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

flutolanil.

Finalised: 3 March 2008

SUMMARY

Flutolanil 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 upon request of the EU-Commission 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.

Finland being the designated rapporteur Member State submitted the DAR on flutolanil in accordance with the provisions of Article 10(1) of the Regulation (EC) No 1490/2002, which was received by the EFSA on 13 June 2005. The peer review was initiated on 29 March 2006 by dispatching the DAR for consultation of the Member States and the sole applicant Nihon Nohyaku Co., Ltd. Subsequently, the comments received on the DAR were examined by the rapporteur Member State and the need for additional data was agreed during a written procedure from November 2006 – January 2007. 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 from May – June 2007.

A final discussion of the outcome of the consultation of experts took place during a written procedure with the Member States from January - February 2008 leading to the conclusions as laid down in this report.

The conclusion was reached on the basis of the evaluation of the representative use as a fungicide tuber treatment prior to planting. Full details of the GAP can be found in the attached end points.
The representative formulated product for the evaluation was "Moncut 40 SC", a suspension concentrate (SC).

Adequate methods are available to monitor all compounds given in the respective residue definition which is flutolanil only. However, there is a data gap for a confirmatory method for soil, it is noted that a confirmatory method is available and is evaluated in addendum 5 Vol. 3 but it has not been peer reviewed. Only single methods for the determination of residues are available however, it was also

[1] OJ No L 224, 21.08.2002, p. 25, as last amended by Regulation (EC) No 1095/2007 (OJ L 246, 21.9.2007, p. 19)

shown that the German S19 method could be used for plant matrices, however no ILV data were provided for this method.
Sufficient analytical methods as well as methods and data relating to physical, chemical and technical properties are available to ensure that at least some quality control measurements of the plant protection product are possible.

During the mammalian toxicology studies, flutolanil was shown to be orally absorbed up to 70% and rapidly excreted. Its acute toxicity was low, it was not irritating and did not cause skin sensitization. In short term studies, the target organ was the liver in the different species. Flutolanil was considered to have no genotoxic potential, no carcinogenic properties, no teratogenic effects or adverse effects on the reproductive parameters, and no specific neurotoxic properties. It was concluded that the metabolites M-4 and M-2, being the main rat metabolites, had the same toxicological profile than flutolanil. The acceptable daily intake (ADI) is 0.09 mg/kg bw/day based on the 2-year rat study, the acceptable operator exposure level (AOEL) is 0.56 mg/kg bw/day based on the 90-day dog study with correction for oral absorption (70%), and the acute reference dose was considered as not necessary. The dermal absorption values were 0.5% for the concentrate and 5% for the dilution.
The operator exposure was below the AOEL with the use of gloves when estimated with the models (UK, German, EUROPOEM). In addition, results of a field study showed that operator exposure is unlikely to be higher than the AOEL. In the same way, the worker and bystander exposure was expected to be lower than the AOEL.

Flutolanil plant metabolism has been investigated in potatoes after seed treatment as well as in peanuts and rice after foliar application. A similar metabolic pathway was observed in the 3 crops. Parent flutolanil is a valid indicator for monitoring residues in harvested plant commodities. Two metabolites and their conjugates contribute significantly to the global toxicological burden and need to be considered in the residue definition for risk assessment.
Supervised residue trials conducted in Northern Europe are available and support the setting of an MRL of 0.05 mg/kg in potatoes. The appropriateness of this MRL for Southern region should be consolidated by further field data.
Livestock exposure to flutolanil residues is low and the establishment of a residue definition and MRLs for animal commodities is not necessary.
Transfer of soil residues is limited and no residue above the LOQ in rotational crop is expected.
The consumer chronic exposure to flutolanil residues is below 2 % of the ADI

In soil under aerobic conditions flutolanil exhibits high to very high persistence and did not form any major (>10% of applied radioactivity (AR)) extractable non volatile soil metabolites. Mineralisation to carbon dioxide accounted for 15.9% AR at 116days. The formation of non extractable residues was also a significant sink accounting for 27.9% AR after 105 days. Flutolanil exhibits medium to low mobility in soil and there was no indication that adsorption was soil pH dependant.
In natural sediment water systems flutolanil dissipated slowly from water and partitioned mostly to sediment. Minor amounts (< 10% AR) of degradation products were detected in the whole systems.

Predicted environmental concentration in surface water systems due to contamination via drainage were calculated using FOCUS surface water Step 3.
The available FOCUS groundwater modelling is based on a 2-year crop rotation period and an incorporation depth in soil of 20 cm. For the representative field uses applied for, the potential for groundwater exposure by flutolanil above the parametric drinking water limit of 0.1 µg/L is low, except for regions with geoclimatic conditions represented by Piacenza and Okehampton FOCUS groundwater scenarios (0.271 and 0.102 µg/L, respectively).

Since the representative use of flutolanil as seed treatment for potatoes is not foreseen as a standard scenario in the Guidance Document for Birds and Mammals, the common cane (*Grus grus*) and the badger (*Meles meles*) were assessed as alternative relevant focal species to represent potatoes-eating birds and mammals respectively. The risk to birds and mammals can be considered low applying refined FIR and the concentration of 92 mg a.s./kg seed potato in the assessment. As for all other groups of non target organisms the ecotoxicological risk can also be considered as being low for the representative use evaluated.

Key words: flutolanil, peer review, risk assessment, pesticide, fungicide

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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, as amended by Commission Regulation (EC) No 1095/2007, regulates for the European Food Safety Authority (EFSA) the procedure of evaluation of the draft assessment reports provided by the designated rapporteur Member State. Flutolanil is one of the 79 substances of the third stage, part A, covered by the Regulation (EC) No 1490/2002 designating Finland as rapporteur Member State.

In accordance with the provisions of Article 10(1) of the Regulation (EC) No 1490/2002, Finland submitted the report of its initial evaluation of the dossier on flutolanil, hereafter referred to as the draft assessment report, to the EFSA on 13 June 2005. Following an administrative evaluation, the EFSA communicated to the rapporteur Member State some comments regarding the format and/or recommendations for editorial revisions and the rapporteur Member State submitted a revised version of the draft assessment report. In accordance with Article 11(2) of the Regulation (EC) No 1490/2002 the revised version of the draft assessment report was distributed for consultation on 29 March 2006 to the Member States and the main applicant Nihon Nohyaku Co., Ltd. as identified by the rapporteur Member State.

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 – January 2007 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 during a written procedure with the Member States in January - February 2008 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 2 February 2007)

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 13 February 2008).

Given the importance of the draft assessment report including its addendum (compiled version of January 2008 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

Flutolanil is the ISO common name for α,α,α-trifluoro-3'-isopropoxy-o-toluanilide (IUPAC).

Flutolanil belongs to the class of benzanilide fungicides such as mepronil and benodanil. It is an inhibitor of succinate dehydrogenase complex, in the respiratory electron transport chain, leading to inhibition of aspartate and glutamate synthesis. It is a Systemic fungicide with protective and curative action, it prevents fungal growth and penetration from infection cushions; it causes collapse of hyphae and infection cushions.
The representative formulated product for the evaluation was " Moncut 40 SC , a suspension concentrate (SC).

The evaluated representative use is as a fungicide tuber treatment prior to planting. Full details of the GAP can be found in the attached end points.

SPECIFIC CONCLUSIONS OF THE EVALUATION

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

The minimum purity of flutolanil as manufactured has not been agreed on because there is an out standing data gap on the batch analysis. From the information available it appears that there are

batches analysed with the same batch numbers that give very different impurity profiles. Addendum 5 to Vol 4 was submitted to address this issue and in it a new specification is proposed. This addendum was received after the meeting of experts and therefore could not be considered as part of the peer review process and for this reason the issue remains unresolved. At the moment no FAO specification exists.

In addition to this the methods of analysis for the impurities show a high % RSD result and the applicant needs to address this issue. Therefore, the technical material as a whole should be regarded as provisional. The technical material contains no relevant impurities.

The content of flutolanil in the representative formulation is 460 g/L (pure).

Beside the specification, 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 flutolanil or the respective formulation. However, the following data gaps were identified:

- Cold temperature stability of the formulation.
- Shelflife study.
- Adherence and distribution on the seed potatoes (it is noted that a study has been submitted and is evaluated in addendum 5 to Vol. 3, however it has not been peer reviewed)

The peer review only considered the nonyl phenol ethoxylate (NPE) containing formulation. However, it is noted that the applicant will no longer support this formulation and an NPE free formulation has been developed.

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

Sufficient test methods and data relating to physical, chemical and technical properties are available. Also adequate analytical methods are available for the determination of flutolanil in the technical material and in the representative formulation as well. There are still some outstanding issues with the methods for the impurities.
Therefore, enough data are available to ensure that quality control measurements of the plant protection product are possible.

Adequate methods are available to monitor all compounds given in the respective residue definition, i.e. flutolanil in food of plant origin (potato only), soil, water and air.

Residues in potatoes can be analysed by a GC-MS method with an LOQ of 0.01 mg/kg it was also shown that the DFG S19 method may also be used but there was no ILV data supplied for it. Soil is also analysed by a GC-MS method with an LOQ of 5 µg/kg and there is a data gap for a confirmatory

method, it is noted that a confirmatory method is available and is evaluated in addendum 5 Vol. 3 but it has not been peer reviewed. Water is analysed by GC-TID with an LOQ for groundwater of 0.1 µg/l and an LOQ for surface water of 1 µg/l. Air is analysed by HPLC-UV with an LOQ of 2.7 µg/m3.
An analytical method for food of animal origin is not required due to the fact that no residue definition is proposed (see 3.2)

A method for body fluids and tissues is also not required as the flutolanil is not classified as toxic or very toxic.

2. Mammalian toxicology

Flutolanil was discussed by the experts in mammalian toxicology in the PRAPeR meeting 24 (round 5, June 2007)
EFSA notes: Considering the technical specification proposed in addendum 2 to Vol.4 (April 2007), the toxicological batches, presenting similar or higher levels of impurities, can be considered as representative of the technical material. However it should be noted that the final technical specification has not yet been agreed (see section 1).

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

Following oral administration in the rat, flutolanil was rapidly excreted (>95% in 72h) into urine (~70%) and faeces (~30%). Based on the data from bile-cannulated animals (bile + urine), the experts agreed to derive an oral absorption of 70%. The highest concentrations were found in the liver and kidney (2 hours after administration) and decreased rapidly. In urine the main metabolites were M-4[2], M-2[3] and M-7[4]. In faeces the metabolites were mainly the unchanged parent, but also M-2 and M-4. There was no evidence of cleavage at the amido bridge in the proposed metabolic pathway.

2.2. Acute toxicity

Flutolanil was found to be of low acute toxicity by oral, dermal or inhalation administration (oral/intraperitoneal/subcutaneous LD_{50} >10000 mg/kg bw, dermal LD_{50} >5000 mg/kg bw, LC_{50} by inhalation >5.98 mg/L). Flutolanil was not an irritant to skin or eyes, and did not cause skin sensitisation (in a Magnusson and Kligman Maximization test). Therefore no classification was proposed for the acute toxicity.

2.3. Short term toxicity

In both rodents and dogs (oral studies: rat 28-day, rat 90-day, mouse 90-day, dog 90-day), the target organ was the liver. Liver weights were increased in most studies, and slight histopathological

[2] M-4 : α,α,α-trifluoro-3'-hydroxy-o-toluanilide
[3] M-2 : α,α,α-trifluoro-4'-hydroxy-3'-isopropoxy-o-toluanilide
[4] M-7 : α,α,α-trifluoro-4'-hydroxy-3'-methoxy-o-toluanilide

alterations were also noted in dogs. In rats, weights of thyroid/parathyroid and serum albumin levels were also increased. The experts discussed the setting of the NOAEL in the 90-day rat study. In the absence of histopathological findings, the weight changes of the liver and the thyroid were not considered adverse and the agreed NOAEL was 299 mg/kg bw/day. In the other species, the NOAELs were 680 mg/kg bw/day for the 90-day mouse study, and 80 mg/kg bw/day for the 90-day dog study.

