CONCLUSION ON PESTICIDE PEER REVIEW

Conclusion on the peer review of the pesticide risk assessment of the active substance flutriafol[1]

European Food Safety Authority[2]

European Food Safety Authority (EFSA), Parma, Italy

SUMMARY

Flutriafol is one of the 84 substances of the third stage part B of the review programme covered by Commission Regulation (EC) No 1490/2002[3], as amended by Commission Regulation (EC) No 1095/2007[4]. In accordance with the Regulation, at the request of the Commission of the European Communities (hereafter referred to as 'the Commission'), the EFSA organised a peer review of the initial evaluation, i.e. the Draft Assessment Report (DAR), provided by the United Kingdom, being the designated rapporteur Member State (RMS). The peer review process was subsequently terminated following the applicant's decision, in accordance with Article 11e, to withdraw support for the inclusion of flutriafol in Annex I to Council Directive 91/414/EEC.

Following the Commission Decision of 5 December 2008 (2008/934/EC)[5] concerning the non-inclusion of flutriafol in Annex I to Council Directive 91/414/EEC and the withdrawal of authorisations for plant protection products containing that substance, the applicant Cheminova A/S made a resubmission application for the inclusion of flutriafol in Annex I in accordance with the provisions laid down in Chapter III of Commission Regulation (EC) No. 33/2008[6]. The resubmission dossier included further data in response to the issues identified in the DAR.

In accordance with Article 18 of Commission Regulation (EC) No. 33/2008, the United Kingdom, being the designated RMS, submitted an evaluation of the additional data in the format of an Additional Report. The Additional Report was received by the EFSA on 15 January 2010.

In accordance with Article 19 of Commission Regulation (EC) No. 33/2008, the EFSA distributed the Additional Report to Member States and the applicant for comments on 19 January 2010. The EFSA collated and forwarded all comments received to the Commission on 5 March 2010.

In accordance with Article 20, following consideration of the Additional Report, the comments received, and where necessary the DAR, the Commission requested the EFSA to conduct a focused peer review in the areas of mammalian toxicology, residues, environmental fate and behaviour, and ecotoxicology and deliver its conclusions on flutriafol.

1 On request from the European Commission, Question No EFSA-Q-2010-00704, issued on 14 October 2010.

2 Correspondence: praper@efsa.europa.eu

3 OJ L224, 21.08.2002, p.25

4 OJ L 246, 21.9.2007, p.19

5 OJ L 333, 11.12.2008, p.11

6 OJ L 15, 18.01.2008, p.5

Suggested citation: European Food Safety Authority; Conclusion on the peer review of the pesticide risk assessment of the active substance flutriafol. EFSA Journal 2010;8(10):1868. [50 pp.] doi:10.2903/j.efsa.2010.1868. Available online: www.efsa.europa.eu/efsajournal.htm

The conclusions laid down in this report were reached on the basis of the evaluation of the representative uses of flutriafol as a fungicide on wheat, as proposed by the applicant. Full details of the representative uses can be found in Appendix A to this report.

Data gaps were identified in the section identity, physical and chemical properties of the active substance and analytical methods.

Data gaps were also identified in the mammalian toxicology section to address the relevance of the impurities present in the technical specification, to set reference values for the plant metabolites triazole alanine and triazole acetic acid, and to characterise the isomer ratio found in residues to which workers are exposed.

Based on the metabolism studies conducted on cereals, oilseed/pulse crops and root crops, the residue for monitoring was limited to the parent flutriafol only. Two separate definitions were proposed for risk assessment; 1) flutriafol and 2) Triazole derivative metabolites (TDM), since TDM were seen to be present in significant proportions and levels in primary and rotational crops. A default MRL value of 0.05 mg/kg was proposed for the crops usually rotated with wheat as there is clear evidence that residues above 0.01 mg/kg are expected in rotational crops. No residue definition could be proposed for animal products and a new metabolism study on ruminant was identified as a data gap. A data gap was also identified concerning the TDM, since no information was provided to include these metabolites in the consumer risk assessment.

Flutriafol is very stable in soil and the aquatic environment. It is expected to exhibit medium to high mobility in soil. A critical area of concern has been identified for potential groundwater contamination.

Two data gaps were identified in the ecotoxicology section. Further information should be provided to address the long-term risk to insectivorous birds. The ecotoxicological relevance of the impurities should be addressed. A high long-term risk to insectivorous birds was identified, based on the available data.

KEY WORDS

Flutriafol, peer review, risk assessment, pesticide, fungicide

TABLE OF CONTENTS

BACKGROUND

Legislative framework

Commission Regulation (EC) No 1490/2002[7], as amended by Commission Regulation (EC) No 1095/2007[8] lays down the detailed rules for the implementation of the third stage of the work programme referred to in Article 8(2) of Council Directive 91/414/EEC. This regulates for the European Food Safety Authority (EFSA) the procedure for organising, upon request of the Commission of the European Communities (hereafter referred to as 'the Commission'), a peer review of the initial evaluation, i.e. the Draft Assessment Report (DAR), provided by the designated rapporteur Member State.

Commission Regulation (EC) No 33/2008[9] lays down the detailed rules for the application of Council Directive 91/414/EEC for a regular and accelerated procedure for the assessment of active substances which were part of the programme of work referred to in Article 8(2) of Council Directive 91/414/EEC but which were not included in Annex I. This regulates for the EFSA the procedure for organising the consultation of Member States and the applicant(s) for comments on the Additional Report provided by the designated RMS, and upon request of the Commission the organisation of a peer review and/or delivery of its conclusions on the active substance.

Peer review conducted in accordance with Commission Regulation (EC) No 1490/2002

Flutriafol is one of the 84 substances of the third stage part B of the review programme covered by Commission Regulation (EC) No 1490/2002, as amended by Commission Regulation (EC) No 1095/2007. In accordance with the Regulation, at the request of the Commission, the EFSA organised a peer review of the DAR provided by the designated rapporteur Member State, the United Kingdom, which was received by the EFSA on 29 May 2006 (United Kingdom, 2006).

The peer review was initiated on 8 November 2006 by dispatching the DAR to Member States and the applicant Cheminova A/S for consultation and comments.

The peer review process was subsequently terminated following the applicant's decision, in accordance with Article 11e, to withdraw support for the inclusion of flutriafol in Annex I to Council Directive 91/414/EEC.

Peer review conducted in accordance with Commission Regulation (EC) No 33/2008

Following the Commission Decision of 5 December 2008 (2008/934/EC)[10] concerning the non-inclusion of flutriafol in Annex I to Council Directive 91/414/EEC and the withdrawal of authorisations for plant protection products containing that substance, the applicant Cheminova A/S made a resubmission application for the inclusion of flutriafol in Annex I in accordance with the provisions laid down in Chapter III of Commission Regulation (EC) No. 33/2008. The resubmission dossier included further data in response to the issues identified in the DAR.

In accordance with Article 18, the United Kingdom, being the designated RMS, submitted an evaluation of the additional data in the format of an Additional Report. The Additional Report was received by the EFSA on 15 January 2010 (United Kingdom, 2010a).

In accordance with Article 19, the EFSA distributed the Additional Report to Member States and the applicant for comments on 19 January 2010. In addition, the EFSA conducted a public consultation on the Additional Report and the DAR. The EFSA collated and forwarded all comments received to the Commission on 5 March 2010. At the same time, the collated comments were forwarded to the RMS

[7] OJ L224, 21.08.2002, p.25
[8] OJ L246, 21.9.2007, p.19
[9] OJ L 15, 18.01.2008, p.5
[10] OJ L 333, 11.12.2008, p.11

for compilation in the format of a Reporting Table. The applicant was invited to respond to the comments in column 3 of the Reporting Table. The comments and the applicant's response were evaluated by the RMS in column 3.

In accordance with Article 20, following consideration of the Additional Report, the comments received, and where necessary the DAR, the Commission decided to further consult the EFSA. By written request, received by the EFSA on 31 March 2010, the Commission requested the EFSA to arrange a consultation with Member State experts as appropriate and deliver its conclusions on flutriafol within 6 months of the date of receipt of the request, subject to an extension of a maximum of 90 days where further information were required to be submitted by the applicants in accordance with Article 20(2).

The scope of the peer review and the necessity for additional information, not concerning new studies, to be submitted by the applicant in accordance with Article 20(2), was considered in a telephone conference between the EFSA, the RMS, and the Commission on 6 April 2010; the applicant was also invited to give its view on the need for additional information. On the basis of the comments received, the applicant's response to the comments, and the RMS' subsequent evaluation thereof, it was concluded that the EFSA should organise a consultation with Member State experts in the areas of mammalian toxicology, residues, environmental fate and behaviour, and ecotoxicology and that further information should be requested from the applicant in the area of mammalian toxicology.

The outcome of the telephone conference, together with EFSA's further consideration of the comments is reflected in the conclusions set out in column 4 of the Reporting Table. All points that were identified as unresolved at the end of the comment evaluation phase and which required further consideration, including those issues to be considered in consultation with Member State experts, and the additional information to be submitted by the applicant, were compiled by the EFSA in the format of an Evaluation Table.

The conclusions arising from the consideration by the EFSA, and as appropriate by the RMS, of the points identified in the Evaluation Table, together with the outcome of the expert discussions where these took place, were reported in the final column of the Evaluation Table.

A final consultation on the conclusions arising from the peer review of the risk assessment took place with Member States via a written procedure in September-October 2010.

This conclusion report summarises the outcome of the peer review of the risk assessment on the active substance and the representative formulation evaluated on the basis of the representative uses as a fungicide on wheat, as proposed by the applicant. A list of the relevant end points for the active substance as well as the formulation is provided in Appendix A. In addition, a key supporting document to this conclusion is the Peer Review Report (EFSA, 2010), which is a compilation of the documentation developed to evaluate and address all issues raised in the peer review, from the initial commenting phase to the conclusion. The Peer Review Report comprises the following documents:

- the comments received,
- the Reporting Table (revision 1-1; 6 April 2010),
- the Evaluation Table (13 October 2010),
- the reports of the scientific consultation with Member State experts (where relevant).

Given the importance of the DAR and the Additional Report including its addendum (compiled version of September 2010 containing all individually submitted addenda) (United Kingdom, 2010b) and the Peer Review Report, both documents are considered respectively as background documents A and B to this conclusion.

THE ACTIVE SUBSTANCE AND THE FORMULATED PRODUCT

Flutriafol is the ISO common name for (*RS*)-2,4′-difluoro-α-(1*H*-1,2,4-triazol-1-ylmethyl)benzhydryl alcohol (IUPAC).

The representative formulated product for the evaluation was 'Flutriafol 125 g/l SC', a suspension concentrate (SC), containing 125 g/l flutriafol, registered under different trade names in Europe.

The representative uses evaluated comprise foliar spraying on winter and spring sown wheat to control *Erysiphe graminis, Rhynchosporium secalis, Septoria, Puccinia* and *Helminthosporium spp*. Full details of the GAP can be found in the list of end points in Appendix A.

CONCLUSIONS OF THE EVALUATION

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

The minimum purity of flutriafol technical material is 920 g/kg. Flutriafol is a racemate. No FAO specification exists.

