TECHNICAL REPORT

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Outcome of the consultation with Member States, the applicant and EFSA on the pesticide risk assessment for fluquinconazole in light of confirmatory data

European Food Safety Authority (EFSA)

Abstract

The European Food Safety Authority (EFSA) was asked by the European Commission to provide scientific assistance with respect to the risk assessment for an active substance in light of confirmatory data requested following approval in accordance with Article 6(1) of Directive 91/414/EEC and Article 6(f) of Regulation (EC) No 1107/2009. In this context EFSA's scientific views on the specific points raised during the commenting phase conducted with Member States, the applicant and EFSA on the confirmatory data and their use in the risk assessment for fluquinconazole are presented. The current report summarises the outcome of the consultation process organised by the rapporteur Member State Ireland and presents EFSA's scientific views and conclusions on the individual comments received.

Key words: fluquinconazole, peer review, confirmatory data, risk assessment, pesticide, fungicide

Requestor: European Commission

Question number: EFSA-Q-2015-00397

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Summary

Fluquinconazole was approved on 1 January 2012 by Commission Implementing Regulation (EU) No 806/2011, in accordance with Regulation (EC) No 1107/2009. It was a specific provision of the approval that the applicant was required to submit to the European Commission further studies in the areas of residues and ecotoxicology by 31 December 2013.

In accordance with the specific provision, the applicant, BASF SE, submitted an updated dossier in December 2013, which was evaluated by the designated rapporteur Member State (RMS), Ireland, in the form of an addendum to the draft assessment report. In compliance with the guidance document SANCO 5634/2009-rev.6.1, the RMS distributed the addendum to Member States, the applicant and EFSA for comments on 6 August 2014. The RMS collated all comments in the format of a reporting table, which was submitted to EFSA on 25 June 2015. EFSA added its scientific views on the specific points raised during the commenting phase in column 4 of the reporting table.

The current report summarises the outcome of the consultation process organised by the RMS, Ireland, and presents EFSA's scientific views and conclusions on the individual comments received.

The **nature of residues in products of animal origin** was considered as sufficiently addressed to derive the residue definitions for risk assessment as a) sum of fluquinconazole and metabolite dione (M615F001) expressed as fluquinconazole, and b) TDMs (triazole derivative metabolites), as already agreed on during the previous peer review (EFSA Journal 2011;9(5):2096). These residue definitions are valid for ruminants only. It is noted that the RMS disagrees on the inclusion of the metabolite dione in the residue definition for risk assessment. Although sufficient residue trials were provided to address the magnitude of the TDMs (1,2,4-triazole, triazolyl alanine, triazolyl acetic acid, triazole lactic acid) both in **primary and rotational crops** and to demonstrate that the **contribution of the residues of the metabolite dione in rotational crops to the overall consumer exposure** can be considered as negligible, no conclusion can be drawn on the acceptability of these trials pending the submission of residue storage stability data on dione and the TDMs compounds. An overall consumer exposure assessment with regard to TDMs residues could not be conducted as the toxicity of TDMs is currently not addressed. EFSA does not see the need for a peer review on these confirmatory data as the storage stability data and the toxicological properties of the TDMs are currently under assessment by the United Kingdom and storage stability data on metabolite dione are required.

The issues related to ecotoxicology were further evaluated in the addendum provided by the RMS. As regards to the **acute risk to insectivorous mammals**, a tier-1 risk assessment according to the EFSA guidance document on birds and mammals (EFSA Journal 2009;7(12):1438) was performed, but considering an omnivore scenario. The **long-term risk to insectivorous and herbivorous birds and mammals** was partly addressed. Several refinement options were applied, but some of them were not agreed by the commenting parties. According to the EFSA guidance document on birds and mammals, some more scenarios should also be considered. It is noted that the applicant has proposed some changes to the original GAP as regards the growth stage of the application. This is connected to the fact that some scenarios were not addressed and also related to a refinement option, which is disagreed if the original GAP is considered. An updated risk assessment was performed addressing the risk to **earthworm-eating mammals**. Based on this assessment, a low risk could be concluded provided that there is at least 15% dilution in food consumption of the vermivorous mammals living in the agricultural area treated with fluquinconazole. However, some uncertainties of this assessment were noted during the commenting. A sufficient **fish full-life-cycle study** was submitted. The risk assessment considering the endpoint from this study indicated a low risk. However, it is considered that the power of the statistical analysis should be further investigated in order to confirm the derived endpoint.

