhynchus mykiss*)	0.015	35 d	0.012		**1.25**	10
	Inverterbrate (*Daphnia magna*)	0.052	21 d	0.012		**4.3**	10
	Sediment dwelling invertebrate (*Chironomus riparius*)	>0.1	28 d	0.041[a]		**> 2.4**	10
	Sediment dwelling invertebrate (*Chironomus riparius*)	2 mg/kg sediment	28 d	0.223 mg/Kg sediment		**9.0**	10

‡ Endpoints identified by EU-Commission as relevant for Member States when applying the Uniform Principles

a Based on total load.

FOCUS Step 2

Exposure resulting from application at 120 g diflufenican/ha to winter wheat, winter barley and winter rye.

Test substance	N/S	Organism	LC/EC_{50}/NOEC mg/L	Time scale	PEC At 1 m mg/L	TER	Annex VI Trigger
		Fish (*Onchorhynchus mykiss*)	> 0.0985	96 h	0.0057	**>17.2**	100
		Invertebrate (*Daphnia magna*)	> 0.24	48 h	0.0057	**>42.1**	100
		Algae (*Scenedesmus subspicatus*)	0.00025	72 h	0.0057	**0.04**	10
		Aquatic higher plant (*Lemna gibba*)	0.039	14 d	0.0057	**6.8**	10
		Fish (*Onchorhynchus mykiss*)	0.015	35 d	0.0057	**2.6**	10
		Inverterbrate (*Daphnia magna*)	0.052	21 d	0.0057	**9.1**	10
		Sediment dwelling invertebrate (*Chironomus riparius*)	>0.1	28 d	0.021[a]	**> 4.76**	10
		Sediment dwelling invertebrate (*Chironomus riparius*)	2 mg/kg sediment	28 d	0.112 mg/Kg sediment	17.9	10

[a] Based on total load.

Refined aquatic risk assessment using higher tier FOCUS modelling.

FOCUS Step 3

State crop and application rate: highest PEC_{water} (D2 ditch scenario) and highest PEC_{sed} (R3 stream scenario)

Test substance	Scenario	Water body type	Test organism	Time scale	Toxicity end point (mg/L)	PEC At 1 m	TER	Annex VI trigger
			Fish (*Onchorhynchus mykiss*)	96 h	> 0.0985	0.000835	> 118.0	100

‡ Endpoints identified by EU-Commission as relevant for Member States when applying the Uniform Principles

Test substance	Scenario	Water body type	Test organism	Time scale	Toxicity end point (mg/L)	PEC At 1 m	TER	Annex VI trigger
			Inverterbrate (*Daphnia magna*)	48 h	> 0.24	0.000835	>287.4	100
			Algae (*Scenedesmus subspicatus*)	72 h	0.00025	0.000835	**0.30**	10
			Aquatic higher plant (*L gibba*)	14 d	0.039 (frond density)	0.000835	46.71	10
			Fish (*Onchorhynchus mykiss*)	35 d	0.015	0.000835	18.0	10
			Inverterbrate (*Daphnia magna*)	21 d	0.052	0.000835	62.3	10
			Sediment dwelling invertebrate (*Chironomus riparius*) based on concn in water	28 d	>0.1	0.000835	>120	10

FOCUS Step 4

Crop and application rate: Toxicity/exposure ratios for the most sensitive algal species, *Scenedesmus subspicatus* at FOCUS Step 4 using PECs from all scenarios using a 5m no-spray buffer zone.

Scenario	Water body type	Test organism	Time scale	Toxicity end point EC_{50} mg/L	Buffer zone distance	PEC At 5 m	TER	Annex VI trigger
D1 ditch			72h	0.00025	5 m	0.000393	**0.64**	
D1 stream			72h	0.00025	5 m	0.000246	**1.02**	10
D2 ditch			72h	0.00025	5 m	0.00042	**0.60**	10
D2 stream			72h	0.00025	5 m	0.00027	**0.92**	10
D3 ditch			72h	0.00025	5 m	0.000206	**1.21**	10
D4 pond			72h	0.00025	5 m	0.000038	**6.58**	10
D4 stream			72h	0.00025	5 m	0.000239	**1.05**	10
D5 pond			72h	0.00025	5 m	0.0000230	10.87	10

‡ Endpoints identified by EU-Commission as relevant for Member States when applying the Uniform Principles