Flutriafol is manufactured as a wet paste, however the specification was given only on a dry weight basis. As a consequence a data gap was identified for a specification of the technical concentrate (TK). Dimethyl sulphate, dimethylformamide and methanol were considered relevant impurities with maximum content of 0.01%, 0.1% and 0.1% respectively. A data gap was identified for a validated analytical method for the determination of the relevant impurities in the technical concentrate. There were impurities in the technical material for which the relevance could not be concluded.

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 flutriafol or the respective formulation; however a data gap was identified for the extinction coefficient at relevant wavelengths and wavelengths ≥ 290 nm. The main data regarding the identity of flutriafol and its physical and chemical properties are given in Appendix A.

Adequate analytical methods are available for the determination of flutriafol in the representative formulation. Adequate analytical methods are available for monitoring the residues of flutriafol in food of plant and animal origin and in the environmental matrices. It should be noted however, that the residue definition for monitoring in food of animal origin is still open. Analytical methods for the determination of residues in body fluids and tissues are not required as flutriafol is not classified as toxic or highly toxic.

2. Mammalian toxicity

Flutriafol was discussed at the PRAPeR Experts' teleconference on mammalian toxicology (PRAPeR TC36) in June 2010. The technical specification is supported by the batches used in the toxicological studies; however the relevance of the impurities was not addressed; a data gap is identified for the relevance of the impurities present in the technical specification. The impurities dimethyl sulphate (maximum concentration level 0.01 %), dimethylformamide and methanol (max. concentration level 0.1%) are toxicologically relevant.

Low to moderate acute toxicity was observed when flutriafol was administered by the oral, dermal or inhalation routes; mild eye irritation and no skin irritation or potential for skin sensitisation were observed; classification with R22 'harmful if swallowed' is proposed regarding acute toxicity. The liver is affected upon short-term and long-term exposure in all species tested, with the relevant short-term NOAEL being 5 mg/kg bw/day derived from the 90-day and 1-year dog studies; the long-term NOAEL is 1.0 mg/kg bw/day taken from the 2-year rat study. No potential for neurotoxicity, genotoxicity or carcinogenicity is attributed to the active substance. Lower fertility index observed in the first generation from the multigeneration study and reduced litter size were associated with parental toxicity. Classification with R63 'risk of harm to the unborn child' is proposed based on

reduced or delayed ossification observed in rat and rabbit foetuses at or below doses showing maternal toxicity, hyoid abnormalities and cleft palate found in preliminary studies together with maternal toxicity.

Toxicity studies were submitted on the metabolites triazole alanine (TA) and triazole acetic acid (TAA); an acceptable daily intake (ADI) of 0.09 mg/kg bw/day is set for TA based on the NOAEL of 90 mg/kg bw/day obtained in the 90-day study in rat, applying a safety factor of 1000 to account for the incomplete data package available for this metabolite. However no conclusion could be reached on the acute reference dose (ARfD) for TA as a critical study (developmental study in rabbit) for this kind of compound is not available. No ADI or ARfD could be concluded for the TAA metabolite due to insufficient data. Data gaps were identified for toxicological information to allow these reference values to be set.

The ADI of flutriafol is 0.01 mg/kg bw/day based on the 2-year rat study, 100 safety factor (SF) applied. The acceptable operator exposure level (AOEL) is 0.05 mg/kg bw/day and the ARfD 0.05 mg/kg bw based on the 90-day and 1-year studies in dog and applying the same SF of 100; no correction for oral absorption being needed to derive the AOEL.

The estimated operator exposure is below the AOEL when no personal protective equipment (PPE) is considered according to the German model. Worker exposure is estimated to represent 75% of the AOEL when no PPE is worn, however, considering the uncertainty about the isomer ratio in residues to which workers are exposed to and the unknown relative toxicity of each isomer (data gap), if a reasonable worst case is assumed (doubling of the toxicity), the use of PPE is required to obtain an estimated degree of exposure below the AOEL. Bystander exposure is calculated to remain below the AOEL.

3. Residues

Metabolism in plants was investigated on cereals (barley, wheat), oilseed/pulse crops (rapeseed) and root crops (sugar beet) using foliar applications and ^{14}C-flutriafol labelled on the carbinol or triazole moiety. Cereals studies were conducted under both outdoor and indoor conditions. In rapeseed and sugar beet, no cleavage of the parent structure was observed and flutriafol was detected as the major component of the residues, accounting at harvest for 56 to 71% TRR. In cereals, flutriafol remains the major component in straw (38-63% TRR), while in grain, residues are mainly composed of the triazole derivative metabolites (TDM), triazole alanine (TA) (up to 58% TRR) and triazole acetic acid (TAA) (up to 28% TRR). The metabolite profile in rotational crops is consistent with that observed in primary crops and confirms that parent and TDM are the residues of concern. Based on these studies, the experts' teleconference on residues (PRAPeR TC34) agreed to limit the plant residue definition for monitoring to flutriafol only. For risk assessment, considering the significant presence of TDM residues in primary and rotational crops and having regard to the conclusion of PRAPeR TC36 on mammalian toxicology, two separate residue definitions were proposed; 1) flutriafol only and 2) Triazole Derivative Metabolites (TDM). However, no final definition can be proposed for TDM at this stage, since a global and harmonized approach is needed for all compounds of the triazole chemical class.

Since a sufficient number of residue trials sufficiently representing the revised GAP using a single application was submitted, the MRL for wheat was derived by EFSA from these trials, and not by calculation from the studies conducted with two applications, as proposed by the RMS. These residue data are supported by the storage stability study, showing flutriafol residues to be stable up to 1 year in wheat matrices.

Radiolabelled and cold rotational crop studies conducted in many locations and over several years were provided. From these experiments, there is clear evidence that flutriafol residues are expected to be present above 0.01 mg/kg in crops sown/planted in rotation with wheat. This issue was discussed during the teleconference and the experts agreed on the need to propose MRLs for the crops usually rotated with wheat. Based on the available studies where the expected levels of flutriafol were

estimated to be in the range of 0.01 to 0.04 mg/kg in various crop groups, it was agreed that a default value of 0.05 mg/kg would be sufficient to cover the possible residues in rotational crops. This proposal is however based on the predicted concentration of flutriafol in soil resulting from a single application on wheat, and it should be revised if further uses and/or higher application rates are envisaged.

The trigger intake of 0.1 mg/kg DM for the investigation of the nature of residues in livestock is exceeded for ruminants. A metabolism study on cattle was provide but considered not appropriate to derive a residue definition, since only a small part of the radioactivity was identified in the different matrices. A new ruminant metabolism study was therefore identified as a data gap. However, it should be noted that based on the available data, the residue levels in ruminant matrices are expected to be low, close to the LOQ and the contribution to the consumer risk assessment limited. A metabolism study on poultry was submitted although the intake was not triggered. Therefore no residue definition and no MRLs were proposed for poultry products. No information was provided concerning the intake of TDM and their possible transfer to animal products, while these metabolites were shown to represent the major part of the residues in rotational crops and in cereal grains. Further information on TDM in animal matrices is therefore identified as a data gap.

No chronic or acute concern was identified, the TMDI and IESTI calculated using the EFSA PRIMo model and the proposed MRL for wheat, being only 4% of the ADI and <2% of the ARfD. Similarly, no concern is identified when this assessment includes a value of 0.05 mg/kg for the possible plant groups planted in rotation with wheat (vegetables, pulses, oilseeds, cereals and sugar beet), the highest TMDI and IESTI being 19% and 15% of the ADI and ARfD respectively. However, these estimations have to be considered as provisional as the contribution of the TDMs was not taken into account, since no information was provided on their possible residue levels in primary crops, rotational crops and in animal matrices.

4. Environmental fate and behaviour

In soil under laboratory aerobic conditions flutriafol is practically stable and no appreciable degradation is observed. Mineralization and non-extractable residues are practically negligible after 126 days. Consequently no degradation products were observed or identified. Similar behaviour is observed under anaerobic conditions. No fully reliable information is available on photolysis of flutriafol in soil. However, no further data were considered necessary to finalise the exposure assessment for the representative uses assessed. Reliable field dissipation trials performed in the United Kingdom and Germany are available. The very high persistence exhibited by flutriafol in soil is confirmed by these trials. PEC soils have been calculated with a DT_{50} of 1500 days as representative worst case.

Batch soil adsorption desorption indicate that flutriafol may be classified as medium to highly mobile in soil. A field leaching study was conducted in Germany over four and half years. Results of this study confirm the potential of flutriafol for leaching to groundwater at levels above 0.1 µg/L.

Flutriafol was stable to hydrolysis under normally occurring environmental conditions (pH 5 – 9; 25 °C). Flutriafol was also stable to aqueous photolysis at pH 7 when exposed to artificial light simulating Florida summer sunlight. Dissipation and degradation of flutriafol was investigated in two water/sediment systems. Flutriafol was practically stable in both systems (DT_{50} > 1000 days). Flutriafol dissipates from the water phase by adsorption to the sediment. $PEC_{SW/SED}$ were calculated by FOCUS SW models up to step 3 for the representative use in winter cereals (FOCUS, 2001).

Potential for contamination of groundwater above the regulatory limit of 0.1 µg/L was investigated by calculation of the 20 years 80th percentile annual average leachate concentrations at 1m depth with

FOCUS GW models PEARL and PELMO (FOCUS, 2000; EFSA, 2004).[11] When flutriafol is applied every year the limit of 0.1 µg/L is exceeded for all 9 scenarios with PEARL and for 6 of 9 scenarios with PELMO. When the product is applied every third year then the limit of 0.1 µg/L is still exceeded by 6 of 9 scenarios with both PEARL and PELMO models. It should be noted that the application every third year should be considered as a restriction for potential mitigation of groundwater contamination (proposed by the applicant) and does not reflect the normal pattern of rotation for the representative use in cereals.

Half-life in the atmosphere is calculated to be <2 days by photochemical degradation. Therefore, flutriafol is not expected to be prone to long range transport through air.

5. Ecotoxicology

The ecotoxicological relevance of the impurities should be addressed. Therefore a data gap was identified.

The acute and short-term risk of flutriafol to insectivorous birds via dietary exposure was assessed as low at tier 1 for the representative use in wheat, in accordance with the guidance document (European Commission, 2002).