Overall, several elements of the ecotoxicology confirmatory data package were not sufficiently addressed and there were divergent views between RMS, EFSA or MSs on several aspects of the risk assessments. A focussed peer-review on the outstanding issues is recommended.

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1. Introduction

1.1. Background and Terms of Reference as provided by the requestor

Fluquinconazole was approved on 1 January 2012 by Commission Implementing Regulation (EU) No 806/2011[1], in accordance with Regulation (EC) No 1107/2009[2]. EFSA previously finalised a Conclusion on this active substance on 25 February 2011 (EFSA, 2011).

It was a specific provision of the approval that the applicant was required to submit to the European Commission by 31 December 2013 further confirmatory information as regards:

- residues of triazole derivative metabolites (TDMs) in primary crops, rotational crops and products of animal origin;
- the contribution of the potential residues of the metabolite dione in rotational crops to the overall consumer exposure;
- the acute risk to insectivorous mammals;
- the long-term risk to insectivorous and herbivorous birds and mammals;
- the risk to earthworm-eating mammals;
- the endocrine disruption potential in aquatic organisms (fish full-life-cycle study).

In accordance with the specific provision, the applicant, BASF SE, submitted an updated dossier in December 2013, which was evaluated by the designated rapporteur Member State (RMS), Ireland, in the form of an addendum to the draft assessment report (Ireland, 2014). In compliance with the guidance document SANCO 5634/2009-rev.6.1 (European Commission, 2013), the RMS distributed the addendum to Member States, the applicant and EFSA for comments on 6 August 2014. The RMS collated all comments in the format of a reporting table, which was submitted to EFSA on 25 June 2015. EFSA added its scientific views on the specific points raised during the commenting phase in column 4 of the reporting table.

The current report summarises the outcome of the consultation process organised by the RMS, Ireland, and presents EFSA's scientific views and conclusions on the individual comments received.

1.2. Interpretation of the Terms of Reference

On 22 December 2014 the European Commission requested EFSA to provide scientific assistance with respect to the risk assessment of confirmatory data following approval of an active substance in accordance with Article 6(1) of Directive 91/414/EEC and Article 6(f) of Regulation (EC) No 1107/2009. EFSA's scientific views on the specific points raised during the commenting phase conducted with Member States, the applicant and EFSA on the risk assessment of confirmatory data for fluquinconazole are presented.

To this end, a technical report containing the finalised reporting table is being prepared by EFSA. The deadline for providing the finalised report is 24 July 2015.

On the basis of the reporting table, the European Commission may decide to further consult EFSA to conduct a full or focused peer review and to provide its conclusions on certain specific points.

[1] Commission Implementing Regulation (EU) No 806/2011 of 10 August 2011 approving the active substance fluquinconazole, in accordance with Regulation (EC) No 1107/2009 of the European Parliament and of the Council concerning the placing of plant protection products on the market, and amending the Annex to Commission Implementing Regulation (EU) No 540/2011 and Commission Decision 2008/934/EC. OJ L 206, 11.8.2011, p. 39-43.

[2] Regulation (EC) No 1107/2009 of the European Parliament and of the Council of 21 October 2009 concerning the placing of plant protection products on the market and repealing Council Directives 79/117/EEC and 91/414/EEC. OJ L 309, 24.11.2009, p. 1-50.