Scenario	Water body type	Test organism	Time scale	Toxicity end point EC_{50} mg/L	Buffer zone distance	PEC At 5 m	TER	Annex VI trigger
D5 stream			72h	0.00025	5 m	0.000259	**0.97**	10
D6 ditch			72h	0.00025	5 m	0.00041	**0.61**	10
R1 pond			72h	0.00025	5 m	0.000075	**3.3**	10
R1 stream			72h	0.00025	5 m	0.00048	**0.52**	10
R3 stream			72h	0.00025	5 m	0.000587	**0.43**	10
R4 stream			72h	0.00025	5 m	0.000680	**0.37**	10

D5 pond with a 5 m no-spray buffer zone produces an acceptable exposure.
Note for clarification on the risk assessment approach agreed in the expert meeting on ecotoxicology (PRAPeR 23) in April 2007:
Examination of the data on recovery of the alga, *Scenedesmus subspicatus*, which is reported in detail in the DAR (Odin-Feurtet 1998d) shows that when this alga is exposed to up to 4.2 µg DFF/L for 3 days it can recover to control levels within 3 days (16x increase within 3 days) when removed to fresh medium. It should be noted that *Scenedesmus subspicatus* is the most sensitive of the 5 algal species tested. It is acknowledged that although this species recovers quickly this may not be the case for less sensitive algal species. Therefore to account for this uncertainty it is proposed that an uncertainty factor of 10 is still used with the EC_{50}. Hence it is assumed that exposure to 0.42 µg DFF/L for 3 days will cause effects but that recovery in fresh medium will be possible within 3 days.

Exposure is not simply a one-off event and the pattern of exposure is important. The effect of multiple exposures is not known so a conservative approach has been taken, i.e. that risk may be considered acceptable provided the peak exposure is below 0.42 µg/L, this exposure does not persist for >3 days (the duration of exposure in the study on which these assumptions were based) and that the other exposure peaks do not exceed the overall NOEC for all species tested, 0.1 µg/L

At FOCUS Step 4, with a 5m no-spray buffer zone and using information on algal recovery the following scenarios are acceptable.

Based on information and PECs in the original DAR which were agreed by experts at the PRAPeR meeting of May 2007, the following scenarios are considered to be acceptable:-

D3 ditch (full scenario) with a no spray buffer zone of 5m
D5 pond (part scenario) with a no spray buffer zone of 5m

Toxicity exposure ratios (TERs) for aquatic organisms and the metabolites AE B107137 and AE 0542291

Test organism	End point EC/LC_{50} mg a.s./L	Step 1 (global max PEC) mg a.s./L	TER	Annex VI trigger
AE B107137				
Fish (*Cyrpinus carpio*)	>17.3	0.005	> 3460	100

‡ Endpoints identified by EU-Commission as relevant for Member States when applying the Uniform Principles

Test organism	End point EC/LC_{50} mg a.s./L	Step 1 (global max PEC) mg a.s./L	TER	Annex VI trigger
Aquatic invertebrate (*D magna*)	> 20.4	0.005	> 4080	100
Alga (*S subspicatus*)	E_bC_{50} > 20.4 E_rC_{50} > 20.4	0.005	> 4080	10
AE 0542291				
Aquatic invertebrate (*D magna*)	> 10.0	0.0064	> 3189	100
Alga (*S subspicatus*)	E_bC_{50} > 36.0 E_rC_{50} > 66.0	0.0064	> 5625 > 10313	10

Exposure to metabolites is acceptable at Step 1.

Bioconcentration

Bioconcentration factor (BCF) ‡	1276 (0.3 µg/L) 1596 (3.0 g/L)
Annex VI Trigger for the bioconcentration factor	> 1000 (diflufenican not readily biodegradable)
Clearance time (CT_{50}) (CT_{90})	2.4 d (0.3 µg/L) 3.3 d (3.0 g/L) 97% depuration by 14 d.
Level of residues in organisms after the 14 day depuration phase	0.010 µg/g (0.3 µg/L 0.123 µg/g (3.0 g/L)

Effects on honeybees (Annex IIA, point 8.3.1, Annex IIIA, point 10.4)

Test substance	Acute oral toxicity (LD_{50} µg/bee)	Acute contact toxicity (LD_{50} µg/bee)
a.s. ‡	>112.3	>100
(18.8% diflufenican, 39.6% flufenacet) (µg formulation/bee) ‡	>198	>200
Field or semi-field tests		
Not tested		

‡ Endpoints identified by EU-Commission as relevant for Member States when applying the Uniform Principles

Hazard quotients for honey bees (Annex IIIA, point 10.4)