The results of a 3-week dermal study in rats were presented in the addendum 3 (May 2007) with a NOAEL higher than 1000 mg/kg bw/day in the absence of adverse findings.

2.4. GENOTOXICITY

Flutolanil has been tested in a range of *in vitro* assays (Ames test, chromosomal aberration tests in mammalian cells, cell mutation test in mouse cells, UDS in rat hepatocytes) and one *in vivo* assay for micronuclei in bone marrow of mice. The weak positive result observed in the presence of metabolic activation in an *in vitro* test for chromosomal aberration in hamster cells occurred only at cytotoxic doses. Furthermore this was not confirmed in the *in vivo* micronucleus test (negative). The experts concluded that flutolanil has no genotoxic potential.

2.5. LONG TERM TOXICITY

The chronic effects of flutolanil were studied in rats (2-year study), mice (18-month study) and dogs (2-year study). There was no evidence of severe toxicity and no carcinogenic properties were demonstrated. In **rats**, the NOAEL is 8.7 mg/kg bw/day, based on slight anaemia in females and histopathological splenic changes in males. In **mice**, the NOAEL is 32 mg/kg bw/day, based on an increased incidence of periacinar hepatocytic fatty vacuolation in males. In **dogs**, the NOAEL is 50 mg/kg bw/day, based on clinical signs (emesis, salivation, excretion of soft faeces) observed during the latter part of the study. Additionally, at the highest dose, hyperaemia of the intestinal tract was observed and some relative organ weights were increased (brain, heart, liver).

2.6. REPRODUCTIVE TOXICITY

The toxicity of flutolanil for the reproductive parameters was investigated in one two-generation reproduction study and in two prenatal toxicity studies. In the rat two-generation study, the parental NOAEL is 157 mg/kg bw/day based on an increased liver weight. No reproductive effects were observed, and the NOAEL for offspring and reproduction is 1614 mg/kg bw/day (highest dose tested).

In the teratogenicity studies, flutolanil did not induce malformations at 1000 mg/kg bw/day in rats or rabbits. The proposed NOAEL for maternal toxicity and teratogenicity is ≥1000 mg/kg bw/day for both species.

2.7. NEUROTOXICITY

Flutolanil does not have a chemical structure that is similar or related to those capable of inducing delayed neurotoxicity. There was no evidence of neurotoxicity in the toxicological studies. It is therefore considered that no specific neurotoxicity studies are required.

2.8. FURTHER STUDIES

Plant metabolites

The metabolites M-4 and M-2 were identified in potato tubers at levels similar to that of flutolanil. Taking into account that these metabolites are the main rat metabolites, the experts agreed that they have the same toxicological profile as the parent compound.

2.9. MEDICAL DATA

No adverse health effects were reported from manufacturing plant workers and no clinical cases or poisoning cases have been reported.

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

ADI

The proposed **ADI is 0.09 mg/kg bw/day**, with the use of a safety factor 100, based on the lowest NOAEL found in the 2-year rat study (8.7 mg/kg bw/day).

The same value for ADI was established in the toxicological evaluation of flutolanil by JMPR (2002).

AOEL

Initially the RMS proposed to base the AOEL on the 90-day rat study. Following the revision of the NOAEL in this study, the experts agreed to use the lowest NOAEL of the 90-day dog study for the setting of the AOEL. Therefore the agreed **AOEL is 0.56 mg/kg bw/day**, with the use of a safety factor 100 and a correction for oral absorption (70%).

ARfD

There is no need to set an ARfD for flutolanil in view of its low acute toxicity, the absence of clinical signs and effects pertinent to administration of single doses, and the absence of developmental effects.

2.11. DERMAL ABSORPTION

One *in vitro* study on human skin was performed with a representative formulation (460 g/L SC formulation) but only with the concentrated formulation. Including the amount found in the epidermis after 24h of exposure, the experts agreed with the dermal absorption value of 0.5% for the concentrate, and decided for a high conservative value of 5% for the dilution of 10% in water.

2.12. EXPOSURE TO OPERATORS, WORKERS AND BYSTANDERS

The representative plant protection product Flutolanil 40SC is a suspension concentrate (SC) containing 460 g flutolanil/L for use on potatoes (at pre-planting).

Operator exposure

The supported method of application is conventional canopied hydraulic or spinning disc potato sprayer equipment mounted on a rolling conveyor. Another common method of application is a tractor sprayer attached to the planting machine. The intended application rate is 200 ml/ton of tubers. During an 8h workday the total amount of tubers handled is around 80 tons (conservative assumption), i.e. the amount of a.s. handled is as high as 7.36 kg as/day.

In the DAR, the estimates with the models (UK POEM, German BBA and EUROPOEM) showed together that the operator exposure was below the proposed AOEL (i.e. 0.37 mg/kg bw/day at that time) in all scenarios, when gloves were used (up to 3% of the AOEL). However it was highlighted that these models did not cover the scenario of seed treatment of potatoes with the use of conveyor or belt-mounted spraying equipment. Therefore no recalculation with the new AOEL (0.56 mg/kg bw/day) and dermal absorption value (5%) was considered necessary.
The supportive field study presented in the DAR using a DP formulation of captan (Stevens and Davis, 1981) was considered inadequate by some experts. The availability of an operator exposure study with flutolanil (performed for the registration in UK) was mentioned during the peer-review. Unfortunately it was provided lately to the RMS and not evaluated completely for the experts' meeting. UK reported that the study was reliable, and was the only realistic assessment in view of the supported use. It was agreed that preliminary results show that operator exposure is unlikely to be higher than the AOEL. The final evaluation by UK has been provided in the addendum 4 to Vol.3 (October 2007, not peer-reviewed), and gave an exposure level of 50% of the AOEL without personal protective equipment when taking into account the agreed AOEL and dermal absorption value.

Worker exposure

There is no model available to predict worker (re-entry) exposure in potato seed handling.
However, the meeting agreed that the German re-entry model could be used in this case. Using this model, the exposure was under 1% of the AOEL for the workers re-entering treated crops without any protective equipment (see addendum 5, December 2007).

Bystander exposure

The field study of Stevens and Davis (1981) was considered as an acceptable surrogate for the estimation of the bystander exposure, giving a presumably highly conservative estimate well below the AOEL (0.1 % of it). In addition to that the experts agreed that the exposure of the bystanders is expected to be lower than that of workers.

3. Residues

Flutolanil was discussed by the experts in residues in the PRAPeR meeting 25 (round 5, June 2007))

3.1. NATURE AND MAGNITUDE OF RESIDUES IN PLANT

3.1.1. PRIMARY CROPS

The metabolism of flutolanil has been investigated in potatoes, peanut and rice. In potatoes the study was conducted in accordance with the representative use (seed treatment). Studies in peanut and rice reflect the plant metabolism after foliar spray. The studies were all conducted with the active substance labelled in the aniline ring. As data show that the amide bridge between the 2 aromatic rings resists plant metabolism, it was agreed that the information provided was sufficient.

Foliar and seed treatments result in similar metabolic pathways. The main metabolic processes involve modification in the aniline ring either by hydroxylation to metabolite M2 or cleavage of the isopropyl moiety leading to metabolite M4. Conjugates of these 2 metabolites and unchanged parent compound form the major constituents of the residue in potato tubers. These metabolites are also major rat metabolites.

The residue definition for monitoring is restricted to the parent compound as it can be considered as a valid indicator for enforcement purposes. The expert meeting discussed the residue definition for risk assessment and agreed on the inclusion of metabolites M2 and M4 and their conjugates as they are considered, in the absence of any toxicological data, of the same level of toxicity as the parent compound, and expected to be present in consumer diet at levels similar to those of parent compound. A conversion factor from monitoring to risk assessment residue definition is also proposed. It was nevertheless recognized that the determination of such conversion factors on the single ground of a metabolism study should be restricted to cases where it clearly appears that consumer exposure is far below the toxicological reference values.

Supervised residue trials in accordance with the representative use are available for Northern Europe. They indicate that flutolanil residues are low, but exceeding the limit of quantification (LOQ) in several cases. The highest residue level for the supported application rate was 0.03 mg/kg. In some trials free M4 metabolite residues were also determined and were always below the LOQ. However this information is of limited value as the analysis method did not included conjugates of the metabolite.

For Southern Europe residue data were also submitted, combining a seed treatment and a soil application at planting. The highest residue found on mature tubers was 0.03 mg/kg. However it is uncertain whether the amount of active substance applied to seed potatoes is conform to the supported rate of application. Therefore although these data seem to have been generated under more critical conditions than the representative use, the expert meeting on residues concluded that further trials covering the use in Southern Europe should be provided.

Processing studies are not necessary as residues are low, and consumer exposure widely below the toxicological reference values.

3.1.2. SUCCEEDING AND ROTATIONAL CROPS

Confined rotational crop studies indicated that the metabolic pathway in rotational crops is similar to that observed in primary crops although an additional route consisting in oxidation of the isopropyl moiety to alcohol and acid derivatives was observed. Parent compound under free or conjugated form was the major component of the residue. The residue definitions proposed for primary crops would be evenly valid for rotational crops.

A field study has been conducted and no residues were found in wheat and rape cultivated as rotational crops.

No significant residues are expected in rotational crops. No label restriction related to rotational crops is needed.

3.2. NATURE AND MAGNITUDE OF RESIDUES IN LIVESTOCK

Livestock exposure resulting from the representative use of flutolanil is very low and livestock metabolism studies are not necessary. Residue definitions and MRLs in animal commodities are not proposed.

A lactating goat metabolism study was although submitted and considered by the expert meeting. Several deficiencies were identified and experts concluded that this study could not serve as appropriate basis for setting a residue definition in animal commodities, in case further uses would increase livestock exposure.

A metabolism study in laying hens was also submitted and confirmed that no residue are to be expected in edible tissues under practical conditions.

3.3. CONSUMER RISK ASSESSMENT

Chronic consumer exposure assessments have been conduced following current WHO methodologies using WHO diet for adult consumer, German diet for 4-6 year old girl as well as UK diet for adults, school children, toddlers and infants, including high consumption patterns. Residues in potatoes were considered to be at the level of the proposed MRL (0.05 mg/kg). No risk has been identified resulting from the supported representative use of flutolanil in potatoes. All calculated chronic exposures were below 1 % of the ADI. The RMS did not use any conversion factor in the exposure assessment. Nevertheless, using a factor of 3 for accounting potential presence of metabolite residues, the consumer exposure would stay below 2 % of the ADI.

Acute exposure assessments were not conducted as no ARfD has been established for flutolanil.

3.4. PROPOSED MRLS

Based on supervised residue trials it is proposed to set MRL for potatoes at 0.05 mg/kg.

4. Environmental fate and behaviour

Flutolanil was discussed at the PRAPeR experts' meeting for environmental fate and behaviour (PRAPeR 22) in May 2007.

Route of degradation of flutolanil under dark aerobic conditions at 20ºC or 25ºC was investigated with [aniline ring-U-^{14}C]labelled compound in two reliable studies with four European soils (20ºC, 100% FC) and one US soil (25ºC, 75%of the 1/3 bar FC). The five soils covered a range of pH (6.0-7.4), clay content (5.1-19.0) and organic carbon content (0.6-3.2%). The European soil samples were treated with an exaggerated dose, corresponding to a field application rate 15 times higher than the amount used as a seed treatment for potatoes prior planting (276 g a.s./ha).

The aerobic degradation of flutolanil resulted in formation of bound residues (max. 27.9% AR after 105 days) and to carbon dioxide (13.4% AR after 116 days). Any other metabolite did not exceed 5% of applied radioactivity. The majority of the bound radioactivity was recovered in humin and humic acid fractions or associated in fulvic acid fraction.