Statistically significant effects were observed in hatchability at the two higher test doses in the Mallard duck reproduction study. A NOEC could not be determined due to the apparent (but not statistically significant) effects in hatchability observed at the two lower test doses. The applicant proposed to use a benchmark dose modelling (BMD) approach to estimate an appropriate dose to serve as chronic toxicity endpoint. The BMD is a model that estimates the benchmark doses (concentration or dose where a percentage of effect was observed). "The use of the benchmark dose approach will come to be viewed as an alternative and often preferable reference point to the no-observed-effect concentration/level (NOEC/NOEL)" was suggested in the guidance the document (EFSA, 2009). This was the first time that this model was used; therefore a more detailed explanation was presented. The use of the BMD modelling was recommended because the methods are not as dependent upon dose selection. The BMD approach only requires that the doses in the study achieve a range of responses to characterise the dose-response curve. The model explicitly accounts for the shape of the dose-response curve. A good-fit of the dose-response curve is required to derive a good estimate of the BMD. The applicant performed a BMD using arcsine square root transformed data on hatchability and a linear model to fit the data. The top dose level was excluded as it was considered an outlier and the lower doses were more relevant to derive the BMD. The RMS used the same data and ran a continuous linear model and a continuous polynomial model to fit the data, with 8.4% or 10% relative effect levels. These produce BMDs (mean) of 10.3-6.0 mg/kg bw/day and BMDLs (lower limit confidence interval of 95%) of 7,4 - 2.8 mg/kg bw/day which are in the same range as the values calculated by the applicant. The use of the BMD approach was discussed and accepted at the experts' meeting on ecotoxicology (PRAPeR 80). Furthermore, the experts discussed which BMD value should be used in the long-term risk assessment for birds. Two types of models were applied to the data, but information regarding the goodness of fit was not available for the RMS calculations. Concern was raised that the modelling (curve fitting) was based on results from only three doses but there are no agreed standards for minimum goodness of fit for deriving BMDs. The first proposal of the experts was to use the median BMD of 6 mg a.s./kg bw/d. Given the uncertainties regarding the goodness of fit of the different models applied, a further proposal was to use the more conservative endpoint lower limit BMDL of 2.8 mg a.s./kg bw/d (based on the lower 95% confidence interval)). There was no consensus, however a majority of Member States experts agreed to using the BMDL of 2.8 mg a.s./kg bw/d.

[11] Simulations utilised a Q_{10} of 2.2 and Walker equation coefficient of 0.7. Additionally a plant uptake factor of 0.7 was used instead of default 0.5 on basis of calculated value following FOCUS Groundwater Guidance.

Even when focal species and PD refinements were considered, the long-term risk of flutriafol to insectivorous birds was assessed as high. A data gap was identified to further address the potential long-term risk to insectivorous birds.

At the experts' meeting (PRAPeR 80) the endpoint that should be used in the long-term risk assessment for mammals was discussed. Experts agreed to use the NOAEL of 13.5 mg a.s./kg bw/d, suggested by the RMS. The acute and long-term risk to mammals via dietary exposure was assessed as low at tier 1 for all representative uses, in accordance with the guidance document (European Commission, 2002).

A risk assessment for earthworm-eating as well as fish-eating birds and mammals (secondary poisoning) was not required since flutriafol is unlikely to bioaccumulate (log P_{ow}= 2.3).

Flutriafol is toxic to aquatic organisms based on the available data. The formulation "Flutriafol 125 g/L" was slightly more toxic than the technical active substance. A low risk was identified for aquatic organisms at the first tier risk assessment (i. e. $FOCUS_{sw}$ step 2).

The risk was assessed as low for the other non-target organisms (i.e. bees, non-target arthropods, earthworms, non-target soil macro-organisms, non-target soil micro-organisms, non-target plants and biological methods of sewage treatment) for the representative uses evaluated.

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

6.1. Soil

Compound (name and/or code)	Persistence	Ecotoxicology
flutriafol	Very high persistent ($DT_{50\ 20°C}$ = 672 – 3492 d).	The risk of flutriafol to earthworms was assessed as low. The risk for soil non-target macro-organisms was assessed as low for use in wheat.

6.2. Groundwater

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 activity
flutriafol	Medium to high (K_{Foc} = 104 – 395 mL/g)	FOCUS GW: yes, 6 to 9 of 9 scenarios exceed the limit of 0.1 µg / L. Lysimeter: not available.	Yes	Yes	No.

6.3. Surface water and sediment

Compound (name and/or code)	Ecotoxicology
flutriafol	Flutriafol is toxic to aquatic organisms. A low risk was identified for aquatic organisms at Tier 1.

6.4. Air

Compound (name and/or code)	Toxicology
flutriafol	Rat LC_{50} inhalation > 5.2 mg/L air/4h (nose-only, solid particulate aerosols), no classification proposed

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

- Specification of the technical concentrate (TK) (relevant for all representative uses evaluated; submission date proposed by the applicant: unknown; see section 1)
- Validated analytical method for the determination of the relevant impurities in the technical concentrate (relevant for all representative uses evaluated; submission date proposed by the applicant: unknown; see section 1)
- The extinction coefficient at relevant wavelengths and wavelengths ≥ 290 nm (relevant for all representative uses evaluated; submission date proposed by the applicant: unknown; see section 1)
- Toxicological and ecotoxicological information on the impurities present in the technical specification to address their relevance (relevant for all representative uses evaluated; submission date proposed by the applicant: unknown; see sections 2 and 5)
- Toxicological information allowing the setting of an ARfD for the metabolite TA and an ADI and an ARfD for the metabolite TAA (relevant for all representative uses evaluated; submission date proposed by the applicant: unknown; see section 2)
- Information on the isomer ratio found in residues to which workers are exposed (or alternatively information on the relative toxicity of the isomers) (relevant for all representative uses evaluated; submission date proposed by the applicant: unknown, according to the RMS additional data from the 'Triazole Derivative Metabolite Group' (TDMG) will be available before the end of 2010; see section 2)
- A new metabolism study on ruminant (relevant for all representative uses evaluated; no submission date proposed by the applicant; refer to the section 3)
- Information allowing the assessment of consumer exposure to triazole derivative metabolites (TDM) in primary crops, rotational crops and products of animal origin are required (relevant for all representative uses evaluated; no submission date proposed by the applicant; refer to section 3)
- A data gap to further address the long-term risk to insectivorous birds was identified (relevant for all representative uses evaluated; submission date proposed by the applicant: unknown; see section 5)

PARTICULAR CONDITIONS PROPOSED TO BE TAKEN INTO ACCOUNT TO MANAGE THE RISK(S) IDENTIFIED

- As a precautionary approach, workers exposed to flutriafol residues should use PPE to maintain the estimated exposure below the AOEL (see section 2).

ISSUES THAT COULD NOT BE FINALISED

- The relevance of the impurities present in the technical specification was not fully addressed.
- Worker exposure was not finalised regarding the recommendation of PPE to be worn, as no characterisation of the isomer ratio found in residues to which workers are exposed was provided (or information on the comparative toxicity of the different isomers).
- The contribution of the residues of the Triazole Derivative Metabolite (TDM) present in primary crops, rotational crops and products of animal origin to the overall consumer exposure was not considered.

- No residue definition and MRL for ruminant products could be proposed, but based on the available data, residues in ruminant matrices are expected to be close to the LOQ, when considering the representative use.

CRITICAL AREAS OF CONCERN

- Potential for groundwater contamination even when the use is restricted to one application every third year. The applicant proposed to restrict the use to once every third year as a mitigation for potential groundwater contamination. It is noted that this measure is envisaged not to be effective in 6 out of 9 scenarios simulated with FOCUS GW tools.

- A high long-term risk to insectivorous birds was identified for the representative uses, based on the available data.

REFERENCES

European Commission, 2002. Guidance Document on Risk Assessment for Birds and Mammals Under Council Directive 91/414/EEC. SANCO/4145/2000.

EFSA (European Food Safety Authority), 2004. Opinion of the Scientific Panel on Plant Health, Plant Protection Products and their Residues on a request of EFSA related to FOCUS groundwater models comparability and the consistency of this risk assessment of groundwater contamination. The EFSA Journal (2004) 93, 1-20.

EFSA (European Food Safety Authority). 2009. Guidance Document on Risk Assessment for Birds & Mammals. EFSA Journal 2009; 7(12):1438.

EFSA (European Food Safety Authority), 2010. Peer Review Report to the conclusion regarding the peer review of the pesticide risk assessment of the active substance flutriafol.

FOCUS, 2000. "FOCUS Groundwater Scenarios in the EU review of active substances". Report of the FOCUS Groundwater Scenarios Workgroup, EC Document Reference SANCO/321/2000-rev.2. 202 pp, as updated by the Generic Guidance for FOCUS groundwater scenarios, version 1.1 dated April 2002.

FOCUS, 2001. "FOCUS Surface Water Scenarios in the EU Evaluation Process under 91/414/EEC". Report of the FOCUS Working Group on Surface Water Scenarios, EC Document Reference SANCO/4802/2001-rev.2. 245 pp.

United Kingdom, 2006. Draft Assessment Report (DAR) on the active substance flutriafol prepared by the rapporteur Member State the United Kingdom in the framework of Directive 91/414/EEC, May 2006.

United Kingdom, 2010a. Additional Report to the Draft Assessment Report on the active substance flutriafol prepared by the rapporteur Member State the United Kingdom in the framework of Commission Regulation (EC) No 33/2008, January 2010.

United Kingdom, 2010b. Final Addendum to Draft Assessment Report and Additional Report on flutriafol, compiled by EFSA, September 2010.

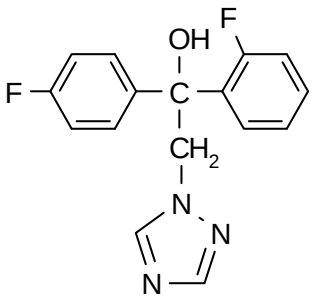
APPENDICES

APPENDIX A – LIST OF END POINTS FOR THE ACTIVE SUBSTANCE AND THE REPRESENTATIVE FORMULATION

Identity, Physical and Chemical Properties, Details of Uses, Further Information

Active substance (ISO Common Name) ‡	flutriafol
Function (*e.g.* fungicide)	fungicide
Rapporteur Member State	UK

Identity (Annex IIA, point 1)

Chemical name (IUPAC) ‡	(*RS*)-2,4'-difluoro-α-(1*H*-1,2,4-triazol-1-ylmethyl)benzhydryl alcohol
Chemical name (CA) ‡	(±)-α-(2-fluorophenyl)-α-(4-fluorophenyl)-1*H*-1,2,4-triazole-1-ethanol
CIPAC No ‡	436
CAS No ‡	76674-21-0
EC No (EINECS or ELINCS) ‡	Not assigned
FAO Specification (including year of publication) ‡	No specification is available.
Minimum purity of the active substance as manufactured ‡	920 g/kg (racemate)
Identity of relevant impurities (of toxicological, ecotoxicological and/or environmental concern) in the active substance as manufactured	dimethyl sulphate: max. 0.01% dimethylformamide: max. 0.1% methanol: max. 0.1% Open for others
Molecular formula ‡	$C_{16}H_{13}F_2N_3O$
Molecular mass ‡	301.3 g/mol
Structural formula ‡	

Physical and chemical properties (Annex IIA, point 2)