Winter cereals

Test substance	Route	Hazard quotient	Annex VI Trigger
120 g a.s./ha	Oral	<1.1	50
120 g a.s./ha	Contact	<1.2	50
750 g product/ha	Oral	<3.8	50
750 g product/ha	Contact	<3.8	50

Effects on other arthropod species (Annex IIA, point 8.3.2, Annex IIIA, point 10.5)

Laboratory tests with standard sensitive species

Species	Test Substance	End point	Effect (LR_{50} g/ha)
Typhlodromus pyri ‡ (adults)	709 g diflufenican/kg WG (187.5 g as/ha)	Mortality Fecundity	7.7% 23.0% reduction
Aphidius rhopalosiphi ‡ (protonymphs)	709 g diflufenican/kg WG (187.5 g as/ha)	Mortality Fecundity	2.8% 39.8% reduction[1]

[1]Statistically significant

Further laboratory and extended laboratory studies ‡

Species	Life stage	Test substance, substrate and duration	Dose (g/ha)	End point	% effect	Trigger value
Aphidius rhopalosiphi ‡	Adult	700 g diflufenican/L	187.5 g as/ha	Mortality Parasitisation	0% 14.3% increase	50 %
Aleochara bilineata ‡	Adult	247 g diflufenican/L	247 g as/ha	Mortality Parasitisation	0.0% 106%	50 %
Poecilus cupreus ‡	Adult	250 g diflufenican/L	250 g as/ha	Mortality Feeding	0.0% 0.0%	50 %

Field or semi-field tests
Not tested

‡ Endpoints identified by EU-Commission as relevant for Member States when applying the Uniform Principles

Effects on earthworms, other soil macro-organisms and soil micro-organisms (Annex IIA points 8.4 and 8.5. Annex IIIA, points, 10.6 and 10.7)

Test organism	Test substance	Time scale	End point
Earthworms			
	a.s. ‡	Acute 14 days	LC_{50} > 500 mg/kg soil[1]
	a.s. ‡	Reproductive toxicity	NOEC 500 mg/kg soil[1]
	Preparation	Acute	/
	Preparation	Chronic	/
	Metabolite AE B107137	Acute	LC_{50} > 500 mg/kg soil[1]
	Metabolite AE 0542291	Acute	LC_{50} > 500 mg/kg soil[1]
	Metabolite 1	Chronic	
Other soil macro-organisms			
Soil mite	a.s. ‡		/
	Preparation (Herold SC600)		NOECcorr 5.4 mg diflufenican/kg soil
Collembola			
	a.s. ‡		/
	Preparation (Diflufenican SC500)		NOEC 438 mg diflufenican/kg soil
Soil micro-organisms			
Nitrogen mineralisation	a.s. ‡		No effects > 25%
	Metabolite AE B107137		No effects > 25%
	Metabolite AE 0542291		No effects > 25%
Carbon mineralisation	a.s. ‡		No effects > 25%
	Metabolite AE B107137		No effects > 25%
	Metabolite AE 0542291		No effects > 25%
Field studies			

[1]Endpoints corrected to allow for logPow of > 2

‡ Endpoints identified by EU-Commission as relevant for Member States when applying the Uniform Principles

Toxicity/exposure ratios for soil organisms

Winter cereals

Test organism	Test substance	Time scale	Soil PEC	TER	Trigger
Earthworms					
	Diflufenican	Acute	0.0405	>1235	10
	AE B107137	Acute	0.05	>10000	10
	AE 0542291	Acute	0.08	>6250	10
	Diflufenican	Chronic	0.0405	1235	5
Other soil macro-organisms					
Soil mite	a.s. ‡		/		
	Preparation (Herold SC600)		0.405	13.3	5
Collembola	a.s. ‡				
	Preparation (Diflufenican SC500)		0.405[1]	1081[1]	5

1Accumulated PEC for diflufenican

Effects on non target plants (Annex IIA, point 8.6, Annex IIIA, point 10.8)

Pre- and post-emergence EC_{50}s for fresh weight for species treated with diflufenican as EXP04005B and with Herold 600 SC.