A degradation study under lower temperatures (10ºC) was conducted using Speyer soil having characteristics close to the one of the soils used in aerobic degradation study at 20ºC. Binding to soil appeared to be the first step of the degradation process, with the maximum amount of non-extractable radioactivity up to 37.7% AR after 365 days. Mineralization accounted for 11.2% AR at the end of the study.

Under anaerobic conditions (25ºC in the dark) mineralization to CO_2 was minimal (0.2% AR after 120 days) and no new metabolites were formed.

In the DAR a study on the potential for photolytic breakdown of labelled flutolanil at the soil surface was reported. However some deficiencies were identified for this experiment and therefore the validity of the study, together with a final report amendment summarized in addendum 2, was discussed in the PRAPeR meeting 22. The experts concluded that although the study should not be relied on, for the applied for intended use (potato seed treatment), the exposure of flutolanil to sunlight should be minimal under good agricultural practice and therefore the EU level assessment can be satisfactorily completed without any further experimental data. Nevertheless, the significant amount (16% AR) of unidentified material produced in the irradiated samples remained addressed. Therefore, a new photolysis study may be required by Member States if uses such as spray treatment, where photolysis may be a relevant route, were requested by a future applicant.

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

Degradation rate of flutolanil under aerobic conditions was investigated in the same studies used to establish the route of degradation in soil. Although DT_{50} values were not reached experimentally in any of the European soils after 105 days of incubation time, a good fit to the data was obtained. A re-evaluation of the kinetic modelling analysis of the degradation/dissipation data for flutolanil under both the laboratory and field conditions was submitted by the applicant a very short time before PRAPeR 22 meeting took place. Only a short summary of the re-evaluation concerning the results obtained in laboratory studies for modelling purpose was presented by RMS at the meeting of experts. The kinetic pathway was simple first order (SFO) kinetics with least squares optimisation. Calculated DT_{50} values were in the range 115-397 days at 20ºC and 110 days at 25ºC. Flutolanil degrades slowly in soil incubated at 10ºC (non linear 1st order DT_{50} = 301 days). After normalisation to FOCUS

reference conditions (20ºC and field capacity (-10kPa or pF2)) the geometric mean of the DT_{50} values calculated for flutolanil is 190 days. The experts agreed that this value is appropriate for FOCUS groundwater modelling. Flutolanil can be classified as high to very high persistent.

The DT_{50} values obtained in the anaerobic conditions studies were very high (4917 days and 6378 days) indicating extremely low degradation.

Soil dissipation of flutolanil under field conditions was assessed in 6 trials located in Northern Europe (northern and southern Germany, the Netherlands and the UK), four with treated potato and two direct soil spray application on to bare soil pre-emergence of potatoes. During the commenting period of the peer review process, concerns were raised on the residue level data for DT_{50}s calculations. Further details on the field trials were provided and evaluated in addendum 2 (dated 24.04.07). At the flutolanil treated potato trial sites, plastic tubes were inserted vertically in the ground and filled with soil. One treated seed potato was placed in each plastic tube. The whole 50 cm tube (with treated seed potato and soil) was extracted (with increments of about 0-20, 20-35 and 35-50) and used to analyse the residue levels above LOQ per layer. The meeting of experts discussed the overall experimental design and whether a reliable soil degradation rate can be assessed. The kinetic re-evaluation of the field dissipation data was not considered by RMS for the experts' meeting and therefore the field DT_{50} values reported in addendum 4 (October 2007) are not peer reviewed. The view of the experts was that as the study design of the treated seed potato trials represents the intended use applied for flutolanil, the derived DT_{50}s can be considered appropriate for PECsoil calculations (see section 4.1.3). However, no agreement could be reached on the suitability of the use of the field DT_{50} derived from the available field trials for FOCUS modelling.

In the DAR calculations on initial soil concentrations and plateau concentrations were performed by RMS assuming an application rate equivalent to 276 g a.s./ha, with a distribution in the top 20 cm of the soil profile and by using the available worst case DT_{50} value from field studies of 303 days. Since the original field DT_{50}s were not considered reliable by the experts of PRAPeR 22 and the new kinetic evaluation was not peer reviewed (see section 4.1.2), it was agreed that PECsoil calculations should be based on the worst case DT_{50} value of 412 days derived from laboratory studies as reported in the DAR. After the meeting the new PECsoil values were presented by the RMS (addendum 4, not peer reviewed) and EFSA is content the calculation procedure followed was correct.

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

In two laboratory adsorption/desorption studies on 9 soils and one river sediment (pH 4.8-8.0; organic matter 0.2-6.2%), $K_f$oc values varied from 457 to 1340 mL/g (mean 781 mL/g, median 641 mL/g) with corresponding 1/n values in the range 0.714-1.164 (mean 0.93). It should be noted that these statistics were obtained assuming that % organic matter = 2 x % organic carbon or % organic matter = 1.72 x % organic carbon, instead of using the agreed equation Koc = 1.724 x Kom (see explanatory notes in addendum 5 of December 2007).

There was no indication that adsorption of flutolanil was pH dependant based on the available information.

An aged batch adsorption/desorption study was performed to characterize the adsorption/desorption properties of aged residues of ^{14}C-flutolanil on four different soil types and one sediment. After 8 months flutolanil still accounted for 74% of the extracted radioactivity. The pattern of dissipation consisted of degradation to volatile residues (4.1% at the end of the study) and trace levels of extractable metabolites.

4.2. FATE AND BEHAVIOUR IN WATER

4.2.1. SURFACE WATER AND SEDIMENT

An aqueous hydrolysis study was conducted in the dark at 25ºC in aqueous buffer solutions at pH 5-9. Flutolanil was shown to be stable to hydrolysis at all relevant pH values.

In a photolysis study first order DT_{50} of flutolanil was estimated to be 277 days. No detectable degradation products were found. Since degradation in a photosensitized system did not occur as a result of photon absorption it was not possible to determine the quantum yield in these circumstances.

Based on the results of an OECD guideline ready biodegradability test, flutolanil is classified as "no readily biodegradable".

In two natural sediment water systems studied in the laboratory in the dark at 20ºC (6 cm water columns overlying 2 cm sediment) ^{14}C-flutolanil dissipated from the water by partitioning to sediment (max. 68.7% AR at 30d) with single first order DT_{50} of 33-53 days. These values for the whole systems were 90-244 days. Mineralization was low (3.7% AR and 5.2% AR) and non-extractable residues accounted for 15.1% AR and 26.3% AR at 105 days. Minor amounts (< 10% AR) of degradation products were detected in the whole systems.

Predicted environmental concentrations (PEC) in surface water systems due to contamination via drainage were calculated using FOCUS surface water Step 3. The simulations were performed using the drainage scenarios relevant for potatoes: scenarios D3, D4 and D6. Although the FOCUS working group recommended using the mean DT_{50} values in the exposure evaluation, the presented PEC calculations were conducted using the maximum DT_{50soil} value of 303 days from field dissipation studies. This input parameter was considered unacceptable by the experts (see section 4.1.2); however, as it can be considered conservative in comparison with the geometric mean of laboratory DT_{50}s (= 190.1 days) no recalculations were required.

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

In the original DAR, the potential for leaching was estimated using FOCUS PRZM model. Simulations were conducted assuming depth of soil incorporation of 15 cm and using as input parameter the mean DT_{50} value (= 237 days) obtained in field dissipation studies and not normalised to FOCUS reference conditions. New PECgw modelling simulations according to FOCUS PRZM and PEARL for all the relevant scenarios was performed before the experts meeting (addendum 2). The experts agreed on these PECgw values from simulations performed with the incorporation depth of 20 cm and a revised geometric mean (= 190.1 days) of normalised DT_{50} values obtained in the laboratory studies. The adsorption parameters (K_{foc} = 683 and 1/n = 0.896) were the arithmetic mean values of

results from laboratory batch-equilibrium studies with the exclusion of the results of sand soils because of the low organic matter content (see addendum 5 for further clarifications on the selection of the K_{foc} value for modelling purpose).

The 80th percentile annual average leachate concentrations at 1 meter depth following one application to potatoes in 2 year crop rotation were <0.1 µg/L for all scenarios in simulations with PRZM model. Simulations performed with PEARL model resulted in PECgw < 0.1 µg/L in all scenarios except for Piacenza (0.271 µg/L) and Okehampton (0.102 µg/L).

4.3. FATE AND BEHAVIOUR IN AIR

The vapour pressure of flutolanil (4.1 x 10^{-7} Pa at 20ºC) is low. Thus it is very probable that the substance will not evaporate in significant amounts. On the basis of Henry's law constant (1.65 x 10^{-5} Pa x m^3 x mol^{-1}) flutolanil has no tendency to volatilize.

The atmospheric half-life of flutolanil was calculated as 0.114 days when considering a day comprising 12 hours of sunlight and 0.057 days when considering a day comprising 24 hours of sunlight. Flutolanil is not expected to be carried in the gaseous phase over long distances or to accumulate in air.

5. Ecotoxicology

5.1. RISK TO TERRESTRIAL VERTEBRATES

The representative use evaluated for flutolanil is as a seed treatment for potatoes. No standard scenario is foreseen for this type of use in the Guidance Document for Birds and Mammals (SANCO/4145/2000). In the DAR the risk was calculated for an herbivorous and granivorous bird and mammal.

The risk to herbivorous birds and mammals was calculated by using the nominal tuber treatment rate of 92 mg a.s./kg seed potato instead of the standard RUD value for spray applications. Based on this assessment the risk to herbivorous birds and mammals can be considered as low except for the long term risk to birds. However the risk to herbivorous birds can still be considered as low based on the unpalatability of potato leaves to birds and mammals.

The model for a granivorous bird and mammal was used to calculate the risk for potato eating birds. The RMS considered this model as not suitable to assess the risk for potato eating birds and mammals.

EFSA recommended that the scenario for granivorous birds and mammals should be revised to take into account 'potato eating' birds and mammals. This was provided in addendum 1A (October 2006). For birds the Common Crane (*Grus grus*) was selected as relevant focal species to represent potatoes -eating birds. Conservative estimates of dietary intake rates and mean body weights were derived from literature and it is assumed that the estimated daily dietary intake represents the FIR. Badger (*Meles melse*) was used as relevant focal species for the mammals. Conservative estimates of dietary intake rates, diet and mean body weights were also derived from literature. The risk to birds and mammals can be considered low applying refined FIR and the concentration of 92 mg a.s./kg seed

potato in the assessment. Although this scenario is not adequately covered by guidance document SANCO/4145/2000, it was regarded as sufficient to address the risk to birds and mammals by RMS, EFSA and several MS.

As the log Pow exceeds 3, the risk from secondary poisoning to birds and mammals was assessed. Based on this assessment, the risk to earthworm- and fish-eating birds and mammals can be considered as low. The risk assessment was revised in addendum 4 (October 2007) due to recalculation of PECsoil following the fate expert meeting (see section 4.1.2). However, the risk to earthworm-eating birds and mammals can still be considered as low.

5.2. RISK TO AQUATIC ORGANISMS

The green algae *Selenastrum capricornutum* is the most sensitive aquatic organism on an acute time scale and the Fathead minnow (*Pimephales promelas*) on a chronic time scale.

The calculation of the risk to aquatic organisms was based on PECsw-values from FOCUS Step 3. Following the GAP, PECsw values were calculated for application of flutolanil once every two years. The risk was calculated more in particular for the scenario D4 stream, Skousbo as this was the scenario with the highest surface water contamination of flutolanil. Based on this assessment the risk to aquatic organisms can be considered as low for the representative use evaluated.