Melting point (state purity) ‡	130 °C (99.4% purity)
Boiling point (state purity) ‡	Not determined or required
Temperature of decomposition (state purity)	approximately 270°C (99.0 % purity)
Appearance (state purity) ‡	White, crystalline solid; odourless technical grade active substance (99.4% purity)
Vapour pressure (state temperature, state purity) ‡	4 x 10^{-7} Pa at 20°C (99.4% purity)
Henry's law constant ‡	1.27 x 10^{-6} Pa m^3 mol^{-1} at 20°C
Solubility in water (state temperature, state purity and pH) ‡	pH 4: 124 mg/L at 20 °C (99.0% purity; preliminary test)
	pH 7: 95 mg/l (20°C; pure water)
	pH 10: 102 mg/L (preliminary test)
Solubility in organic solvents ‡ (state temperature, state purity)	1,2-dichloroethane: 19-20 g/l acetone: 116-135 g/l ethyl acetate: 29-34 g/l methanol: 115-134 g/l heptane: <10 g/l xylene: <10 g/l Solubility at 21°C (94.4% purity)
Surface tension ‡ (state concentration and temperature, state purity)	68.7 mN/mat 20°C (6.97 x 10^{-2} g/L solution) Typical technical – purity not stated.
Partition co-efficient ‡ (state temperature, pH and purity)	log $P_{O/W}$ = 2.3 at 20°C (not pH dependent)
Dissociation constant (state purity) ‡	pKa = 2.3 at 25°C (99.4% purity)
UV/VIS absorption (max.) incl. ε ‡ (state purity, pH)	No adsorption
Flammability ‡ (state purity)	Not highly flammable (purity not stated)
Explosive properties ‡ (state purity)	No explosive properties (purity not stated)
Oxidising properties ‡ (state purity)	None expected (purity not stated)

- **Summary of representative uses evaluated (*flutriafol*)***

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 (for explanation see the text in front of this section)			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	g as/hL min–max (l)	Water L/ha min–max	g as/ha min–max (l)		
Wheat (Winter and Spring sown)	Northern Europe	Flutriafol 125 g/L SC	F	*Erysiphe graminis, Rhynchosporium secalis, Septoria, Puccinia, Helminthosporium spp*	SC	125 g/L	Foliar sprayer	Between BBCH 40 - 55	1	nr	40 –60	200 - 300	125	nr	Application should be not later than growth stage 55 and not earlier than *growth* stage 40 [1] [2] [3] [4]
Wheat (Winter and Spring sown)	Southern Europe	Flutriafol 125 g/L SC	F	*Erysiphe graminis, Rhynchosporium secalis, Septoria, Puccinia, Helminthosporium spp*	SC	125 g/L	Foliar sprayer	Between BBCH 40 - 55	1	nr	40 – 60	200 - 300	125	nr	Application should be not later than growth stage 55 and not earlier than growth stage 40 [1] [2] [3] [4] [5]

[1] Potential for groundwater contamination has been identified for all FOCUS GW scenarios. If the use was to be restricted to application every third year, the limit of 0.1 µg/L would be exceeded in six of nine scenarios (this restriction was proposed by the applicant as potential mitigation not as normal rotation of the crop).
[2] A high long-term risk to insectivorous birds was identified.
[3] The relevance of the impurities was not fully addressed
[4] Worker exposure was not finalised regarding the recommendation of PPE to be worn, as no characterisation of the isomer ratio found in residues to which workers are exposed was provided.
[5] The contribution of the residues of the Triazole Derivative Metabolite (TDM) present in primary crops, rotational crops and products of animal origin to the overall consumer exposure was not considered. Furthermore, no residue definition and MRL for ruminant products could be proposed

* 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).	(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).**
nr not relevant	(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
(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)	(k) Indicate the minimum and maximum number of application possible under practical conditions of use
(b) Outdoor or field use (F), greenhouse application (G) or indoor application (I)	(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
(c) *e.g.* biting and suckling insects, soil born insects, foliar fungi, weeds	(m) PHI - minimum pre-harvest interval
(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	

Methods of Analysis

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

Technical as (analytical technique)	Validated HPLC method
Impurities in technical as (analytical technique)	Validated HPLC method
Plant protection product (analytical technique)	Validated HPLC method

Analytical methods for residues (Annex IIA, point 4.2)

Residue definitions for monitoring purposes

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

Monitoring/Enforcement methods

Food/feed of plant origin (analytical technique and LOQ for methods for monitoring purposes)	HPLC-MS/MS LOQ: 0.01 mg/kg, flutriafol Wheat (plant, grain, straw) ILV: HPLC-MS/MS LOQ: 0.01 mg/kg, flutriafol Wheat (plant, grain, straw)
Food/feed of animal origin (analytical technique and LOQ for methods for monitoring purposes)	GC-MSD LOQ: 0.01 mg/kg, flutriafol (milk, muscle, kidney, liver, egg) Residue definition still open
Soil (analytical technique and LOQ)	GC-TID LOQ: 0.01 mg/kg, flutriafol
Water (analytical technique and LOQ)	Primary method: GC-NPD with DB-5 column LOQ: 0.05 µg/l, flutriafol (drinking water, groundwater, surface water) Confirmatory method: GC-NPD with DB-1701
Air (analytical technique and LOQ)	GC-TID LOQ: 0.003 mg/m^3 , flutriafol
Body fluids and tissues (analytical technique and LOQ)	Not required

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

	RMS/peer review proposal
Active substance	None

Impact on Human and Animal Health

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

Rate and extent of oral absorption ‡	Rapid and extensive absorption: > 90 % based on urinary and biliary excretion.
Distribution ‡	Widely distributed; highest levels in red blood cells due to extensive binding.
Potential for accumulation ‡	No evidence for accumulation.
Rate and extent of excretion ‡	Rapidly excreted with approximately equal proportions present in the urine and faeces. Extensive biliary excretion (~ 80 %) with evidence for enterohepatic circulation.
Metabolism in animals ‡	Extensive metabolism; only trace amount of unchanged parent detected. Limited cleavage of the molecule.
Toxicologically relevant compounds ‡ (animals and plants)	Flutriafol
Toxicologically relevant compounds ‡ (environment)	Flutriafol

Acute toxicity (Annex IIA, point 5.2)

Rat LD_{50} oral ‡	1140-1480 mg/kg bw	**R22**
Mouse LD_{50} oral	179 – 365 mg/kg bw	
Rabbit LD_{50} oral	300 – 400 mg/kg bw (female)	
Guinea pig LD_{50} oral	300 – 400 mg/kg bw (male)	
Rat LD_{50} dermal ‡	> 1000 mg/kg bw	
Rat LC_{50} inhalation ‡	> 5.2 mg/L air/4h (nose-only, solid particulate aerosols)	
Skin irritation ‡	Non-irritant	
Eye irritation ‡	Mild-irritant	
Skin sensitisation ‡	No evidence of skin sensitisation (M&K, LLNA)	

Short term toxicity (Annex IIA, point 5.3)

Target / critical effect ‡	Rat and dog: Decreased Body weight gain; Red blood cell (anaemia) and liver (lipid metabolism) Mouse: lipid accumulation in the liver	
Relevant oral NOAEL ‡	90-day & 1-year dog: 5 mg/kg bw/day 90-day rat: 13.3 mg/kg bw/day 90-day mouse: LOAEL: 7.5 mg/kg bw/day	
Relevant dermal NOAEL ‡	No data – not required	
Relevant inhalation NOAEL ‡	No data – not required	

Genotoxicity ‡ (Annex IIA, point 5.4)

	Equivocal evidence *in vitro*; negative *in vivo*. Not considered to be genotoxic on the basis of all studies.	

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

Target/critical effect ‡	Liver: increased liver weight and histopathology (rat and mouse)	
Relevant NOAEL ‡	1.0 mg/kg bw/day; 2-year rat 1.2 mg/kg bw/day; 2-year mouse	
Carcinogenicity ‡	Flutriafol is unlikely to pose a risk to humans	

Reproductive toxicity (Annex IIA, point 5.6)

Reproduction toxicity

Reproduction target / critical effect ‡	Reproductive effects: lower fertility index in the first generation; Parental toxicity: liver histopathology, decreased body weight and organ weight changes at the top dose level; Offspring's toxicity: Reduced litter size.	
Relevant parental NOAEL ‡	3.5 mg/kg bw/day	
Relevant reproductive NOAEL ‡	13.5 mg/kg bw/day	
Relevant offspring NOAEL ‡	13.5 mg/kg bw/day	

Developmental toxicity

Developmental target / critical effect ‡	Maternal toxicity: clinical signs, decreased body weight gain, increased post implantation loss (rat & rabbit); Developmental toxicity: Reduced litter size, hyoid abnormalities, reduced/delayed ossification (rat & rabbit), cleft palate observed in preliminary studies in rat	
Relevant maternal NOAEL ‡	7.5 mg/kg bw/day (rabbit) 50 mg/kg bw/day (rat)	
Relevant developmental NOAEL ‡	7.5 mg/kg bw/day (rabbit) LOAEL: 10 mg/kg bw/day (rat)	**R63**

Neurotoxicity (Annex IIA, point 5.7)

Acute neurotoxicity ‡	No neuropathy – NOAEL 750 mg/kg bw Altered urination patterns – NOAEL 125 mg/kg bw Reduced body weight gain – LOAEL 125	

	mg/kg bw	
Repeated neurotoxicity ‡	Not neurotoxic – NOAEL 172 mg/kg bw/day Reduced body weight gain – NOAEL 29 mg/kg bw/day	
Delayed neurotoxicity ‡	Not applicable	

Other toxicological studies (Annex IIA, point 5.8)

Mechanism studies ‡	None submitted
Studies performed on metabolites or impurities ‡	

TA

Toxicokinetics and metabolism	> 80 % orally absorbed and then eliminated via urine (within 24 h) mostly as unchanged parent compound; negligible amount retained in organs and tissues or expired air.
Acute toxicity	Rat LD_{50} oral > 5000 mg/kg bw
Short term toxicity	90-day oral rat: NOAEL = 90 mg/kg bw/day (↓ triglycerides) 90-day oral dog: NOAEL = 200 mg/kg bw/day (↓ body weights and food consumption)
Genotoxicity	TA is unlikely to be genotoxic
Reproduction toxicity	Reproductive and parental toxicity: NOAEL 240 mg/kg bw/day (↑ proportion of male offspring, ↓ litter weight at birth; ↑ precoital interval, histopathological findings in the kidneys of uncertain significance)
Developmental toxicity	Maternal toxicity: NOAEL 1000 mg/kg bw/day (no adverse effects at the highest dose tested) Developmental toxicity: NOAEL 100 mg/kg bw/day (delayed ossification)
ADI (TA)	0.09 mg/kg bw/day (90-day study in rat, SF 1000 due to incomplete data set)
ARfD (TA)	Insufficient data to conclude

TAA

Toxicokinetics and metabolism	> 80 % orally absorbed and then eliminated via urine (within 24 h) mostly as unchanged parent compound.
Acute toxicity	Rat LD_{50} oral > 5000 mg/kg bw
Short term toxicity	14-day oral rat: NOAEL: 704 mg/kg bw/day
Genotoxicity	Ames test negative
ADI/ARfD (TAA)	Insufficient data to conclude

Medical data ‡ (Annex IIA, point 5.9)

No adverse reactions reported

Summary (Annex IIA, point 5.10)	Value	Study	Safety factor
ADI ‡	0.01 mg/kg bw/day	2-year rat	100
AOEL ‡	0.05 mg/kg bw/day	90-day dog & 1-year dog	100
ARfD ‡	0.05 mg/kg bw	90-day dog & 1-year dog	100

Dermal absorption ‡ (Annex IIIA, point 7.3)

Flutriafol 125 g/L SC	Concentrate: 0.5 % 0.025 g/L spray dilution: 30 % Based on rat *in vivo* data and comparative *in vitro* data (rat/human skin)

Exposure scenarios (Annex IIIA, point 7.2)

Operator	Tractor mounted equipment (application rate 0.125 kg flutriafol/ha) — % of AOEL *According to the German model*: Without PPE 45 % With PPE (gloves when M/L) 44 % *According to the UK POEM:* Without PPE 272 % With PPE (gloves when M/L) 262 % With PPE (gloves during M/L & application) 42 %
Workers	Estimates of exposure for flutriafol predicted for workers entering wheat treated with 'Flutriafol 125 g/l SC' suggest levels of exposures will be within the AOEL (75 % of the AOEL without PPE) assuming that the isomer ratio is maintained in the residues workers are exposed to.
Bystanders	According to drift data or published study, bystander's exposure is estimated at < 1 % of AOEL Exposure to vapour post application according to a surrogate monitoring study: Adults (60 kg) 7.6 % of AOEL Children (15 kg) 17 % of AOEL Spray drift fallout into adjacent properties, children's exposure predicted at < 1 % of AOEL.