2. Assessment

The comments received on the pesticide risk assessment for the active substance fluquinconazole in light of confirmatory data and the conclusions drawn by EFSA are presented in the format of a reporting table.

The comments received are summarised in column 2 of the reporting table. The RMS' considerations of the comments are provided in column 3, while EFSA's scientific views and conclusions are outlined in column 4 of the table.

The finalised reporting table is provided in Appendix A of this report.

Documentation provided to EFSA

1. Ireland, 2014. Addendum to Volume 3 B7 and B9 of the assessment report on fluquinconazole, confirmatory data, July 2014. Available online: www.efsa.europa.eu.

2. Ireland, 2015. Reporting table, comments on the pesticide risk assessment for fluquinconazole in light of confirmatory data, June 2015.

References

ACD/ChemSketch, Advanced Chemistry Development, Inc., ACD/Labs Release: 12.00 Product version: 12.00 (Build 29305, 25 Nov 2008.

European Commission, 2013. Guidance document on the procedures for submission and assessment of confirmatory information following approval of an active substance in accordance with Regulation (EC) No 1107/2009. SANCO 5634/2009-rev. 6.1

EFSA (European Food Safety Authority), 2009. Guidance on Risk Assessment for Birds and Mammals on request from EFSA. EFSA Journal 2009;7(12):1438, 358 pp. doi:10.2903/j.efsa.2009.1438

EFSA (European Food Safety Authority), 2011. Conclusion on the peer review of the pesticide risk assessment of the active substance fluquinconazole. EFSA Journal 2011;9(5):2096, 112 pp. doi:10.2903/j.efsa.2011.2096. Available online: www.efsa.europa.eu

FOCUS (Forum for the Co-ordination of Pesticide Fate Models and their Use), 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 Generic guidance for FOCUS groundwater scenarios, v. 1.1, April 2002.

Ireland, 2005. Draft Assessment Report (DAR) on the active substance fluquinconazole prepared by the rapporteur Member State Ireland in the framework of Directive 91/414/EEC, February 2005. Available online: www.efsa.europa.eu

Ireland, 2010. Additional Report to the Draft Assessment Report on the active substance fluquinconazole prepared by the rapporteur Member State Ireland in the framework of Commission Regulation (EC) No 33/2008, April 2010. Available online: www.efsa.europa.eu

Abbreviations

a.s.	active substance
µg	microgram
BBCH	Biologische Bundesanstalt, Bundessortenamt und CHemische Industrie
b.w.	bodyweight
CRD	The UK Chemicals Regulation Directorate (Directorate of the Health & Safety Executive)
DAR	draft assessment report
DAT	days after treatment
DT_{50}	period required for 50 percent disappearance (define method of estimation)
GAP	good agricultural practice
DF	deposition factor
DG SANCO	European Commission Directorate General Health and Consumers
ED	endocrine disruption
EU	European Union
FFLC	fish full-life-cycle study
FOMC	first-order multi-compartment model
GD	guidance
GLP	good laboratory practice
GS	growth stage
LD_{50}	lethal dose, median; dosis letalis media
LOQ	limit of quantification (determination)
MS	Member State
NEU	Northern Europe
NOEC	no observed effect concentration
PBI	plant-back interval
PD	proportion of different food types
PEC	predicted environmental concentration
$PEC_{plateau}$	predicted plateau concentration
PEC_{soil}	predicted environmental concentration in soil
PEC_{twa}	predicted time-weighted average concentration
PT	proportion of diet obtained in the treated area
RA	risk assessment
RMS	rapporteur Member State
RUD	residue per unit dose
SEU	Southern Europe
TDMs	triazole derivative metabolites
TER	toxicity exposure ratio

TRR	total radioactive residue
VTG	vitellogenin

Appendix A – Collation of comments from Member States, applicant and EFSA on the pesticide risk assessment for the active substance fluquinconazole in light of confirmatory data and the conclusions drawn by EFSA on the specific points raised