The original dossier of flutolanil did not include studies on the toxicity of the formulation to aquatic organisms. Because it was considered unlikely that the proposed product use as seed treatment for potatoes would lead to exposure of the aquatic environment. The applicant, however, submitted the algal growth inhibition test with *Pseudokirchneriella subcapitata* in April 2007. An assessment of the study was included in addendum 2 (April 2007), without changing the conclusion of the aquatic risk assessment.

Flutolanil was observed in concentrations above 10% in the sediment during the water-sediment study. Nevertheless no studies on sediment dwelling organisms are considered necessary as the NOEC for *Daphnia magna* exceeds 0.1 mg a.s./L (NOEC = 0.53 mg a.s./L).

No major metabolites were identified in surface water, sediment or in ground water.

A study on the potential for bioconcentration in fish is available as the LogPow exceeds 3. The resulting BCF equals 100 and the CT_{50} equals 0.46 days. Therefore the risk for bioconcentration in fish is considered to be low.

Flutolanil is not an herbicide, therefore no studies with higher aquatic plants are considered necessary.

5.3. RISK TO BEES

The acute and oral toxicity of flutolanil to bees was tested. The oral LC_{50} exceeds 208.7 µg/bee and the contact LC_{50} exceeds 200 µg/bee. It is not considered appropriate to calculate HQ values to assess the risk as these values are only applicable for spray applications. No direct exposure to bees is expected due to the use as a potato seed dressing. However as flutolanil shows systemic properties, the risk to bees needs to be assessed. It is stated in the DAR that potato plants are rarely attractive to bees. The EFSA is of the opinion that it should be kept in mind that incidents with high bee mortality were observed in the Netherlands in potatoes. In these cases the bees were attracted to the potato plants by honeydew. Nevertheless the risk to bees is considered to be low in this case based on the low toxicity observed in the laboratory.

5.4. RISK TO OTHER ARTHROPOD SPECIES

The effects of flutolanil on the two indicator species *Aphidius rhopalosiphi* and *Typhlodromus pyri* were tested in a laboratory study. A maximum effect of 2.5% on mortality was observed at 4.5 kg a.s./ha.

Furthermore, 3 ground dwelling species were tested. The predator beetles *Poecilus cupreus* and *Aleochara bilineata* and the spider *Poecilus* sp. A maximum effect of 6.7 % on mortality was observed at 4.5 kg a.s./ha for *P. cupreus* and *Poecilus* sp. A reduction of 2.2% and 42.7 % of the mean number of emerged beetles was observed at 0.6 and 4.5 kg a.s./ha respectively for *A. bilineata*. An extended laboratory study with this species is available. In this study the observed effect on beetle emergence was 20.3% at 4.5 kg a.s./ha and 21.9% at 11.2 kg a.s./ha.

The lead formulation was applied to glass plates or sprayed on the test substrate in the available studies. This does not correspond to the method of application as a tuber dressing. Nevertheless the risk to non-target arthropods is considered to be low as effects were far below 50% at dose rates far above the representative use rate of 276 g a.s./ha.

5.5. RISK TO EARTHWORMS

An acute toxicity study on earthworms with flutolanil is available. The LC_{50} was corrected for the high organic matter content in the test soil as the Log Pow exceeds 2. Based on this study the acute risk to earthworms can be considered as low for the representative use evaluated.

Also a long term study on earthworms was submitted due to the high persistence in soil (DT_{90} in the field > 1 year). Two chronic studies with the lead formulation EXP10066A were made available. In the first study a standard artificial soil was used. The artificial soil in the second study had a reduced organic matter content. Therefore no corrections for the high Log Pow were made. The NOEC from the second study, performed with the soil with reduced organic matter content, was slightly higher. Based on these studies the long term risk to earthworms can be considered as low for the representative use evaluated.

The risk assessment was revised in addendum 4 (October 2007) due to recalculation of PECsoil following the fate expert meeting (see section 4.1.2). However, the risk to earthworm can still be considered as low.

No major metabolites were identified in soil.

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

The soil DT_{90} in the field exceeds 1 year. Therefore immediately a litter bag study is triggered. Such a study is available as well as a study on the effects of EXP10066A on the reproduction of *Folsomia candida*.

The formulation EXP10066A was applied twice in the litter bag study. The first application was conducted at 15 kg a.s./ha. The second application was made at 11.3 kg a.s./ha with the litter bags on the soil surface. Significant reduction (22.6%-30%) of organic material decomposition was observed. The method of application and the used treatment rate do not reflect the representative use as a potato tuber dressing at 276 g a.s./ha. Therefore the RMS set a Level 4 data requirement for a clarification of the effects of flutolanil on soil litter degradation under more realistic exposure conditions. A new litterbag study was assessed in addendum 1A (October 2006). The study was conducted in Germany, using an acceptable application rate of 670.5 g flutolanil/ha, which was confirmed by chemical analyse. Based on the results obtained with an application rate of 2.4 times the intended dose, it was concluded that flutolanil 40SC will not cause long-term adverse impacts on organic matter decomposition under practical field conditions.

The risk of EXP10066A to *F. candida* is considered to be low for the representative use evaluated.

No major metabolites were identified in soil.

5.7. RISK TO SOIL NON-TARGET MICRO-ORGANISMS

A study on the effects of EXP10066A on soil micro-organisms is available. Effects on soil respiration and nitrogen mineralisation were below 25% after 42 days at 1392 g a.s./ha.. This exposure rate is higher than the PEC in soil from the representative use evaluated. The risk to soil micro-organisms can therefore be considered as low.

No major metabolites were identified in soil.

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

EXP10066A was tested on six plant species at a rate of 11.2 kg a.s./ha. No effects were observed on seedling emergence and plant growth. Therefore the NOEC was set at the highest tested concentration

of 11.2 kg a.s./ha. This far above the nominal application rate for the representative use evaluated. The risk to non-target plants is considered to be low.

5.9. RISK TO BIOLOGICAL METHODS OF SEWAGE TREATMENT

No study on the effects of flutolanil on biological methods of sewage treatment was originally submitted to the RMS. The study was requested during the review process and it was subsequently submitted to RMA in April 2007 and assessed in addendum 2 (October 2007). Based on the data with an EC50 above 1000 mg as/L no risk is expected for sewage sludge micro-organisms after seed potato treatment of flutolanil.

6. Residue definitions

Soil

Definitions for risk assessment: flutolanil

Definitions for monitoring: flutolanil

Water

Ground water

Definitions for exposure assessment: flutolanil

Definitions for monitoring: flutolanil

Surface water

Definitions for risk assessment: flutolanil

Definitions for monitoring: flutolanil

Air

Definitions for risk assessment: flutolanil

Definitions for monitoring: flutolanil

Food of plant origin

Definitions for risk assessment: sum of flutolanil, metabolite M2[5], metabolite M4[6] and their conjugates, expressed as flutolanil

Definitions for monitoring: flutolanil

Food of animal origin

Definitions for risk assessment: not required considering the low livestock exposure

Definitions for monitoring: not required considering the low livestock exposure

[5] M2: α,α,α-trifluoro-4'-hydroxy-3'-isopropoxy-o-toluanilide

[6] M4: α,α,α-trifluoro-3'-hydroxy-o-toluanilide

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

Soil

Compound (name and/or code)	**Persistence**	**Ecotoxicology**
flutolanil	High to very high persistence Single first order $DT_{50\ lab}$ = 119-412 d (20°C, pF 2)	No risk to soil living organisms.

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**
flutolanil	Low to medium mobility (Kf_{oc} = 457-1340 mL/g)	FOCUS PRZM 2.4.1: no in all 9 FOCUS scenarios FOCUS PEARL 3.3.3: yes in 2 out of 9 scenarios (0.271 µg/L in Piacenza scenario and 0.102 µg/L in Okehampton scenario)	Yes	Yes	Yes

Surface water and sediment

Compound (name and/or code)	Ecotoxicology
flutolanil	No risk to aquatic organisms.

Air

Compound (name and/or code)	Toxicology
flutolanil	low acute toxicity by inhalation (rat LC_{50}>5.98 mg/L).

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

- It should be addressed why the concentration of analytes in identically numbered batches is different in value and different impurities are present (relevant for all uses evaluated, data gap identified by meeting of experts May 2007; information has been provided and is evaluated in addendum 5 Vol. 4 but have not been peer reviewed refer to chapter 1).
- The high % RSD values for the impurity analysis needs to be addressed (relevant for all uses evaluated, data gap identified by meeting of experts May 2007; date of submission unknown refer to chapter 1).
- Shelflife study (relevant for all uses evaluated, data gap identified by meeting of experts May 2007; date of submission unknown refer to chapter 1).
- Cold temperature stability of the formulation (relevant for all uses evaluated, data gap identified by meeting of experts May 2007; date of submission unknown refer to chapter 1).
- Adherence and distribution on the seed potato (relevant for all uses evaluated, data gap identified by meeting of experts May 2007; data have been provided and are evaluated in addendum 5 Vol. 3 but have not been peer reviewed refer to chapter 1).
- Confirmatory method for soil (relevant for all uses evaluated, data gap identified by meeting of experts May 2007; data have been provided and are evaluated in addendum 5 Vol. 3 but have not been peer reviewed refer to chapter 1).
- A new kinetic assessment of the field dissipation studies was submitted by the applicant but not evaluated by RMS for the experts' meeting. The revised field DT_x are available (addendum 4, dated 05.10.2007) but not peer review (not relevant to finalise the EU level risk assessment; refer to point 4.1.2).
- Supervised residue trials in Southern Europe (relevant for the use on potatoes in Southern Europe; data gap identified by meeting of experts; submission date proposed by the notifier: end of 2010; refer to point 3.1).

CONCLUSIONS AND RECOMMENDATIONS

Overall conclusions

The conclusion was reached on the basis of the evaluation of the representative use as a fungicide tuber treatment prior to planting. Full details of the GAP can be found in the attached end points. The representative formulated product for the evaluation was "Moncut 40 SC", a suspension concentrate (SC).

Adequate methods are available to monitor all compounds given in the respective residue definition which is flutolanil only. However, there is a data gap for a confirmatory method for soil, it is noted that a confirmatory method is available and is evaluated in addendum 5 Vol. 3 but it has not been peer reviewed. Only single methods for the determination of residues are available however, it was also

shown that the German S19 method could be used for plant matrices, however no ILV data were provided for this method.
Sufficient analytical methods as well as methods and data relating to physical, chemical and technical properties are available to ensure that at least some quality control measurements of the plant protection product are possible.

During the mammalian toxicology studies, flutolanil was shown to be orally absorbed up to 70% and rapidly excreted. Its acute toxicity was low, it was not irritating and did not cause skin sensitization. In short term studies, the target organ was the liver in the different species. Flutolanil was considered to have no genotoxic potential, no carcinogenic properties, no teratogenic effects and no adverse effects on the reproductive parameters, and no specific neurotoxic properties. It was concluded that the metabolites M-4 and M-2, being the main rat metabolites, had the same toxicological profile than flutolanil. The **acceptable daily intake (ADI) is 0.09 mg/kg bw/day** based on the 2-year rat study, the **acceptable operator exposure level (AOEL) is 0.56 mg/kg bw/day** based on the 90-day dog study with correction for oral absorption (70%), and the acute reference dose was considered as not necessary. The dermal absorption values were 0.5% for the concentrate and 5% for the dilution.
The operator exposure was below the AOEL with the use of gloves when estimated with the models (UK, German, EUROPOEM). In addition, results of a field study showed that operator exposure is unlikely to be higher than the AOEL. In the same way, the worker and bystander exposure was expected to be lower than the AOEL.