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

	RMS/peer review proposal
Flutriafol	**Xn** 'Harmful' **R22** 'Harmful if swallowed' **R63** 'Risk of harm to the unborn child'

Residues

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

Plant groups covered	Cereals: (barley, wheat) Oilseeds/pulses: (oilseed rape) Root crops (sugarbeet)
Rotational crops	Wheat, sugar beet, peas, oilseed rape
Metabolism in rotational crops similar to metabolism in primary crops?	Yes; parent, triazole alanine (TA) and triazole acetic acid (TAA) major components in rotational crops
Processed commodities	Not required
Residue pattern in processed commodities similar to residue pattern in raw commodities?	Not applicable
Plant residue definition for monitoring	Flutriafol
Plant residue definition for risk assessment	1. Flutriafol 2. TDM (provisional, pending the definition of a common and harmonised approach for all the active substances of the triazole chemical class)
Conversion factor (monitoring to risk assessment)	To be determined following the outcome of TDM review

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

Animals covered	Lactating cattle (but not appropriate, data gap), laying hen
Time needed to reach a plateau concentration in milk and eggs	No residues in milk 7 days in Eggs
Animal residue definition for monitoring	Open (residue definition required for ruminant product only, pending submission of a new metabolism study)
Animal residue definition for risk assessment	Open
Conversion factor (monitoring to risk assessment)	Open
Metabolism in rat and ruminant similar (yes/no)	Open
Fat soluble residue: (yes/no)	Open

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

There is clear evidence that flutriafol residues above 0.01 mg/kg could be present in crops sown/planted in rotation with wheat. Although insufficient data are available to quantify residues in all potential following crops, existing data suggest that an MRL of 0.05 mg/kg is appropriate for vegetables, pulses, oilseeds, sugar beet and cereals.

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

Flutriafol was found to be stable for up to 12 months in wheat plant, straw and grain.

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

	Ruminant:	Poultry:	Pig:
	Conditions of requirement of feeding studies		
Maximum Expected intakes by livestock ≥ 0.1 mg/kg diet (dry weight basis) (yes/no - If yes, specify the level)	Yes 0.51/1.27 mg/kg DM Dairy/beef cattle	No 0.016 mg/kg DM	No 0.019 mg/kg DM
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 : (Max) mg/kg		
Dose Rate	5 mg/kg DM (10N/4N)	5 mg/kg DM (300 N)	
Muscle	<0.01[a]	<0.01[a]	
Liver	0.28[a]	0.066[a]	
Kidney	<0.01[a]	-	
Fat	<0.01[a]	0.063[a]	
Milk	<0.01[a]		
Eggs		0.035[a]	

[a]: Residue levels for the parent flutriafol only. The acceptability of these feeding studies is pending the submission on a new ruminant metabolism study and the finalisation of the animal residue definitions for monitoring and risk assessment.

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 Southern Region field (F) or glasshouse (G)	Trials results relevant to the representative uses (a)	Recommendation/ comments	MRL estimated from trials according to representative use	HR (c)	STMR (b)
Wheat grain	N and S	North: 6x <0.01, <0.02, 0.02 South: 6x <0.02, 0.02	Trials on wheat conducted with a single application at 125 g a.s./ha, and PHI in the range of 30-76 days. Treatment in Northern trials performed from stages BBCH 38 to 59 (almost within the recommended stages). Growth stages not stated for southern trials, but PHIs consistent with the northern ones.	0.05	0.02	0.02
Wheat straw	N and S	North: 0.07, 3x 0.19, 0.24, 0.32, 0.43, 0.95 South: 0.34, 0.51, 0.55, 2.16		-	2.16	0.33

(a) Numbers of trials in which particular residue levels were reported *e.g.* 3x <0.01, 0.01, 6x 0.02, 0.04, 0.08, 2x 0.1, 2x 0.15, 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

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

ADI	0.01 mg/kg bw/day
TMDI (% ADI) according to EFSA PRIMO Model	Highest TMDI: - 4% ADI (WHO Cluster B) when considering the MRL on wheat only. - 19% ADI (UK toddler) when considering a default value of 0.05 mg/kg on cereals, vegetables, pulses, oilseeds and sugar beet (possible rotational crops)
TMDI (% ADI) according to national (to be specified) diets	-
IEDI (WHO European Diet) (% ADI)	-
NEDI (specify diet) (% ADI)	-
ARfD	0.05 mg/kg bw
IESTI (% ARfD) according to EFSA PRIMo Model	<2% ARfD (wheat) 15% ARfD (potatoes) when considering a default value of 0.05 mg/kg for the possible rotational crops.
NESTI (% ARfD) according to national (to be specified) large portion consumption data	
Factors included in IESTI and NESTI	

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

Plant products

Wheat	0.05

Animal products

	Open. Required for ruminant products, but pending the finalisation of the animal residue definitions.

Rotational crops (default value of 0.05 mg/kg[b])

Vegetables (fresh or frozen)	0.05[b]
Oilseeds/pulses	0.05[b]
Sugar plants	0.05[b]
Cereals (Others)	0.05[b]

[b]: default value based on a predicted peak plateau in soil of 0.107 mg/kg, resulting from a single application on wheat at a dose rate of 125 g a.s./ha. Should be reconsidered if further uses or higher dose rates are envisaged.

When the MRL is proposed at the LOQ, this should be annotated by an asterisk (*) after the figure.

Fate and Behaviour in the Environment

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

Mineralisation after 126 days	0.1-2.2 % after 126 d, [^{14}C-triazole]-label (n= 9) 1.2-2.6 % after 126 d, [^{14}C-carbinol]-label (n= 2)
Non-extractable residues after 126 days	0.9-6.1 % after 126 d, [^{14}C- triazole]-label (n= 9) 2-2.8% after 126 d, [^{14}C- carbinol]-label (n= 2)
Metabolites requiring further consideration - name and/or code, % of applied (range and maximum)	None.

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

Anaerobic degradation

Non-extractable residues after 126 days	3.4 % after 126d, [^{14}C- triazole]-label (n= 1)
Metabolites that may require further consideration for risk assessment	None

Soil photolysis

Metabolites that may require further consideration for risk assessment	No fully reliable information on soil photolysis was available. In addition no further information was considered necessary to support the current exposure assessments for the proposed uses.

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	use rate[12] [g/ha]	pH	t. °C / % MWHC	DT_{50} /DT_{90} *(ext.)* (d)	DT_{50} *(ext.)* (d) 20°C pF2/10kPa	St. (r^2)	Method of calculation
Sandy clay loam	100	6.8	20 °C / 40 %	1125/3736	nc	0.81	SFO
Sandy clay loam	100	6.8	20 °C / 40 %	2017/6700	nc	0.87	SFO
Loamy sand	100	5.8	20 °C / 40 %	1290/4286	nc	0.89	SFO
Loamy sand	100	5.8	20 °C / 40 %	1264/4200	nc	0.91	SFO
Clay loam	100	7.7	20 °C / 40 %	811/2694	nc	0.94	SFO
Sandy clay loam	100	6.4	20 °C / 40 %	3492/11599	nc	0.78	SFO
Loamy sand	100	6.5	20 °C / 40 %	672/2231	nc	1.00	SFO
Sandy loam	100	5.6	20 °C / 40 %	2464/8185	nc	0.97	SFO
Sand	750	6.2	20 °C / 40 %	nc[13]	nc	nc	-
Sand	750	7.5	20 °C / 40 %	2513/8347	nc	0.70	SFO
Loamy sand	750	5.7	20 °C / 40 %	1820/6048	nc	0.92	SFO
Sandy clay loam	100	6.8	20 °C / 15 %	nc	nc	nc	-
Sandy clay loam	100	6.8	30 °C / 40 %	1058/3514	nc	0.61	SFO
Sandy clay loam	1000	6.8	20 °C / 40 %	2031/6748	nc	0.92	SFO
Geometric mean at 20°C, 40% MWHC				1587			
Median at 20°C, 40% MWHC				1820			

nc: not calculated

[12] Corresponding to an application rate [g a.s./ha]
[13] could not be calculated as data do not show consistent decline

Field studies

Parent	Aerobic conditions							
Soil type (in all studies: application to bare soil).	Location (country or USA state).	time of appl.[14]	pH	Depth (cm)	DT_{50} (d) actual	DT_{90}(d) actual	St. (r^2)	Method of calculation
Loamy sand	UK	spr	6.5	0-30	942	3128	0.78	SFO
Clay loam	UK	spr	8.1	0-30	4089	13583	0.24	SFO
Sandy clay loam	UK	spr	6.9	0-30	3164	10512	0.22	SFO
ni[15]	DE	spr	ni	0-30	1303	4327	0.79	SFO
ni	DE	spr	ni	0-30	963	3200	0.75	SFO
ni	DE	spr	ni	0-30	1511	5018	0.55	SFO
ni	DE	aut	ni	0-30	1041	3457	0.73	SFO
ni	DE	aut	ni	0-30	720	2392	0.85	SFO
ni	DE	aut	ni	0-30	935	3105	0.58	SFO
Sandy loam	DE	spr	7.1	0-25	316	1051	0.75	SFO
Geometric mean (n=10)					1177			
Median (n=10)					1002			

pH dependence (yes / no) (if yes type of dependence) ‡	no
Soil accumulation and plateau concentration	Peak plateau concentration of 0.107 mg/kg reached after approximately 30 years of continuous application of 125 g a.s./ha per annum assuming an SFO DT_{50} of 1500 d.
Anaerobic conditions	No significant degradation observed

[14] spr = spring application
aut = autumn application
[15] ni = not indicated

Soil adsorption/desorption (Annex IIA, point 7.1.2)

Parent					
Soil Type	OC %	pH ($CaCl_2$)[a]	Kf (ml/g)	Kfoc	1/n
Roquefort (Loamy sand)	2.47	3.94	9.754	395	0.97
Lillyfield (Coarse sand)[a]	0.45	4.7	1.3	295	0.88*
Hyde Farm (Loam)[a]	1.9	5.6	5.7	304	0.92*
Bayonvillers (Silt loam)[a]	1.2	6.8	1.9	157	0.92*
Mussig (Clay loam)	4.67	7.53	5.766	123	0.94
Hesingue	2.73	5.4	2.8	104	0.585
Senozan	1.26	7.0	1.6	130	0.891
Mechtildshausen	1.46	7.1	1.8	122	0.868
Speyer 2.2	2.29	5.7	4.9	214	0.916
Arithmetic mean				205	0.91**
pH dependence, Yes or No			Results indicated a possible negative correlation between increasing pH and decreasing sorption (measured as K_{foc}). However based on the relatively small change in sorption over a relatively wide pH range, the RMS concluded that pH dependent sorption of flutriafol in agricultural soils is unlikely.		