	Diflufenican (as EXP04005B)		Herold 600SC	
Species	Pre-emergence EC_{50} (g a.s./ha)	Post-emergence EC_{50} (g a.s./ha)	Pre-emergence EC_{50} (g a.s./ha)	Post-emergence EC_{50} (g a.s./ha)
Brassica napus	482.6	2.88	214.2	92.07
Cucumis sativa	490.0	5.51	218.41	27.75
Lycopersicon esculentum	350.2	5.50	> 332	ND
Phaseolus vulgaris	> 1000	212.78	/	/
Avena sativa	>1000	> 1000	207.9	227.5
Lolium perrene	171.8	> 1000	/	/
Allium cepa	/	/	190.4	> 332.3
Glycine max	/	/	> 332.3	55.14

‡ Endpoints identified by EU-Commission as relevant for Member States when applying the Uniform Principles

Pre- and post-emergence EC_{50}s for survival and fresh weight for species treated with diflufenican as AE F088657 00 SC42

Species	Pre-emergence EC_{50} (g a.s./ha)	Post-emergence EC_{50} (g a.s/ha)
Cucumis sativa	>428	>428
Brassica napus	>428	>428
Raphanus sativus	415.9	>428
Glycine max	>428	>428
Beta vulgaris	>428	174.8
Helianthus annuus	>428	>428
Lycopersicon esculentum	>428	290.8
Avena sativa	>428	>428
Allium cepa	>428	>428
Lolium perrene	>428	>428

TERs based on EXP04005B

Seedling emergence	Diflufenican:- Comparison of the maximum PEC_{soil} at 1m from the treated crop 0.0112 mg diflufenican/kg soil, with the lowest pre-emergence EC_{50} of 0.229mg diflufenican/kg soil (converted from an application rate of 171.8 g diflufenican/ha), gives a TER of 20.4which exceeds the proposed trigger of 5. Hence, risk to non-target plants pre-emergence immediately adjacent to treated crop and taking account of potential accumulation of diflufenican in soil is acceptable. The risk posed by other formulations should be considered at Member State level.
Vegetative vigour	Diflufenican:- Comparison of the deposition at 1m from the treated crop, 3.324 mg diflufenican/ha, with the lowest post-emergence EC_{50} of 2.88 mg diflufenican/ha, gives a TER of 0.87 which is below the proposed trigger of 5. A buffer zone of 10m reduces the drift to 0.348 mg diflufenican/ha and increases the TER for 8.28, which exceeds the trigger of 5 and provides adequate protection.

‡ Endpoints identified by EU-Commission as relevant for Member States when applying the Uniform Principles

TERs based on AE F088657 00 SC42

Seedling emergence	Diflufenican:- Comparison of the maximum PEC_{soil} at 1m from the treated crop, 0.0112 mg diflufenican/kg soil, with the lowest pre-emergence EC_{50} of 0.019mg diflufenican/kg soil (converted from an application rate of 171.8 g diflufenican/ha), gives a TER of 1.7 which falls short of the proposed trigger of 5. Comparison of the PEC at 5m of 0.0023 mg/kg soil witth the EC_{50} of 0.019 mg/kg soil gives a TER of 8.3 which exceeds the trigger of 5 and provides adequate protection.
Vegetative vigour	Diflufenican:- Comparison of the deposition at 1m from the treated crop, 3.324 mg diflufenican/ha, with the lowest post-emergence EC_{50} of 76.6 g diflufenican/ha, gives a TER of 23.0 which exceeds he proposed trigger of 5 and does not indicate a requirement for risk mitigation

Use of diflufenican is acceptable provided appropriate risk mitigation is used. Member States should consider potential risk and appropriate management of that risk on a national basis at product authorization

Effects on biological methods for sewage treatment (Annex IIA 8.7)

Test type/organism	Endpoint
Activated sludge	3 h EC_{50} > 1000 mg diflufenican/L
Pseudomonas sp	/

Ecotoxicologically relevant compounds

Compartment	
soil	Diflufenican
water	Diflufenican
sediment	Diflufenican
groundwater	Diflufenican

‡ Endpoints identified by EU-Commission as relevant for Member States when applying the Uniform Principles

Classification and proposed labelling with regard to ecotoxicological data (Annex IIA, point 10 and Annex IIIA, point 12.3)

	RMS/peer review proposal	
Diflufenican	N	Dangerous for the environment
	R50	Very toxic to aquatic organisms
	R53	May cause long term adverse effects in the aquatic environment.
	S60	This material and its container should be disposed of as hazardous waste
	S61	Avoid release to the environment. Refer to special instructions/safety data sheets.

	RMS/peer review proposal	
Preparation	N	Dangerous for the environment
	R50	Very toxic to aquatic organisms
	R53	May cause long term adverse effects in the aquatic environment.
	S60	This material and its container should be disposed of as hazardous waste
	S61	Avoid release to the environment. Refer to special instructions/safety data sheets.