Flutolanil plant metabolism has been investigated in potatoes after seed treatment as well as in peanuts and rice after foliar application. A similar metabolic pathway was observed in the 3 crops. Parent flutolanil is a valid indicator for monitoring residues in harvested plant commodities. Two metabolites and their conjugates contribute significantly to the global toxicological burden and need to be considered in the residue definition for risk assessment.
Supervised residue trials conducted in Northern Europe are available and support the setting of an MRL of 0.05 mg/kg in potatoes. The appropriateness of this MRL for Southern region should be consolidated by further field data.
Livestock exposure to flutolanil residues is low and the establishment of a residue definition and MRLs for animal commodities is not necessary.
Transfer of soil residues is limited and no residue above the LOQ in rotational crop is expected.
The consumer chronic exposure to flutolanil residues is below 2 % of the ADI.

The information submitted on the fate and behaviour in the environment is generally sufficient to enable the required environmental exposure concentrations to be estimated that are required for environmental risk assessment at EU level. For the representative field uses applied for, the potential for groundwater exposure by flutolanil above the drinking water limit of µg/L is low except for regions with geoclimatic conditions represented by Piacenza and Okehampton FOCUS groundwater scenarios (0.271 and 0.102 µg/L, respectively).

Since the representative use of flutolanil as seed treatment for potatoes is not foreseen as a standard scenario in the Guidance Document for Birds and Mammals, the common cane (*Grus grus*) and the badger (*Meles meles*) were assessed as alternative relevant focal species to represent potatoes-eating birds and mammals, respectively. The risk to birds and mammals can be considered low applying refined FIR and the concentration of 92 mg a.s./kg seed potato in the assessment. As for all other groups of non target organisms the ecotoxicological risk can also be considered as being low for the representative use evaluated.

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

- For the uses assessed, Member States must pay particular attention to the protection of groundwater under vulnerable situations in geoclimatic conditions represented by the Piacenza and Okehampton FOCUS groundwater scenarios.

Critical areas of concern

- The minimum purity of the active substance is not agreed nor is the specification for the impurities.

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

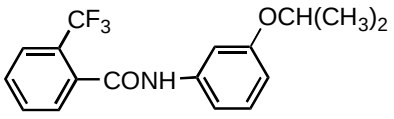
(Abbreviations used in this list are explained in appendix 2)

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

Active substance (ISO Common Name) ‡	Flutolanil
Function (e.g. fungicide)	Fungicide

Rapporteur Member State	Finland
Co-rapporteur Member State	-

Identity (Annex IIA, point 1)

Chemical name (IUPAC) ‡	α,α,α-trifluoro-3'-isopropoxy-o-toluanilide
Chemical name (CA) ‡	N-[3-(1-methylethoxy)phenyl]-2-(trifluoromethyl) benzamide
CIPAC No ‡	524
CAS No ‡	66332-96-5
EC No (EINECS or ELINCS) ‡	Not allocated
FAO Specification (including year of publication) ‡	Not allocated
Minimum purity of the active substance as manufactured ‡	open
Identity of relevant impurities (of toxicological, ecotoxicological and/or environmental concern) in the active substance as manufactured	none
Molecular formula ‡	$C_{17}H_{16}F_3NO_2$
Molecular mass ‡	323.3 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) ‡	103.9 to 105.2 °C (99.8 %)
Boiling point (state purity) ‡	Boiling start at 300 °C and is accompanied by decomposition. (99.8 %)
Temperature of decomposition (state purity)	Boiling start at 300 °C and is accompanied by decomposition. (99.8 %)
Appearance (state purity) ‡	White powder (99.8 %)
Vapour pressure (state temperature, state purity) ‡	4.1 · 10-7 Pa at 20 °C (99.8 %) 1.0 · 10-6 Pa at 25 °C (99.8 %)
Henry's law constant ‡	1.65 · 10-5 Pa · m3 · mole-1
Solubility in water (state temperature, state purity and pH) ‡	8.01 mg/l at 20 °C (99.0 %)
Solubility in organic solvents ‡ (state temperature, state purity)	Solubility at 20 °C in g/l (99.3 %) Acetone: 606 Acetonitrile: 334 Dichloromethane: 378 Ethyl acetate: 365 n-Hexane: 0.39 Methanol: 322 n-Octanol: 42 Toluene: 35
Surface tension ‡ (state concentration and temperature, state purity)	71.3 mN/m at 20 oC (90 % saturated solution) (99.8 %)
Partition co-efficient ‡ (state temperature, pH and purity)	log PO/W = 3.17 at 21 °C (unbuffered solution) (100 %)
Dissociation constant (state purity) ‡	Structure of flutolanil has no acidic or basic substituents which could dissociate.
UV/VIS absorption (max.) incl. ε ‡ (state purity, pH)	Neutral solution: λmax = 208.5 nm ε = 11709 l · mol-1 · cm-1 λmax = 292.0 nm ε = 33109 l · mol-1 · cm-1 (99.8 %)
Flammability ‡ (state purity)	Not flammable (99.3 %)
Explosive properties ‡ (state purity)	Not explosive (99.3 %)
Oxidising properties ‡ (state purity)	Not oxidising (99.3 %)

‡ 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 (c)	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)		
Seed treatment for potatoes prior to planting	N/S-EU	Moncut 40 SC	F	Black scurf and stem canker	SC	460 g/L	Canopied hydraulic or spinning disc equipment (with or without electrostatics	Apply to seed tubers	1 application per batch, where the treated potatoes are only planted in the same soil area once in a 24 month period		Not relevant	2.0 L spray solution per tonne	92 g as/tonne tubers which corresponds to 230 – 276 g as/ha. Calculated for a planting rate of 3 tonne/ha	Not relevant	

* 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)
(c) *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)	GC-FID, packed column
Impurities in technical as (analytical technique)	New analytical profile of batches is required with fully validated analytical methods.
Plant protection product (analytical technique)	HPLC, UV-detection at 240 nm, RP-18 column

Analytical methods for residues (Annex IIA, point 4.2)

Residue definitions for monitoring purposes

Food of plant origin		flutolanil
Food of animal origin		none
Soil		flutolanil
Water	surface	flutolanil
	drinking/ground	flutolanil
Air		flutolanil

Monitoring/Enforcement methods

Food/feed of plant origin (analytical technique and LOQ for methods for monitoring purposes)	GC-MSD, 0.01 mg/kg flutolanil (potatoes)
Food/feed of animal origin (analytical technique and LOQ for methods for monitoring purposes)	Not relevant
Soil (analytical technique and LOQ)	GC/ MSD, 5 µg/kg flutolanil confirmatory method open
Water (analytical technique and LOQ)	GC/TID, 0.1 µg/l flutolanil (drinking water) GC/TID, 1.0 µg/l flutolanil (surface water)
Air (analytical technique and LOQ)	HPLC/UV, 2.7 µg/m^3 flutolanil
Body fluids and tissues (analytical technique and LOQ)	Not relevant, flutolanil is not toxic or very 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) in mammals (Annex IIA, point 5.1)

Rate and extent of oral absorption ‡	70%; based on urinary excretion within 24h
Distribution ‡	Uniformly distributed
Potential for accumulation ‡	No evidence for accumulation
Rate and extent of excretion ‡	>95% excreted within 72 h via urine (70%) and faeces (26%)
Metabolism in animals ‡	Extensively metabolised; excreted as metabolites (mainly M-4) in urine and as unchanged flutolanil in faeces
Toxicologically relevant compounds ‡ (animals and plants)	Flutolanil and metabolites (M2 and M4)
Toxicologically relevant compounds ‡ (environment)	Flutolanil

Acute toxicity (Annex IIA, point 5.2)

Rat LD_{50} oral ‡	> 10,000 mg/kg bw	
Rat LD_{50} dermal ‡	> 5,000 mg/kg bw	
Rat LC_{50} inhalation ‡	> 5.98 mg/l air /4 h (whole body)	
Skin irritation ‡	Non-irritant	
Eye irritation ‡	Non-irritant	
Skin sensitisation ‡	Non-sensitizing (M&K)	

Short term toxicity (Annex IIA, point 5.3)

Target / critical effect ‡	Increased weight of liver (rat, dog) and thyroid/parathyroid (rat) and histopathological alterations in liver (dog)	
Relevant oral NOAEL ‡	299 mg/kg bw/d (90-d rat) 80 mg/kg bw/d (90-d dog) 680 mg/kg bw/d (90-d mouse)	
Relevant dermal NOAEL ‡	>1000 mg/kg bw/day (21-d rat)	
Relevant inhalation NOAEL ‡	No data available - not required	

Genotoxicity ‡ (Annex IIA, point 5.4)

No genotoxic potential	

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

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

Target/critical effect ‡	Histological changes in spleen (rat) Histological alterations in liver (male mouse) Clinical signs (emesis, salivation, excretion of soft faeces) (dog)	
Relevant NOAEL ‡	8.7 mg/kg bw/d (2-yr rat), 32 mg/kg bw/day (79-wk mouse), 50 mg/kg bw/d (2-yr dog)	
Carcinogenicity ‡	No carcinogenic potential	

Reproductive toxicity (Annex IIA, point 5.6)

Reproduction toxicity

Reproduction target / critical effect ‡	Parental: increased liver weight Reproduction and offspring: no effect up to the highest dose	
Relevant parental NOAEL ‡	157 mg/kg bw/day	
Relevant reproductive NOAEL ‡	1614 mg/kg bw/day	
Relevant offspring NOAEL ‡	1614 mg/kg bw/day	

Developmental toxicity

Developmental target / critical effect ‡	Maternal: no effect up to the highest dose (rat and rabbit) Foetal: no effect up to the highest dose (rat and rabbit)	
Relevant maternal NOAEL ‡	> 1000 mg/kg bw/d (rat and rabbit)	
Relevant developmental NOAEL ‡	>1000 mg/kg bw/d (rat and rabbit)	

Neurotoxicity (Annex IIA, point 5.7)

Acute neurotoxicity ‡	No data available - not required	
Repeated neurotoxicity ‡	No data available - not required	
Delayed neurotoxicity ‡	No data available - not required	

Other toxicological studies (Annex IIA, point 5.8)

Mechanism studies ‡	No data available - not required

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

Studies performed on metabolites or impurities ‡	No data available - not required

Medical data ‡ (Annex IIA, point 5.9)

No evidence of adverse effects to workers of manufacturing plants, agricultural workers and consumers

Summary (Annex IIA, point 5.10)

	Value	Study	Safety factor
ADI ‡	0.09 mg/kg bw/d	2-yr rat	100
AOEL ‡	0.56 mg/kg bw/d	90-d dog study	100*
ARfD ‡	Not allocated, not necessary		

*Corrected for oral absorption 70%

Dermal absorption ‡ (Annex IIIA, point 7.3)

SC formulation (461 g/L)	In vitro study with human skin : Concentrate: 0.5% Spray dilution (10%): 5%

Exposure scenarios (Annex IIIA, point 7.2)

Operator	The estimated exposure for the formulation containing 460 g/L flutolanil according to the EUROPOEM II, UK POEM and BBA –model (application rate 0.09 kg a.i./ton) showed that the exposure to flutolanil is lower than the AOEL proposed by the RMS in the DAR (up to 3% without PPE for the tractor application during planting). The exposure with spraying equipment mounted on a rolling conveyer was measured in a field study (required for the UK registration), showing an exposure level of 50% of the AOEL without PPE.
Workers	<1% of the AOEL without PPE (German re-entry data)
Bystanders	<0.1% of the AOEL (surrogate field study)

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

	RMS/peer review proposal
Substance (flutolanil)	No classification

‡ 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	Seed treatment : Potato (R) Foliar treatment : peanut (P/O) and rice (C).
Rotational crops	Oats (C), wheat (C), raddish (R), lettuce (L).
Metabolism in rotational crops similar to metabolism in primary crops?	Yes
Processed commodities	Study on the effect of processing not required, considering the low residue level in raw potatoes
Residue pattern in processed commodities similar to residue pattern in raw commodities?	Yes
Plant residue definition for monitoring	Flutolanil.
Plant residue definition for risk assessment	Sum of flutolanil, metabolites M2 and M4 and their conjugates, expressed as flutolanil
Conversion factor (monitoring to risk assessment)	3 (for potatoes)

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

Animals covered	Not required
Time needed to reach a plateau concentration in milk and eggs	Not required
Animal residue definition for monitoring	Not required
Animal residue definition for risk assessment	Not required
Conversion factor (monitoring to risk assessment)	Not required
Metabolism in rat and ruminant similar (yes/no)	Not required
Fat soluble residue: (yes/no)	Not required

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

No residues of flutolanil were found in wheat and rape cultivated as rotational crops under field conditions.