[a] pH converted from value measured in H_2O to approximate value in $CaCl_2$ assuming a standard difference of 0.7 units (FOCUS groundwater guidance)
*1/n values not available in original study report but calculated independently by the Rapporteur from raw data.
**mean 1/n value reported in GLP study reports = 0.96

Aged sorption

Parent kinetic sorption parameters				
Soil Type	OC %	pH ($CaCl_2$)	fNE (-)	K_{des} (d^{-1})
Hesingue	2.73	5.4	0.574	0.064
Senozan	1.26	7.0	0.223	0.020
Mechtildshausen	1.46	7.1	0.494	0.032
Speyer 2.2	2.29	5.7	0.919	0.018
Arithmetic (fNE)/geometric (K_{des}) mean			0.55	0.03

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

Column leaching	No data submitted and none required.
Aged residues leaching	Aged for (d): 100 d at 20°C and 40% MWHC Time period (d): 45 d Eluation (mm): 12.5 mm per day
	Analysis of soil residues post ageing (soil residues pre-leaching): No analysis conducted but recovery of radioactivity after 100 d ageing was 89.6 to 94.7% of applied and assumed to be unchanged flutriafol Majority of residues retained in top 15 cm after leaching.
	Leachate: 0.9% applied radioactivity in leachate

Lysimeter/ field leaching studies	A field leaching study was conducted over 4 and a half years in Germany on a sandy soil with low organic carbon irrigated to ensure a total precipitation of > 800 mm/annum. Flutriafol was applied to wheat at a rate of 2 x 125 g a.s./ha. Soil pore water was collected using suction probes at 0.4, 0.8 and 1.2m depth. Results at different depths and at different sample points were variable throughout the trial. At 0.4 m depth, the level of flutriafol in the leachate was generally below 0.5 µg/L, but a number of peaks were observed, the maximum being a peak of 1.4 µg/L in July 2005. At 0.8 m depth, the level of flutriafol was generally below 0.2 µg/L. At 1.2 m depth, the level of flutriafol in the leachate increased and decreased irregularly, with a maximum peak of 2.9 µg/L in May 2007.

PEC (soil) (Annex IIIA, point 9.1.3)

Parent Method of calculation	DT_{50} (d): 1500 days Kinetics: 1st order Field or Lab: representative value from field studies.
Application data	Crop: wheat Depth of soil layer: (e.g. 5 cm). Soil bulk density: 1.5 g/cm^3 % plant interception: 90% for each application Number of applications: 1 Interval (d): - Application rate(s): 125 g as/ha

PEC$_{(s)}$ (mg/kg)	Single application Actual	Single application Time weighted average
Initial	0.017	0.017
Short term 24h	0.017	0.017
2d	0.017	0.017
4d	0.017	0.017
Long term 7d	0.017	0.017
28d	0.016	0.016
50d	0.016	0.016
100d	0.016	0.016
365d	0.014	0.015
Plateau concentration	0.091 mg/kg after approx. 30 yrs. Peak accumulated residue of 0.107 mg/kg.	

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

Hydrolytic degradation of the active substance and metabolites > 10%.	Flutriafol was stable to hydrolysis at pH 5, 7 and 9 at 25°C over 30 d.
Photolytic degradation of active substance and metabolites above 10%	Flutriafol was photolytically stable in aqueous buffer at pH 7 and 25°C when exposed to artificial light equivalent to 66 d of Florida summer sunshine.
Quantum yield of direct phototransformation in water at □ > 290 nm	No measurable photodegradation. Quantum yield assumed to be zero.
Readily biodegradable (yes/no)	Not readily biodegradable.

Degradation in water / sediment

Parent	Distribution (Maximum in sediment: 66.2-75.5% after 60 to 100 d)									
Water / sediment system	H w	H sed	t. °C	DT_{50}-DT_{90} whole	St. (r^2)	$DT_{50}D T_{90}$ water	St. (r^2)	DT_{50}-DT_{90} sed	St. (r^2)	Method of calculation
Virginia water	7.9	6.7	20	n.c	-	27[a]		n.c.	-	SFO
Old Basing	7.3	7.8	20	n.c	-	27[a]		n.c.	-	SFO
Geometric mean/median			-	-	-	27/27	-	-	-	-

Mineralization and non extractable residues					
Water / sediment system	pH w	pH sed	Mineralization x % after n d. (end of the study).	Non-extractable residues in sed. Max x % after n d	Non-extractable residues in sed. Max x % after n d (end of the study)
Virginia water	7.9	6.7	0.3% after 100 d	5.0% after 100 d	5.0% after 100 d

Old Basing	7.3	7.8	0.1% after 100 d	2.1% after 100 d	2.1% after 100 d

- [a]: this is a dissipation DT50 since it includes loss from the water phase due to partitioning to sediment
- n.c.: not calculated due to minimal degradation. DT50 assumed to be 1000d for both water and sediment for the purposes of FOCUSsw modeling.
-

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

Parent Parameters used in FOCUSsw step 1 and 2	Version control no. of Focus calculator: Molecular weight (g/mol): 301.3 Water solubility (mg/L): 95 Koc (L/kg): 205 DT_{50} soil (d): 939 days (field. In accordance with FOCUS SFO) DT50 water/sediment system (d): 1000 (representative worst case from sediment water studies) DT50 water (d): 1000 DT50 sediment (d): 1000 Crop interception (%): 70 (full crop cover at Step 2)
Parameters used in FOCUSsw step 3 (if performed)	Version control no.'s of FOCUS software: Koc: 205 Vapour pressure: 0 1/n: 0.91 (Freundlich exponent for soil)
Application rate	Crop: winter cereals Number of applications: 1 Interval (d): - Application rate(s): *125* g as/ha Application window: 1 April – 15 July
Main routes of entry	2.759 % drift from 1 metre (Step 1) 2.438% drift from 1 metre (Step 2) 10% runoff/drainage (at FOCUSsw Step 1) 2-4% runoff/drainage (at FOCUSsw Step 2 NE/SE March-May)

FOCUS STEP 1 Scenario	Day after overall maximum	PEC_{SW} (µg/L)		PEC_{SED} (µg/kg)	
		Actual	TWA	Actual	TWA
	0	33.87	-	67.08	-
	1	33.60	33.74	68.88	67.98
	2	33.58	33.66	68.84	68.42
	4	33.53	33.61	68.74	68.61
	7	33.46	33.56	68.60	68.63
	14	33.30	33.47	68.27	68.53
	21	33.14	33.39	67.94	68.39
	28	32.98	33.31	67.61	68.23
	42	32.66	33.14	66.95	67.92
	50	32.48	33.05	66.58	67.73
	100	31.37	32.49	64.31	66.59

Total load PECsw appropriate for use in the water spiked sediment dweller risk assessment = 42.8 µg/l.

FOCUS STEP 2 Scenario	Day after overall maximum	PEC_{SW} (µg/L)		PEC_{SED} (µg/kg)	
		Actual	TWA	Actual	TWA
Northern EU	0	2.93	-	5.85	-
	1	2.86	2.89	5.85	5.85
	2	2.85	2.87	5.85	5.85

	4	2.85	2.86	5.84	5.85
	7	2.84	2.86	5.83	5.84
	14	2.83	2.85	5.80	5.83
	21	2.82	2.84	5.77	5.81
	28	2.80	2.83	5.74	5.80
	42	2.78	2.82	5.69	5.77
	50	2.76	2.81	5.66	5.75
	100	2.67	2.76	5.46	5.66

FOCUS STEP 2 Scenario	Day after overall maximum	PEC_{SW} (µg/L)		PEC_{SED} (µg/kg)	
		Actual	TWA	Actual	TWA
Southern EU	0	4.88	-	9.86	-
	1	4.81	4.85	9.86	9.86
	2	4.81	4.83	9.85	9.86
	4	4.80	4.82	9.84	9.85
	7	4.79	4.81	9.82	9.84
	14	4.77	4.79	9.77	9.82
	21	4.75	4.78	9.72	9.79
	28	4.72	4.77	9.68	9.77
	42	4.68	4.75	9.58	9.72
	50	4.65	4.73	9.53	9.70
	100	4.49	4.65	9.20	9.53

Total load PECsw appropriate for use in the water spiked sediment dweller risk assessment = 6.1 µg/l.

FOCUS STEP 3 Scenario	Water body	PEC_{SW} (µg/L) Actual	PEC_{SED} (µg/kg) Actual	Main route of entry to surface water
D1	Ditch	3.361	13.759	Drainage
D1	Stream	2.127	7.604	Drainage
D2	Ditch	5.290	15.994	Drainage
D2	Stream	3.299	2.345	Drainage
D3	Ditch	1.001	2.976	Spray drift for surface water Drainage for sediment
D4	Pond	1.481	7.190	Drainage
D4	Stream	1.320	2.354	Drainage
D5	Pond	1.035	6.112	Spraydrift for surface water Drainage for sediment
D5	Stream	0.818	1.523	Drainage
D6	Ditch	0.881	1.358	Drainage
R1	Pond	0.207	0.681	Runoff
R1	Stream	1.898	0.930	Runoff
R3	Stream	2.682	1.170	Runoff
R4	Stream	2.247	0.723	Runoff

Only maximum initial values are reported as only these values were used in the aquatic risk assessment.

PEC (groundwater) (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 – Modelling using FOCUS model with appropriate FOCUS gw scenarios, according to FOCUS guidance. Model used: FOCUS PEARL (version 3.3.3) and FOCUS PELMO v 3.3.2 Scenarios (list of names): Châteaudun, Hamburg, Jokioinen, Kremsmünster, Okehampton, Piacenza, Porto, Sevilla, Thiva

	Crop: Winter cereals Median parent $DT_{50field}$ 1002 d (n=10, un-normalised; moisture correction routines disabled). K_{foc}: parent, mean: 205 ml/g, $^1/_n$= 0.91 Q_{10} = 2.2 TSCF = 0.7 (calculated following FOCUS GW guidance)
Application rate	Application rate: 125 g a.s./ha. No. of applications: 1 at BBCH 40-55 (crop interception 90%) Time of application (month or season): spring (March-May). Application dates were chosen based on typical agricultural practice: 15-March for Sevilla; 15-April for Piacenza, Porto & Thiva; 29-April for Châteaudun; 15-May for Hamburg, Kremsmünster & Okehampton; 29-May for Jokioinen.