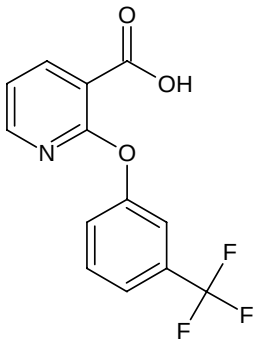
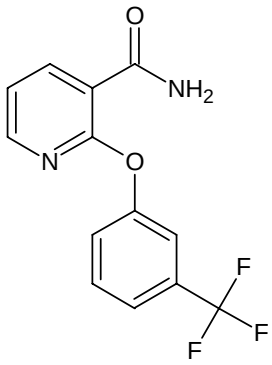
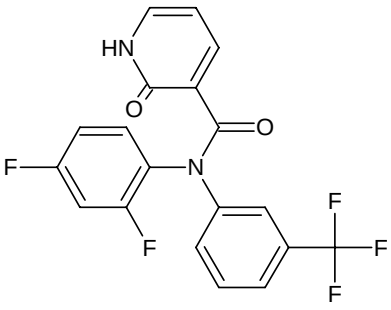
‡ Endpoints identified by EU-Commission as relevant for Member States when applying the Uniform Principles

APPENDIX 2 – ABBREVIATIONS USED IN THE LIST OF ENDPOINTS

ADI	acceptable daily intake
AOEL	acceptable operator exposure level
ArfD	acute reference dose
a.s.	active substance
bw	body weight
CA	Chemical Abstract
CAS	Chemical Abstract Service
CIPAC	Collaborative International Pesticide Analytical Council Limited
d	day
DAR	draft assessment report
DM	dry matter
DT_{50}	period required for 50 percent dissipation (define method of estimation)
DT_{90}	period required for 90 percent dissipation (define method of estimation)
ε	decadic molar extinction coefficient
EC_{50}	effective concentration
EEC	European Economic Community
EINECS	European Inventory of Existing Commercial Chemical Substances
ELINKS	European List of New Chemical Substances
EMDI	estimated maximum daily intake
ER50	emergence rate, median
EU	European Union
FAO	Food and Agriculture Organisation of the United Nations
FOCUS	Forum for the Co-ordination of Pesticide Fate Models and their Use
GAP	good agricultural practice
GCPF	Global Crop Protection Federation (formerly known as GIFAP)
GS	growth stage
h	hour(s)
ha	hectare
hL	hectolitre
HPLC	high pressure liquid chromatography or high performance liquid chromatography
ISO	International Organisation for Standardisation
IUPAC	International Union of Pure and Applied Chemistry
K_{oc}	organic carbon adsorption coefficient
L	litre
LC	liquid chromatography
LC-MS	liquid chromatography-mass spectrometry
LC-MS-MS	liquid chromatography with tandem mass spectrometry

LC_{50}	lethal concentration, median
LD_{50}	etal dose, median; dosis etales media
LOAEL	lowest observable adverse effect level
LOD	limit of detection
LOQ	limit of quantification (determination)
µg	microgram
mN	milli-Newton
MRL	maximum residue limit or level
MS	mass spectrometry
NESTI	national estimated short term intake
NIR	near-infrared-(spectroscopy)
nm	nanometer
NOAEL	no observed adverse effect level
NOEC	no observed effect concentration
NOEL	no observed effect level
PEC	predicted environmental concentration
PEC_A	predicted environmental concentration in air
PEC_S	predicted environmental concentration in soil
PEC_{SW}	predicted environmental concentration in surface water
PEC_{GW}	predicted environmental concentration in ground water
PHI	pre-harvest interval
pK_a	negative logarithm (to the base 10) of the dissociation constant
PPE	personal protective equipment
ppm	parts per million (10^{-6})
ppp	plant protection product
r^2	coefficient of determination
RPE	respiratory protective equipment
STMR	supervised trials median residue
TER	toxicity exposure ratio
TMDI	theoretical maximum daily intake
UV	ultraviolet
WHO	World Health Organisation
WG	water dispersible granule
yr	year

APPENDIX 3 – USED COMPOUND CODE(S)

Code/Trivial name	Chemical name	Structural formula
AE B107137 [M&B38181]	2-[3-(trifluoromethyl)phenoxy]pyridine-3-carboxylic acid	
AE 0542291 [M&B43625]	2-[3-(trifluoromethyl)phenoxy]pyridine-3-carboxamide	
AE 0592370	*N*-(2,4-difluorophenyl)-2-oxo-*N*-[3-(trifluoromethyl)phenyl]-1,2-dihydropyridine-3-carboxamide	
AE C522392	2,4-difluoroaniline