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

18 months for potato, wheat (grain and straw) and rape (grain)

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

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

	Ruminant:	Poultry:	Pig:
	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)	No	No	No
Potential for accumulation (yes/no):	No	No	No
Metabolism studies indicate potential level of residues ≥ 0.01 mg/kg in edible tissues (yes/no)	No	No	No
	Feeding studies (Specify the feeding rate in cattle and poultry studies considered as relevant) Residue levels in matrices : Mean (max) mg/kg		
Muscle	Not relevant	Not relevant	Not relevant
Liver	Not relevant	Not relevant	Not relevant
Kidney	Not relevant	Not relevant	Not relevant
Fat	Not relevant	Not relevant	Not relevant
Milk	Not relevant		
Eggs		Not relevant	

‡ 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 (c)	STMR (b)
Potato	North	2 x <0.01*, 2 x 0.014, <0.02, 0.22, 0.03, 0.035	*In two trials application rate exceeded about 27 % and 40 % the intended application rate. No residue levels above the LOQ were found.	0.05	0.035	0.017
Potato	South		Data gap.			

(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
(c) Highest residue

‡ 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	0.09 mg/kg
TMDI (% ADI) according to WHO European diet	Calculated with a conversion factor of 3 and using MRL 0.7 %
TMDI (% ADI) according to national (to be specified) diets	Calculated with a conversion factor of 3 and using MRL 0.3 % (The German diet, children from 2 to under 5 years old – 16.15 kg) PSD spreadsheet version 1.0 (www.pesticides.gov.uk).: <1% adult 2 % infants 2 % toddlers 1% children 4-6 yrs <1% 11-14 yrs <1% 15-18 yrs <1% vegetarian <1% elderly (residential and own home)
IEDI (WHO European Diet) (% ADI)	Not required
NEDI (specify diet) (% ADI)	Not required
Factors included in IEDI and NEDI	Not required
ARfD	Not required
IESTI (% ARfD)	Not required
NESTI (% ARfD) according to national (to be specified) large portion consumption data	Not required
Factors included in IESTI and NESTI	Not required

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	
Potato tuber/distribution in the edible/non edible portion /peel	1	Not required as residue level is low	Not relevant	Not calculated

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

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

Potato	0.05 mg/kg

‡ 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 ‡	- European soils: 2.9-9.9 % after 105 d (n7= 4)), 20 oC - US soil: 13.4 % after 116 d (27.5 % after 365 d) (n=1), 25 oC
Non-extractable residues after 100 days ‡	- European soils: 9.4-27.9 % after 105 d (n=4), 20 oC - US soil: 15.9 % after 116 d (26.7 % after 365 d) (n=1), 25 oC
Metabolites requiring further consideration ‡ - name and/or code, % of applied (range and maximum)	No (the only metabolite appearing over 5 % was CO2)

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

Anaerobic degradation ‡

Mineralization after 100 days	0.2 % / 120 d (0.4 % / 365 d) (n=1) Sterile conditions: no data available
Non-extractable residues after 100 days	4.6 % / 120 d (7.4 % / 365 d) (n=1)
Metabolites that may require further consideration for risk assessment - name and/or code, % of applied (range and maximum)	No (after 365 days total amount of flutolanil 86 %)

Soil photolysis ‡

Metabolites that may require further consideration for risk assessment - name and/or code, % of applied (range and maximum)	The study is not relied upon (PRAPeR 22, May 2007), but it is not required for the representative use evaluated (seed treatment for potatoes prior planting)

[7] n corresponds to the number of soils.

‡ 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 ‡

Parent	Aerobic conditions						
Soil type	Org. Carbon[2]	pH	t. °C / % MWHC	DT_{50} /DT_{90} (d)	DT_{50} (d) 20 °C pF2/10kPa	St. (r^2)	Method of calculation
Loamy sand	2.3	6.0 (KCl)	20 °C/100 % FC	115/382[3]	115	1.8	SFO
Sandy loam	2.4	7.1 (KCl)	20 °C/100 % FC	380/1262[3]	380	1.1	SFO
Loam	1.0	7.2 (KCl)	20 °C/100 % FC	151/501[3]	151	0.9	SFO
Sand	0.6	7.4 (KCl)	20 °C/100 % FC	397/1318[3]	397	2.1	SFO
Sandy loam	3.2	7.4[1]	25 °C/75 % FC	110/365[3]	133	4.5	SFO
Loamy sand	2.2	5.7 ($CaCl_2$)	10 °C/40 % MWH	295/979[3]	135	1.7	SFO
Geometric mean/median					190/143 (n = 6)		SFO

1 = based on average determinations on soil samples taken from the same location five years before the test started, no information on the measurement method
2 = calculated by the RMS
3 = calculated by the RMS by the equation DT90 = 3.32 x DT50

No metabolites requiring further consideration

Field studies ‡ **field studies available, revised DT50 values not peer reviewed.**

pH dependence ‡ (yes / no) (if yes type of dependence)	No
Soil accumulation and plateau concentration ‡	No field accumulation studies The plateau concentration (0.1301 mg/kg) was calculated to be achieved after 16 years (a 2-year rotation, 276 g as/ha) [1]

1 = based on the worst case laboratory DT_{50} value of 412 days, as calculated in the original DAR; agreed by PRAPeR 22 as worst case

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

Laboratory studies ‡

Parent	Anaerobic conditions						
Soil type	Org. Matter (%)[3]	pH	t. °C / % MWHC	DT_{50} / DT_{90} (d)	DT_{50} (d) 20 °C pF2/10kPa	St. (r^2)	Method of calculation
Sandy loam	1.8	6.1	25 °/*	4917**/- 6378***/-	N.a.****	N.a. ****	****
Geometric mean/median							

* = Water saturated soil

** = Test concentration 5 mg/kg

*** = Test concentration 50 mg/kg

**** = The first order decline curve was calculated based on the concentrations of flutolanil as a percentage of recovered radioactivity. However, very little degradation was detected over the course of the study (after 365 days total amount of flutolanil 86 %) and the substance can be classified as stable in anaerobic conditions.

No metabolites requiring further consideration

Soil adsorption/desorption (Annex IIA, point 7.1.2)

Parent ‡							
Soil Type	OC %	Soil pH	Kd (mL/g)	Koc (mL/g)	Kf (mL/g)	Kfoc (mL/g)	1/n
Sand	0.2	6.5	-	-	1.34	1340[1,3]	1.164
Clay	2.4	6.7	-	-	10.6	883[1]	0.909
Mississippi sediment	3.9	7.5	-	-	10.3	528[1]	0.943
Clay loam	4.9	7.8	-	-	16.0	653[1]	0.943
Sandy loam	6.2	6.1	-	-	35.5	1150[1]	0.980
Sand	0.3	8.0 (w)	-	-	0.996	571[2,3]	0.962
Loam	0.8	8.0 (w)	-	-	2.76	594[2]	0.855
Clay loam	4.9	7.4 (w)	-	-	13.0	457[2]	0.714
Clay loam	1.1	6.2 (w)	-	-	4.02	628[2]	0.901
Loamy sand	2.7	4.8 (w)	-	-	15.8	1005[2]	0.926
Arithmetic mean/median						781[4]/64[1]/735	0.93/0.935 /0.924
pH dependence, Yes or No			No				

1 = assuming organic matter (%) = 2.0 x organic carbon (%)

2 = assuming organic matter (%)= 1.72 x organic carbon (%)

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

3 = these values were omitted in PECgw modelling due to their low organic matter content

4 = the arithmetic mean value used in PECgw modelling (683, n = 8) was calculated assuming organic matter = 1.724 x organic carbon

No metabolites requiring further consideration

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

Column leaching ‡	Elution (mm): 200 mm Time period (d): 2 d
	Leachate: less than 0.24 % total residues/radioactivity in leachate The radioactivity of soil column was not analyzed.
Aged residues leaching ‡	After 8 months of aging flutolanil still accounted for 84 % of the extracted radioactivity. Thus it was considered inappropriate to continue the experiment and the study was found unnecessary.
Lysimeter/ field leaching studies ‡	Not considered necessary

PEC (soil) (Annex IIIA, point 9.1.3)

Parent Method of calculation	DT_{50} (d): 412 days (worst case value from laboratory studies) Kinetics: 1st order
Application data	Crop: potato Depth of soil layer: 20 cm Soil bulk density: 1.5g/cm^3 % plant interception: Pre-emergence therefore no crop interception Number of applications:1 Application rate(s): 276 g as/ha (a potato seed planting rate 3000 kg/ha) Application scenario: treated potatoes grown once every 2 years

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

$PEC_{(s)}$[1] (mg/kg)		Single application Actual	Single application Time weighted average	Multiple application Actual	Multiple application Time weighted average
Initial		0.1301[2]		Not applicable. As the product is a seed treatment it is only applied once	
Short term	24h	0.1299	0.1300		
	2d	0.1297	0.1299		
	4d	0.1292	0.1297		
Long term	7d	0.1286	0.1293		
	28d	0.1241	0.1271		
	50d	0.1196	0.1248		
	100d	0.1099	0.1197		
Plateau concentration		0.1301 mg/kg after 16 yr (a 2-year crop rotation)			

1 = Maximum PEC(s) values, occurring 16 years after the first application.

2 = Application 276 g as/ha results in a PECs,initial of 0.092 mg/kg

No metabolites requiring further consideration

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

Hydrolytic degradation of the active substance and metabolites > 10 % ‡	Stable to hydrolysis (pH 5-9: at the end of a 30-day study recovery of applied radioactivity 103-108 %, flutolanil accounted for 98.3-99.5 %, no hydrolysis products were observed)
Photolytic degradation of active substance and metabolites above 10 % ‡	DT50: 277 d (SFO, r2 = 0.812) No relevant metabolites Xenon arc lamp, 30 d
Quantum yield of direct phototransformation in water at Σ > 290 nm	N.a.
Readily biodegradable ‡ (yes/no)	No (the change of BOD/28 days was 0 %)

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

Degradation in water / sediment

Parent	Distribution (max in water 96.8-97.8% after 0.25 d. Max. Sed 34.0-68.7% after 30 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
Pond, NL	8.3[1]-7.0[2]	7.3	20	90-299	0.987	53-176	0.878	n.a.	n.a.	SFO
				n.a.	n.a.	25-274	0.984	n.a.	n.a.	SQRT 1. order
Ditch, NL	7.2[1]-6.5[2]	6.7	20	244-811	0.956	33-110	0.623	n.a.	n.a.	SFO
				543-5992	0.952	n.a.	n.a.	n.a.	n.a.	SQRT 1. order
				n.a.	n.a.	3.4-92	0.911	n.a.	n.a.	SQRT 1.5 order
Geometric mean/median				148-492 / 167-555 (n=2)		42-139 / 43-143 (n=2)				SFO

1 = before study start
2 = study end

No metabolites requiring further consideration

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 (end of the study)
Pond, NL	8.3[1]-7.0[2]	7.3	5.2 % after 105 d	26.3 % after 105 d
Ditch, NL	7.2[1]-6.5[2]	6.7	3.7 % after 105 d	15.1 % after 105 d

1 = before study start
2 = study end

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

Parent Parameters used in FOCUSsw step 1 and 2	PECsw values were not calculated using FOCUS step 1 and 2
Parameters used in FOCUSsw step 3 (if performed)	Version control no.'s of FOCUS software: FOCUS-MACRO 4.4.2 (running MACRO version 4.3b) to calculate concentrations entering water bodies via drainage, FOCUS-TOXCWA 1.1.1 (running TOXSWA

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

	version 2.1.1F1) to calculate the fate in the water Molecular weight (g/mol): 323.3 Water solubility (mg/L): 8.01 Vapour pressure (Pa): 4.1 x 10^{-7} Koc (L/kg): 780.9 (arithmetic mean of 10 studies) 1/n: 0.93 (arithmetic mean of 10 studies) DT50 soil (d): 303 (max. DT50 from field dissipation studies) [1] DT50 sediment (d): 543 (max. DT50 for whole water/sediment system) DT50 water (d): 543 (max. DT50 for whole water/sediment system)
Application rate	Crop: potatoes Crop interception: 0 (seed treatment) Number of applications:1 Interval: treated potatoes grown once every 2 years Application rate: 276 g as/ha (a potato seed planting rate 3000 kg/ha) Application window: 10-40 d prior to emergence (model automatically selects an application date) Main routes of entry: drainage

1 = This input parameter was considered unacceptable by PRAPeR 22. However, it was considered conservative in comparison with the geometric mean of laboratory DT_{50}s (190 days) and thus no recalculations are required.