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

PEARLv3.3.3 / winter cereals	Scenario	Application every year (1/1)	Applications every other year (1/2)	Applications every third year (1/3)
	Châteaudun	0.570	0.275	0.174
	Hamburg	0.598	0.274	0.173
	Jokioinen	0.237	0.122	**0.076**
	Kremsmünster	0.554	0.271	0.166
	Okehampton	0.602	0.281	0.181
	Piacenza	0.924	0.477	0.294
	Porto	0.175	**0.080**	**0.048**
	Sevilla	0.263	0.152	**0.080**
	Thiva	0.834	0.393	0.251

The model outputs were consulted to confirm that the duration of the groundwater simulations in each case were sufficient to reach an approximate plateau in the simulated scenarios.

PELMO v3.3.2 / winter cereals	Scenario	Application every year (1/1)	Applications every other year (1/2)	Applications every third year (1/3)
	Châteaudun	0.420	0.191	0.122
	Hamburg	0.502	0.228	0.147
	Jokioinen	**0.080**	**0.072**	**0.044**
	Kremsmünster	0.471	0.226	0.148
	Okehampton	0.503	0.234	0.148
	Piacenza	0.835	0.396	0.277
	Porto	**0.099**	**0.045**	**0.027**
	Sevilla	**0.003***	**0.020**	**0.012**
	Thiva	0.511	0.245	0.164

*the lower leaching observed for the Sevilla scenario following application every year relative to that seen for application every second or third year is considered to be an artifact of the very low leaching observed during the standard 20 year simulation. For this scenario only, the longer term simulations allowed an increased leaching risk to be identified even when the application frequency was reduced.

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

Direct photolysis in air	Not studied - no data requested
Quantum yield of direct phototransformation	Not studied - no data requested

Photochemical oxidative degradation in air	DT_{50} of 1.1 d derived by the Atkinson method of calculation assuming an OH radical concentration in the troposphere of 1.5 x 10^6 molecules cm^{-3}
Volatilisation	from plant surfaces (similar to BBA guideline): < 3% after 24 hours
	from soil (similar to BBA guideline): < 3% after 24 hours
Metabolites	None.

PEC (air)

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

$PEC_{(a)}$

Maximum concentration	Assumed to be negligible

Residues requiring further assessment

Environmental occurring metabolite requiring further assessment by other disciplines (toxicology and ecotoxicology).	Soil, Surface Water, Sediment, Groundwater and Air: Parent flutriafol only

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)	France, 1987-1989. Samples taken from River Seine and River Marne. Concentrations < LOQ of 0.05µg/l.
Groundwater (indicate location and type of study)	France, 1987-1989. Samples taken from 11 wells ranging from shallow (<15m) to deep (>30m) reported to cover the most significant agricultural areas of France Concentrations < LOQ of 0.05µg/l. UK, Lincolnshire, 1999. Samples taken from two boreholes situated on a vulnerable aquifer in an area of potentially high flutriafol usage. Concentrations < LOQ of 0.1µg/l. UK: 2704 samples taken from 1550 boreholes between year 2000 and year 2005. In 39 out of 1550 boreholes, the residue level of Flutriafol was above the LOD (0.008 to 0.036 µg/L) in at least one sample. One finding at one site in England was above the regulatory trigger value of 0.1 µg/L in 2003 as well as four findings at two sites in England in 2005. According to the Environmental Agency the borehole with the finding in 2003 was located in an urban industrial area.
Air (indicate location and type of study)	No appropriately validated monitoring data available.

Points pertinent to the classification and proposed labeling

with regard to fate and behaviour data	Not ready biodegradable. Candidate for R53

Ecotoxicology

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

Species	Test substance	Time scale	End point
Birds ‡			
red-legged partridge	a.s.	Acute	LD_{50} = 616 mg a.s./kg bw
mallard duck	a.s.	Short-term	LC_{50} = 435 mg a.s./kg bw/d
bobwhite quail	a.s.	Long-term	NOEC = 35.8 mg a.s./kg bw/d
mallard duck	a.s.	Long-term	BMD_L of 2.8 mg/kg bw/d [1]
Mammals ‡			
mouse	a.s.	Acute	LD_{50} = 179 mg a.s./kg bw[2]
rat	Preparation	Acute	LD_{50} > 2000 mg Formulation/kg bw
rat	a.s.	Long-term	NOAEL = 13.5 mg a.s./kg bw/d

[1]Bench Mark Dose approach used in absence of NOEC. BMD_L of 2.8 mg/kg bw/d proposed –
[2]LD_{50} value for the mouse is not considered to be reliable due to the prolonged fasting period prior to dosing, however this value is considered to be worse-case.

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

Two applications of 0.125 kg flutriafol/ha to wheat

Indicator species/Category	Time scale	ETE (mg a.s./kg bw/d)	TER	Annex VI Trigger
Tier 1 (Birds)				
Insectivorous bird cereals/early & late	Acute	6.76	91.1	10
	Short-term	3.77	115	10
	Long-term	3.77	**0.74**	5
Tier 1 (Mammals)				
Insectivorous mammal	Acute	1.10	163	10
	Long-term	0.40	33.8	5
Refined Risk (Birds) using $BMDL_{10}$				
Skylark	Long-term	1.47	1.9	5

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

Group	Test substance	Time-scale	Test species	Endpoint	Toxicity (µg a.s./l)
Fish	a.s.	Acute	*Lepomis macrochirus*	96 h LC_{50}	33000 ^{mm}
	formulation	Acute	*Oncorhynchus mykiss*	96 h LC_{50}	920 ^{mm}
	a.s.	Chronic[1]	*Pimephales promelas*	33 d NOEC	4800 ^{mm}
	formulation	Chronic	*Oncorhynchus mykiss*	28 d NOEC	390 ^{mm}
Aquatic inverte-brate	a.s.	Acute	*Daphnia magna*	48 h EC_{50}	67000 ^{mm}
	formulation	Acute	*Daphnia magna*	48 h EC_{50}	890 ^{nom}
	a.s.	Chronic	*Daphnia magna*	21 d NOEC	310 ^{mm}
	formulation	Chronic	*Daphnia magna*	21 d NOEC	13 ^{nom}
Algae	a.s.	Acute	*Scenedesmus subspicatus*	72 h E_bC_{50}	1900 ^{nom}
	formulation	Acute	*Pseudokirchneriella subcapitata*	72 h E_bC_{50}	500 ^{mm}
Lemna	formulation	Acute	*Lemna gibba*	7 day E_bC_{50}	650^{mm}

Sediment dwelling organism	a.s.	Chronic	*Chironomus riparius*	26 d NOEC	1600 [nom]

[mm] Based on mean measure values
[nom] Based on nominal values
[1]Early Life Stage study

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

FOCUS Step 1 – active substance

Two applications of 0.125 kg flutriafol/ha to wheat

Test substance	Organism	Toxicity end point (µg a.s./L)	Time scale	PEC_i (µg a.s./L)	TER	Annex VI Trigger
a.s.	Fish	33000	Acute	33.87	974	100
a.s.	Fish	4800	Chronic	33.87	142	10
a.s.	Aquatic invertebrates	67000	Acute	33.87	1978	100
a.s.	Aquatic invertebrates	310	Chronic	33.87	**9.2**	10
a.s.	Algae	1900	Chronic	33.87	56	10
a.s.	Sediment-dwelling organisms	1600	Chronic	42.8	37	10

* Total load PEC_{SW} appropriate for the sediment dweller risk assessment

FOCUS Step 2 – active substance

Test substance	N/S [1]	Organism	Toxicity end point (µg/L)	Time scale	PEC [2]	TER	Annex VI Trigger
a.s.	N	Aquatic invertebrates	310	Chronic	2.93	106	10
a.s.	S	Aquatic invertebrates	310	Chronic	4.88	64	10

[1] Northern/Southern Europe
[2] Maximum values have been used

Risk from spray drift of formulation

Test substance	Species	Time scale	Toxicity values (µg a.s./L)	Waterbody	Initial PEC_{sw} (µg a.s./L)	TER	TER trigger
Formulation	Fish	Acute	LC_{50} = 920	Ditch	0.80	1150	100
				Stream	0.60	1533	
				Pond	0.03	30667	
Formulation	Aquatic inverte-brates	Acute	EC_{50} = 890	Ditch	0.80	1113	100
				Stream	0.60	1483	
				Pond	0.03	29667	
Formulation	Algae	Acute	E_bC_{50} = 500	Ditch	0.80	625	10
				Stream	0.60	833	
				Pond	0.03	16667	
Formulation	*Lemna*	Acute	E_bC_{50} = 650	Ditch	0.80	813	10
				Stream	0.60	1083	
				Pond	0.03	21667	
Formulation	Fish	Chronic	NOEC = 390	Ditch	0.80	488	10
				Stream	0.60	650	
				Pond	0.03	13000	
Formulation	Aquatic inverte-brates	Chronic	NOEC = 13	Ditch	0.80	16	10
				Stream	0.60	22	
				Pond	0.03	433	

Bioconcentration				
	Active substance	Metabolite1	Metabolite2	Metabolite3
$logP_{O/W}$	2.3			
Bioconcentration factor (BCF) ‡	6.5			
Annex VI Trigger for the bioconcentration factor	100			
Clearance time (days) (CT_{50})	< 1 day			
(CT_{90})	3-7 days			
Level and nature of residues (%) in organisms after the 14 day depuration phase	0%			

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

Test substance	Acute oral toxicity (LD_{50} µg a.s./bee)	Acute contact toxicity (LD_{50} µg a.s./bee)
a.s. ‡	> 2	> 50
Preparation	> 49	> 52.5
Field or semi-field tests		
Not required		

One application of 0.125 kg flutriafol/ha to wheat

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

Test substance	Route	Hazard quotient	Annex VI Trigger
a.s.	Contact	< 2.5	50
a.s.	oral	< 62.5 *	50
Preparation	Contact	< 2.38	50
Preparation	oral	2.55	50

* Function of concentrations tested in study, 7% mortality at 2 µg a.s./bee, which was the highest dose tested.