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

FOCUS STEP 3 Scenario	Water body	Day after overall maximum	PEC_{SW} (µg/L)		PEC_{SED} (µg/kg)	
			Actual	TWA	Actual	TWA
D3, Vredepeel, NL - application date 05/04 (day 95) - emergence date 10/05	Ditch	0 h	<0.001 (28 Jan)[1]		0.001 (1 Apr)[1]	
		24 h	<0.001	<0.001	0.001	0.001
		2 d	<0.001	<0.001	0.001	0.001
		4 d	<0.001	<0.001	0.001	0.001
		7 d	<0.001	<0.001	0.001	0.001
		14 d	<0.001	<0.001	0.001	0.001
		21d	<0.001	<0.001	0.001	0.001
		28 d	<0.001	<0.001	0.001	0.001
		42 d	<0.001	<0.001	0.001	0.001
D4, Skousbo, DK - application date 18/04 (day 108) - emergence date 22/05	Pond	0 h	0.027 (28 Jan)[1]		0.256 (1 May)[1]	
		24 h	0.027	0.027	#[2]	0.256
		2 d	0.026	0.027	#[2]	0.256[3]
		4 d	0.026	0.026	#[2]	0.256[3]
		7 d	0.026	0.026	#[2]	0.256[3]
		14 d	0.025	0.026	#[2]	0.256[3]
		21 d	0.024	0.026	#[2]	0.256[3]
		28 d	0.023	0.025	#[2]	0.255[3]
		42 d	0.021	0.025	#[2]	0.254[3]
D4, Skousbo, DK - application date 18/04 (day 108) - emergence date 22/05	Stream	0 h	0.060 (9 Dec)[1]		0.096 (27 Jan)	
		24 h	0.012	0.034	0.096	0.096
		2 d	0.008	0.028	0.095	0.096
		4 d	0.008	0.022	0.094	0.096
		7 d	0.012	0.018	0.092	0.095
		14 d	0.014	0.015	0.085	0.094
		21 d	0.010	0.015	0.079	0.091
		28 d	0.006	0.014	0.073	0.089
		42 d	0.014	0.011	0.065	0.084

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

FOCUS STEP 3 Scenario	Water body	Day after overall maximum	PEC_{SW} (µg/L)		PEC_{SED} (µg/kg)	
			Actual	TWA	Actual	TWA
D6 (1), Thiva, GR - application date 05/03 (day 64) - emergence date 10/04	Ditch	0 h	0.027 (19 Jan)[1]		0.042 (20 Jan)[1]	
		24 h	0.010	0.019	0.042	0.042
		2 d	0.006	0.014	0.041	0.042
		4 d	0.004	0.011	0.040	0.042
		7 d	0.003	0.009	0.038	0.041
		14 d	0.001	0.006	0.033	0.039
		21 d	0.001	0.005	0.031	0.037
		28 d	0.001	0.005	0.032	0.036
		42 d	0.002	0.004	0.036	0.036
D6 (2), Thiva, GR - application date 29/06 (day 180) - emergence date 05/08	Ditch	0 h	0.037 (19 Jan)[1]		0.056 (20 Jan)[1]	
		24 h	0.013	0.026	0.056	0.056
		2 d	0.008	0.019	0.055	0.056
		4 d	0.006	0.015	0.053	0.055
		7 d	0.004	0.012	0.050	0.054
		14 d	0.001	0.008	0.044	0.051
		21 d	0.001	0.006	0.041	0.049
		28 d	0.001	0.006	0.041	0.048
		42 d	0.003	0.006	0.048	0.048

1 = in parenthesis the date when the global maximum value was reached
2 = the simulation period was not long enough to calculate PECsed
3 = The TWACsed values were generated by the model but should not be used in risk assessment as actual PECsed values could not be calculated

No metabolites requiring further consideration

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

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 modelling, values used – Model(s) used: FOCUS PRZM V2.4.1 and FOCUS PEARL V3.3.3: Scenarios: Chateaudun, Hamburg, Jokioinen, Kremsmünster, Okehampton, Piacenza, Porto, Sevilla, Thiva Crop: Potatoes $DT_{50, parent}$: 190 d (geometric mean, n=6, ModelMaker optimization and normalisation to pF2, 20 °C with Q10 of 2.2) $K_{foc, parent}$: 683 L/kg (arithmetic mean, n=8, the sand soils were omitted from the calculations due their low organic matter content) $^1/_n$= 0.896 Metabolites: No metabolites requiring further consideration Lysimeter or field leaching studies were not carried out.
Application rate	Application rate: 276 g/ha (potato seed planting rate 3000 kg/ha, incorporation depth 20 cm) No. of applications: 1 application/2 years (a 2-year crop rotation period) Time of application: the date of planting for PEARL, 15 days pre-emergence for PRZM (January-May)

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

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

	Scenario	Parent (µg/L)	Metabolite (µg/L)[1]		
			1	2	3
PRZM 2.4.1/potatoes	Chateaudun	<0.001	-	-	-
	Hamburg	0.011	-	-	-
	Jokioinen	<0.001	-	-	-
	Kremsmunster	<0.001	-	-	-
	Okehampton	0.047	-	-	-
	Piacenza	0.081	-	-	-
	Porto	<0.001	-	-	-
	Sevilla	<0.001	-	-	-
	Thiva	<0.001	-	-	-

	Scenario	Parent (µg/L)	Metabolite (µg/L)[1]		
			1	2	3
PEARL 3.3.3/potatoes	Chateaudun	0.033	-	-	-
	Hamburg	0.046	-	-	-
	Jokioinen	0.004	-	-	-
	Kremsmunster	0.054	-	-	-
	Okehampton	0.102	-	-	-
	Piacenza	0.271	-	-	-
	Porto	<0.001	-	-	-
	Sevilla	<0.001	-	-	-
	Thiva	0.013	-	-	-

1= no metabolites requiring further consideration

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

Parent	1st year	2nd year	3rd year
No data available, not required.			

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

Direct photolysis in air ‡	No data available (flutolanil has a low vapour pressure, 4.7×10^{-8}, and as such its concentration in the atmosphere is likely to be negligible)
Quantum yield of direct phototransformation	No data available (flutolanil is not susceptible to direct

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

	phototransformation and therefore it is not possible to determine the quantum yield)
Photochemical oxidative degradation in air ‡	Half-life: 0.114 days (a day:12 hours of sunlight), 0.057 days (a day: 24 hours of sunlight) (The concentration of OH radicals 9.5 x 10^5) (These estimations were carried out with respect to the OH-radical reaction, only.)
Volatilisation ‡	Not available
Metabolites	None

PEC (air)

Method of calculation	Not available

$PEC_{(a)}$

Maximum concentration	Not applicable

Residues requiring further assessment

Environmental occurring residues requiring further assessment by other disciplines (toxicology and ecotoxicology) and or requiring consideration for groundwater exposure.	Soil: flutolanil Surface Water: flutolanil Sediment: flutolanil Ground water: flutolanil Air: flutolanil

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

Soil (indicate location and type of study)	No data provided - none requested
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, 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)

Species	Test substance	Time scale	End point (mg/kg bw/day)	End point (mg/kg feed)
Birds ‡				
Bobwhite quail	a.s.	Acute	LD_{50} > 2000	
Mallard duck	a.s.	Acute	LD_{50} > 2000	
	Preparation	Acute	-	-
	Metabolite 1	Acute	-	-
Bobwhite quail	a.s.	Short-term	LD_{50} > 961	LC_{50} > 5243
Mallard duck	a.s.	Short-term	LD_{50} = 1249	LC_{50} > 5243
Bobwhite quail	a.s.	Long-term	NOEL = 247	NOEC = 1920
Mallard duck	a.s.	Long-term	NOEL = 267	NOEC = 1920
Mammals ‡				
Rat	a.s.	Acute	LD_{50} > 10000	
	Preparation	Acute	-	
	Metabolite 1	Acute	-	
Rat	a.s.	Long-term	NOEL = 157	NOEC = 2000
Additional higher tier studies ‡ Not required				

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

Potato with an application rate of 276 g/ha

Indicator species/Category[2]	Time scale	ETE	TER[1]	Annex VI Trigger[3]
Tier 1 (Birds)				
Granivorous bird	Acute	35.0	> 57	10
Herbivorous bird	Acute	69.9	> 29	10
Potato eating bird	Acute	6.5	> 308	10
Granivorous bird	Short-term	35.0	> 27	10
Herbivorous bird	Short-term	69.9	> 13	10
Potato eating bird	Short-term	6.5	> 148	10
Granivorous bird	Long-term	35.0	7.1	5

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

Indicator species/Category[2]	Time scale	ETE	TER[1]	Annex VI Trigger[3]
Herbivorous bird	Long-term	69.9	3.5	5
Potato eating bird	Long-term	6.5	38	5
Earthworm eating bird	Long-term	0.214	1004	5
Fish eating bird	Long-term	0.0005	494000	5
Higher tier refinement (Birds) Not necessary				
Tier 1 (Mammals)				
Granivorous mammal	Acute	21.2	> 473	10
Herbivorous mammal	Acute	25.8	> 388	10
Potato eating mammal	Acute	24.5	> 41	10
Granivorous mammal	Long-term	21.2	7.4	5
Herbivorous mammal	Long-term	25.8	6.1	5
Potato eating mammal	Long-term	24.5	6.4	5
Earthworm eating mammal	Long-term	0.270	505	5
Fish eating mammal	Long-term	0.0003	523333	5
Higher tier refinement (Mammals) Not necessary				
	Acute			10
	Long-term			5

1 in higher tier refinement provide brief details of any refinements used (e.g., residues, PT, PD or AV)
2 for cereals indicate if it is early or late crop stage
3 If the Annex VI Trigger value has been adjusted during the risk assessment of the active substance (e.g. many single species data), it should appear in this column.

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[1] (mg/L)
Laboratory tests ‡				
Fish				
Indicate species.	*a.s.*	*96 hr (flow-through)*	*Mortality, EC_{50}*	
Salmo gairdneri	*Technical flutolanil*	*96 h (static)*	*Mortality, LC_{50}*	*5.4 (mm)*
Lepomis macrochirus		*96 h (static)*	*Mortality LC_{50}*	*> 5.4 (mm)*
Pimephales promelas		*96 h (static)*	*Mortality LC_{50}*	*4.8 (mm)*

‡ 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[1] (mg/L)
Pimephales promelas		*30 d (flow-through)*	*Growth NOEC*	*0.233 (mm)*
Aquatic invertebrate				
Daphnia magna	*Technical flutolanil*	*48 hr (static)*	*Mortality EC_{50}*	*> 6.8 (mm)*
Daphnia magna		*21 d (semistatic)*	*Reproduction NOEC*	*0.53 (mm)*
Sediment dwelling organisms				
Not conducted, not required				
Algae				
Selenastrum capricornuntum	*Technical flutolanil*	*72 h (static)*	*Biomass: EbC_{50}* *Growth rate: ErC_{50}* *NOEC*	*0.97 (mm)* *>3.2 (mm)* *0.18*
Pseudokirchneriella subcapitata (formerly Selenastrum capricornuntum)	*Flutolanil 40SC*	*72 h (static)*	*Growth rate: ErC_{50}* *NOEC*	*12.3 (a.s., nom)* *<0.41 (a.s., nom)*
Higher plant				
Not conducted, not required				
Microcosm or mesocosm tests				
Not required				

1 indicate whether based on nominal (nom) or mean measured concentrations (mm). In the case of preparations indicate whether end points are presented as units of preparation or a.s.

No studies on the toxicity of the product to other aquatic organisms than algae, no studies on the toxicity of metabolites to aquatic organisms.

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

FOCUS Step1 PEC_{sw} values were not calculated using FOCUS step 1 and 2

FOCUS Step 2 PEC_{sw} values were not calculated using FOCUS step 1 and 2

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

Refined aquatic risk assessment using higher tier FOCUS modelling.

FOCUS Step 3

Potato with an application rate of 276 g/ha

Test substance	Scenario[1]	Water body type[2]	Test organism[3]	Time scale	Toxicity end point (mg/L)	PEC[4]	TER	Annex VI trigger[5]
Technical flutolanil	D4, Skousbo	Stream	Fathead minnow	acute	4.8	0.060 µg/L, max. PECsw	80000	100
			Fathead minnow	chronic	0.233		3883	10
			Daphnia magna	acute	>6.8		>113333	100
			Daphnia magna	chronic	0.53		8833	10
			Selenastrum capricornuntum	72 h	0.97		16167	10

1 drainage (D1-D6) and run-off (R1-R4)
2 ditch/stream/pond
3 include critical groups which fail at Step 2.
4 indicate whether PECsw, or PECsed and whether maximum or twa values used
5 If the Annex VI Trigger value has been adjusted during the risk assessment of the active substance, it should appear in this column. E.g. if it is agreed during the risk assessment of mesocosm, that a Trigger value of 5 is required, it should appear as a minimum requirement to MS in relation to product approval.

FOCUS Step 4 PECsw values were not calculated using FOCUS step 4

Bioconcentration				
	Active substance	Metab.[2] 1	Metab. 2	Metab. 3
logPO/W	3.17	-	-	-
Bioconcentration factor (BCF)[1] ‡	100*	-	-	-
Annex VI Trigger for the bioconcentration factor	100 (for not readily biodegradable substances)	-	-	-
Clearance time (days) (CT_{50})	0.46 d	-	-	-
(CT_{90})	-	-	-	-
Level and nature of residues (%) in organisms after the 14 day depuration phase	None detected	-	-	-

1 only required if log PO/W >3.
2 no studies on metabolites, not required
* based on ^{14}C-flutolanil

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

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. ‡	> 208.7	> 200
Preparation[1]	-	-
Metabolite 1	-	-
Field or semi-field tests		
No data is submitted nor required, because the laboratory toxicity of flutolanil to honey bees is low and no risk is anticipated.		

1 No studies on the effects of the product EX10066 or metabolites on honey bees, not required

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

Potato with an application rate of 276 g/ha

Test substance	Route	Hazard quotient	Annex VI Trigger
a.s.	Contact	Not applicable	50
a.s.	oral	Not applicable	50
Preparation[1]	Contact	-	50
Preparation	oral	-	50

1 No studies on the effects of the product EX10066 on honey bees, not required

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

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

Laboratory tests with standard sensitive species

The tests were performed using two dose rates (according to ESCORT 1). Thus the results could not be used to derive the LR_{50} or HQ values. Besides, HQ approach is validated for spray application, not seed treatment.

Species	Test Substance	End point	Effect (LR_{50} g/ha[1])
Typhlodromus pyri ‡		Mortality	-
Aphidius rhopalosiphi ‡		Mortality	-

[1] for preparations indicate whether end point is expressed in units of a.s. or preparation

Potato with an application rate of 276 g/ha

Test substance	Species	Effect (LR_{50} g/ha)	HQ in-field	HQ off-field[1]	Trigger
	Typhlodromus pyri	-	-	-	2
	Aphidius rhopalosiphi	-	-	-	2

[1] indicate distance assumed to calculate the drift rate

Further laboratory and extended laboratory studies ‡

Species	Life stage	Test substance, substrate and duration	Dose (g/ha)	End point	% effect[1]	Trigger value
Aphidius Rhopalosiphi	Adult females, < 48 h	EXP10066A (464 g/L), Glass plate	450 (initial residues)	Mortality Reproduction	2.5 0	50 %
Aphidius Rhopalosiphi	Adult females, < 48 h	EXP10066A (464 g/L), Glass plate	4500 (initial residues)	Mortality Reproduction	2.5 -31	50 %
Typhlodromus pyri	Protonymph to adult	EXP10066A (464 g/L), Glass plate	450 (initial residues)	Mortality Reproduction	-2.1 -6	50 %
Typhlodromus pyri	Protonymph to adult	EXP10066A (464 g/L), Glass plate	4500 (initial residues)	Mortality Reproduction	1.1 -5	50 %

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

Species	Life stage	Test substance, substrate and duration	Dose (g/ha)	End point	% effect[1]	Trigger value
Poecilus cupreus	Adult (approx. 6 week old)	EXP10066A (464 g/L), Quartz sand	450 4500 (initial residues)	Mortality	0 6.7	50 %
Pardosa sp.		EXP10066A (464 g/L), Quartz sand	450 4500 (initial residues)	Mortality	0 6.7	50 %
Aleochara bilineata	Adult (1-3 days old)	EXP10066A (454 g/L), Quartz sand	600 4500	Reproduction	2.2 42.7	50 %
Aleochara bilineata	Adult (1-4 days old)	EXP10066A (458 g/L), (natural soil)	4500 7800 11200	Reproduction	20.3 15.2 21.9	50 %

[1] positive percentages relate to adverse effects, negative result indicate smaller mortality or higher reproduction when compared to controls

Field or semi-field tests
No data submitted nor required

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	$LC_{50, corr}$ >500 g a.s./kg d.w.soil (mg a.s/ha)
	a.s. ‡	Chronic 8 weeks	-
	Preparation	Acute	-
	EXP10066A EXP10066A (mixed in soil with reduced organic matter)	Chronic 8 weeks Chronic 8 weeks	NOEC[1] = 12.9 mg a.s./kg soil NOEC[1] = 38.0 mg a.s./kg soil
	Metabolite 1[2]	Acute	-

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

Test organism	Test substance	Time scale	End point
	Metabolite 1[2]	Chronic	-
Other soil macro-organisms			
Soil mite	a.s. ‡		-
	Preparation		-
	Metabolite 1[2]		-
Collembola			
	a.s. ‡	-	-
	EXP10066A	Chronic 28 days	NOECcorr = 18.8 mg a.s./kg d.w.soil
	Metabolite 1[2]		
Soil micro-organisms			
Nitrogen mineralisation	a.s. ‡		-
	EXP10066A		-0.71 % effect at 1.35 kg as/ha after 42 days (5 x intended use)
	Metabolite 1[2]		
Carbon mineralisation	a.s. ‡		-
	EXP10066A		-6.5 % effect at 1.35 kg as/ha after 28 days (5 x intended use)
	Metabolite 1[2]		
Field studies Significant reduction (22.6-30%) of organic material decomposition was observed by EXP 10066 treatment after the application on soil at 15-kg a.s./ha followed by on Litter-bag at 11.3 kg/ha. Comparing the application rates by seed tuber treatment at 276 g a.s./ha, however, the rates are more than 50 times higher. In the litter bag test conducted with an application rate of 670 g a.s./ha (plateau concentration plus maximum application rate) the decomposition in the test group was 88.4-102.3 % of the control. However, decomposition relative to the control was approximately 94 % at 162 days after exposure and at subsequent assessments (test period 616 days).			

[1] Because logKow of flutolanil is 3.17 the NOEC should be divided by 2. However, based on the effects obtained in the sublethal study the toxicity of flutolanil is smaller in soil with reduced organic matter, therefore the correction to the NOEC have not been done (even if the correction had been performed, there would be no risk).

[2] no studies on the effects of metabolites on soil organisms (not required).

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

Toxicity/exposure ratios for soil organisms

Potato with an application rate of 276 g/ha

Test organism	Test substance	Time scale	Soil PEC[2]	TER	Trigger
Earthworms					
	a.s. ‡	Acute	0.130 (plateau)	3846	10
	a.s. ‡	Chronic	-	-	5
	Preparation	Acute	-	-	10
	Preparation	Chronic	0.130 (plateau)	99 292*	5
	Metabolite 1[3]	Acute	-	-	10
	Metabolite 1[3]	Chronic	-	-	5
Other soil macro-organisms					
Soil mite	a.s. ‡	-			
	Preparation	-			
	Metabolite 1[3]	-			
Collembola	a.s. ‡	-			
	Preparation		0.130 (plateau)	145	
	Metabolite 1[3]	-			

[1] to be completed where first Tier triggers are breached

[2] indicate which PEC soil was used (e.g. plateau PEC)

[3] no studies on the effects of metabolites on soil organisms (not required)

* in the soil with reduced organic matter contents

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

Preliminary screening data

Application of EXP10066A at a rate of 11.2 kg a.i./ha (40 times the intended use) did not cause any effects on the plant growth (tested on six terrestrial non-target plant species representing six plant families). NOEC was determined to be greater than 11.2 kg a.i./ha.

Laboratory dose response tests

Most sensitive species	Test substance	ER_{50} (g/ha) vegetative vigour	ER_{50} (g/ha) emergence	Exposure (g/ha)[2]	TER	Trigger
No data available, not required.						

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

Additional studies (e.g. semi-field or field studies)

-

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

Test type/organism	Endpoint
Activated sludge	EC_{50} >1000 mg a.i./L
Pseudomonas sp	Not conducted (not required)

Ecotoxicologically relevant compounds (consider parent and all relevant metabolites requiring further assessment from the fate section)

Compartment	
soil	-
water	-
sediment	-
groundwater	-

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

	RMS/peer review proposal
Active substance	N, R50/53

	RMS/peer review proposal
Preparation	N, R50/53

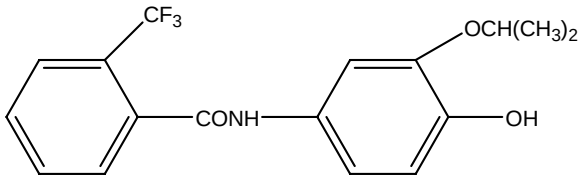
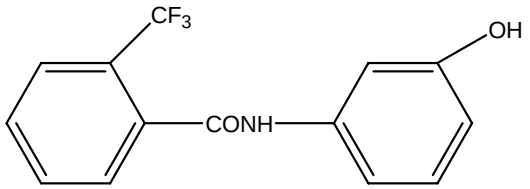
‡ Endpoints identified by EU-Commission as relevant for Member States when applying the Uniform Principles

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}	lethal dose, median; dosis letalis 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
M-2	α,α,α-trifluoro-4'-hydroxy-3'-isopropoxy-o-toluanilide	
M-4	α,α,α-trifluoro-3'-hydroxy-o-toluanilide	
M-7	α,α,α-trifluoro-4'-hydroxy-3'-methoxy-o-toluanilide