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

Laboratory tests with standard sensitive species

Species	Test Substance	End point	Effect (LR_{50} g a.s./ha)
Typhlodromus pyri ‡	Formulation	Mortality	204.5
Aphidius rhopalosiphi ‡	Formulation.	Mortality	> 1125

Risk assessment for standard sensitive species - one application of 0.125 kg flutriafol/ha to wheat

Test substance	Species	Effect (LR_{50} g a.s./ha)	HQ in-field	HQ off-field[1]	Trigger
Formulation	*Typhlodromus pyri*	204.5	0.613	0.002	2
Formulation	*Aphidius rhopalosiphi*	> 1125	< 0.11	< 0.00004	2

[1] Drift value is set at 2.77% for 1 application in field crops at 1m distance

One application of 0.125 kg flutriafol/ha to wheat

Further laboratory and extended laboratory studies ‡

Species	Life stage	Test substance/ substrate/ duration	End point	Dose (g a.s./ha) [$]	Effect	Trigger value
Pterostrichus cupreus	Adult	Formulation/soil/6 days	Mortality	0 500	0% 0%	50 % (control corrected)
			Immobility	0 500	0% 0%	
Pardosa spp.	Adult	Formulation/soil/6 days	Mortality	0 500	12% 10%	
			Immobility	0 500	2% 0%	
			Feeding	0 500	1.00 * 1.15 *	
A. rhopalosiphi	Adult	Formulation/barley seedlings/48 hours	Mortality	0 125	0% 0%	
			Parasitism	0 125	34 [#] 35 [#]	
Episyrphus balteatus	Larvae	Formulation/bean seedlings /until emergence	Larvae pupated	0 125	77% 93%	
			Adults emerged	0 125	100% 96%	

[$] Initial residues * Feeding index 0-2 [#] No. aphid mummies/female

Field or semi-field tests
Not 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			
Eisenia fetida	a.s. ‡	Acute 14 days	$LC_{50\ corr}$ > 500 mg a.s./kg soil
Eisenia fetida	Preparation	Acute 14 days	$LC_{50\ corr}$ > 500 mg a.s./kg soil
Eisenia fetida	Preparation	Chronic 56 days	$NOEC_{corr}$ 6.1 mg a.s./kg soil
Organic matter breakdown			
Straw decay	Preparation	30 days	NOEC = 18 mg a.s./kg straw
Soil micro-organisms			
Nitrogen mineralisation	a.s. ‡	28 days	< 25 % effect at day 28 at 1.67 mg a.s./kg dw soil

Test organism	Test substance	Time scale	End point
	Preparation	77 days	< 25 % effect at day 77 at 1.6 mg a.s./kg dw soil
Carbon mineralisation	a.s. ‡	29 days	< 25 % effect at day 28 at 1.67 mg a.s./kg dw soil
	Preparation	50 days	< 25 % effect at day 50 at 1.6 mg a.s./kg dw soil
Field studies			
10 yr field study (multiple applications) on earthworms, conducted with formulation: NOEC = 0.52 mg a.s./kg soil, equivalent to 100 g a.s./ha/yr (calculated)			
4 yr field study (multiple applications) on soil micro-arthropods, conducted with formulation: NOEC = 0.45 mg a.s./kg soil (from mean residue data at end of study)			
3 yr field study (single applications) on soil micro-arthropods, conducted with formulation: NOEC = 2 mg a.s./kg soil (calculated)			
5 yr field study (multiple applications) on soil micro-organisms/microbial processes, conducted with Formulation: NOEC = 0.4 mg a.s./kg soil (measured)			
3 yr field study (single application) on microbial activity, conducted with formulation: 28% reduction in carbon mineralisation (total C) at 0.69 mg a.s./kg soil. < 25% reduction in carbon mineralisation at 0.31 mg a.s./kg soil. < 25% reduction in nitrogen mineralisation at 0.69 mg a.s./kg soil. Based on mean measured concentrations.			

One application of 0.125 kg flutriafol/ha to wheat

Toxicity/exposure ratios for soil organisms

Test organism	Test substance	Time scale	Soil PEC (mg a.s. /kg soil)	TER	Trigger
Earthworms					
Eisenia fetida	A.s./preparation $LC50_{corr}$ > 500 mg a.s./kg	Acute – 1st yr	0.017	> 29412	10
		Acute – subsequent yrs	0.107 (peak plateau)	> 4673	10
	'Flutriafol 125 g/L SC' $NOEC_{corr}$ 6.1 mg a.s./kg	Chronic – 1st yr	0.017	359	5
		Chronic – subsequent yrs	0.107 (peak plateau)	57	5

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

Field study on earthworms: No significant long-term effects on earthworms at calculated soil concentrations higher than the peak

accumulated plateau PEC_{soil} of 0.107 mg a.s./kg soil, and at an application rate higher than proposed in the GAP. Field studies on soil macro-organisms: No significant long-term effects at concentrations well above the maximum PEC_{soil} Straw decay laboratory study: No significant effects at concentrations well above residues levels in straw at the proposed application rate. Field studies on soil micro-organisms: 28% effect at 0.69 mg a.s./kg soil, which is slightly above the Annex VI trigger of 25% but at a much higher dose than the maximum PEC_{soil} (0.107 mg a.s./kg soil) from the proposed use. No other effects > 25% at doses above the maximum PEC_{soil}

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

EC_{50} > 134 g a.s./ha (seedling emergence and vegetative vigour). TER 36.2 at 1m.

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

Not required

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

Test type/organism	end point
Activated sludge	NOEC = 1000 mg a.s./L
Pseudomonas sp	NOEC = 104 µ a.s./kg soil

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

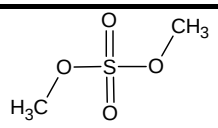
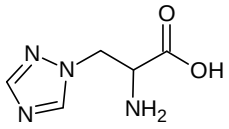
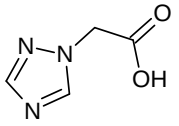
Compartment	
soil	flutriafol
water	flutriafol
sediment	flutriafol
groundwater	n.a.

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	R51/R53

	RMS/peer review proposal
Preparation	R51/R53

APPENDIX B – USED COMPOUND CODE(S)

Code/Trivial name*	Chemical name	Structural formula
dimethyl sulphate	dimethyl sulfate	
Triazole alanine (TA)	3-(1*H*-1,2,4-triazol-1-yl)-DL-alanine	
Triazole acetic acid (TAA)	1*H*-1,2,4-triazol-1-ylacetic acid	

* The name in bold is the name used in the conclusion.

ABBREVIATIONS

1/n	slope of Freundlich isotherm
ε	decadic molar extinction coefficient
°C	degree Celsius (centigrade)
µg	microgram
µm	micrometer (micron)
a.s.	active substance
AChE	acetylcholinesterase
ADE	actual dermal exposure
ADI	acceptable daily intake
AF	assessment factor
AOEL	acceptable operator exposure level
AP	alkaline phosphatase
AR	applied radioactivity
ARfD	acute reference dose
AST	aspartate aminotransferase (SGOT)
AV	avoidance factor
BCF	bioconcentration factor
BMD	benchmark dose modelling
BMDL	benchmark dose modelling low
BUN	blood urea nitrogen
bw	body weight
CAS	Chemical Abstract Service
CFU	colony forming units
ChE	cholinesterase
CI	confidence interval
CIPAC	Collaborative International Pesticide Analytical Council Limited
CL	confidence limits
d	day
DAA	days after application
DAR	draft assessment report
DAT	days after treatment
DM	dry matter
DT_{50}	period required for 50 percent disappearance (define method of estimation)
DT_{90}	period required for 90 percent disappearance (define method of estimation)
dw	dry weight
EbC_{50}	effective concentration (biomass)
EC_{50}	effective concentration
ECHA	European Chemical Agency
EEC	European Economic Community
EINECS	European Inventory of Existing Commercial Chemical Substances
ELINCS	European List of New Chemical Substances
EMDI	estimated maximum daily intake
ER_{50}	emergence rate/effective rate, median
ErC_{50}	effective concentration (growth rate)
ETE	estimated theoretical exposure
EU	European Union
EUROPOEM	European Predictive Operator Exposure Model
f(twa)	time weighted average factor
FAO	Food and Agriculture Organisation of the United Nations
FIR	Food intake rate
FOB	functional observation battery
FOCUS	Forum for the Co-ordination of Pesticide Fate Models and their Use
g	gram

GAP	good agricultural practice
GC	gas chromatography
GC-MSD	gas chromatography with mass-selective detection
GC-NPD	gas chromatography with nitrogen phosphorous detector
GC-TID	gas chromatography with thermionic detector
GCPF	Global Crop Protection Federation (formerly known as GIFAP)
GGT	gamma glutamyl transferase
GM	geometric mean
GS	growth stage
GSH	glutathion
h	hour(s)
ha	hectare
Hb	haemoglobin
Hct	haematocrit
hL	hectolitre
HPLC	high pressure liquid chromatography or high performance liquid chromatography
HPLC-MS	high pressure liquid chromatography – mass spectrometry
HPLC-MS-MS	high pressure liquid chromatography with tandem mass spectrometry
HQ	hazard quotient
IEDI	international estimated daily intake
IESTI	international estimated short-term intake
ILV	inter laboratory validation
ISO	International Organisation for Standardisation
IUPAC	International Union of Pure and Applied Chemistry
JMPR	Joint Meeting on the FAO Panel of Experts on Pesticide Residues in Food and the Environment and the WHO Expert Group on Pesticide Residues (Joint Meeting on Pesticide Residues)
K_{doc}	organic carbon linear adsorption coefficient
kg	kilogram
K_{Foc}	Freundlich organic carbon adsorption coefficient
L	litre
LC	liquid chromatography
LC_{50}	lethal concentration, median
LC-MS	liquid chromatography-mass spectrometry
LC-MS-MS	liquid chromatography with tandem mass spectrometry
LD_{50}	lethal dose, median; dosis letalis media
LDH	lactate dehydrogenase
LOAEL	lowest observable adverse effect level
LOD	limit of detection
LOQ	limit of quantification (determination)
m	metre
M/L	mixing and loading
MAF	multiple application factor
MCH	mean corpuscular haemoglobin
MCHC	mean corpuscular haemoglobin concentration
MCV	mean corpuscular volume
mg	milligram
mL	millilitre
mm	millimetre
MRL	maximum residue limit or level
MS	mass spectrometry
MSDS	material safety data sheet
MTD	maximum tolerated dose
MWHC	maximum water holding capacity

NESTI	national estimated short-term intake
ng	nanogram
NOAEC	no observed adverse effect concentration
NOAEL	no observed adverse effect level
NOEC	no observed effect concentration
NOEL	no observed effect level
OM	organic matter content
Pa	Pascal
PD	proportion of different food types
PEC	predicted environmental concentration
PEC_{air}	predicted environmental concentration in air
PEC_{gw}	predicted environmental concentration in groundwater
PEC_{sed}	predicted environmental concentration in sediment
PEC_{soil}	predicted environmental concentration in soil
PEC_{sw}	predicted environmental concentration in surface water
pH	pH-value
PHED	pesticide handler's exposure data
PHI	pre-harvest interval
PIE	potential inhalation exposure
pK_a	negative logarithm (to the base 10) of the dissociation constant
P_{ow}	partition coefficient between *n*-octanol and water
PPE	personal protective equipment
ppm	parts per million (10^{-6})
POEM	Predictive Operator Exposure Model
ppp	plant protection product
PT	proportion of diet obtained in the treated area
PTT	partial thromboplastin time
QSAR	quantitative structure-activity relationship
r^2	coefficient of determination
RMS	rapporteur Member State
RPE	respiratory protective equipment
RUD	residue per unit dose
SC	suspension concentrate
SD	standard deviation
SFO	single first-order
SSD	species sensitivity distribution
STMR	supervised trials median residue
$t_{1/2}$	half-life (define method of estimation)
TDM	Triazole Derivative Metabolites
TDMG	Triazole Derivative Metabolite Group
TER	toxicity exposure ratio
TER_A	toxicity exposure ratio for acute exposure
TER_{LT}	toxicity exposure ratio following chronic exposure
TER_{ST}	toxicity exposure ratio following repeated exposure
TK	technical concentrate
TLV	threshold limit value
TMDI	theoretical maximum daily intake
TRR	total radioactive residue
TSH	thyroid stimulating hormone (thyrotropin)
TWA	time weighted average
UDS	unscheduled DNA synthesis
UV	ultraviolet
W/S	water/sediment
w/v	weight per volume
w/w	weight per weight

WBC	white blood cell
WG	water dispersible granule
WHO	World Health Organisation
wk	week
yr	year