3. Residues

Residue Data B.7				
No.	**Column 1** **Reference to addendum to assessment report**	**Column 2** **Comments from Member States / applicant / EFSA**	**Column 3** **Evaluation by rapporteur Member State** /comments by the applicant	**Column 4** **EFSA's scientific views on the specific points raised in the commenting phase conducted on the RMS's assessment of confirmatory data**
3(1)	Confirmatory data July 2014 - Residues of TDMs in products of animal origin	**EFSA:** A ruminant metabolism study radiolabelled on the triazole ring moiety demonstrated the presence of parent fluquinconazole and the 1, 2, 4-triazole metabolite at significant levels in milk (23 % and 57 % TRR, resp.) and in tissues (up to 53 % and 62 % TRR, resp.). The triazole acetic acid metabolite was detected at a trace level in muscle (1 % TRR) while not detected in the other matrices. In fat, fluquinconazole and the 1, 2, 4-triazole metabolite were recovered at low proportions (12 % and 2.2 % TRR, resp.) whilst the rest of the radioactivity (82 % TRR) was characterized as the parent compound and the triazole acetic acid metabolite. The metabolism study is considered as acceptable and the residue definitions in milk and ruminants matrices	**BASF (16 Dec 2014)** The findings of dion in the rotational crop samples are negligible. For explanation please see Appendix 1 – end of word file **BASF (11 Dec 2014)** Feeding study addressing TDM residues in cereals grain are reported and are part of TDM data package submitted to RMS UK. (The CRD reference is COP 2011/00502: 'TRIAZOLE DERIVATIVE METABOLITES CONSUMER RISK DATA' and COP 2012/01449 for the additional residue data submitted on 3rd July 2012.) **RMS Response December 2014:** Residue definition for enforcement: Agree that the residue definition should	Addressed. The ruminant metabolism study labelled on the triazole ring (Triazole-3(5)-^{14}C) of the parent molecule was considered as acceptable. The residue definition for enforcement is set as fluquinconazole only. The residue definitions for risk assessment are set as: a) Sum of fluquinconazole and metabolite dione (M615F001) expressed as fluquinconazole b) TDMs The proposed residue definitions are valid for ruminants only. It is noted that there is a disagreement between the views of the RMS and EFSA concerning the inclusion of the

Residue Data B.7				
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		are proposed as follows: -Enforcement: Fluquinconazole only, -Risk assessment: 1) Fluquinconazole and metabolite dione, expressed as fluquinconazole; 2) provisionally, Triazole Derivative Metabolites (TDMs). EFSA is also of the opinion that based on the residue levels of TDMs in wheat grain and straw residue trials, the calculated dietary burden triggers a feeding study to address the potential transfer of TDMs to animal products.	be Fluquinconazole only. Residue definition for risk assessment (1): The RMS disagrees with the inclusion of the dione metabolite in the residue definition for risk assessment as it is significantly less toxic than parent fluquinconazole. The dione metabolite does not contain the triazole moiety, which is considered to infer the carcinogenicity to the molecule, therefore the same toxicity as the parent is not anticipated. This was bourne out in the separate database for the dione metabolite which was submtitted. No genotoxic potential is attributed to the dione metabolite either *in vitro* or *in vivo*. The dione metabolite also has no acute toxicity unlike parent Fluquinconazole. Furthermore, the dione metabolite was found at significantly lower levels in the ruminant metabolism studies than parent fluquinconazole. It should also be noted that the original residue trials submitted as part of the DAR did not analyse for the dione	metabolite dione in the residue definition for risk assessment, although the previous peer review (EFSA, 2011) agreed on. This residue definition was derived based on the findings in the cow metabolism study (^{14}C-phenyl) and the results of the residue trials in primary crops (significant residue levels of metabolite dione in wheat straw) (Addendum – Confirmatory information, 2014; Ireland, 2014). Furthermore, although the metabolite dione was shown to be less acutely toxic than the parent compound, this metabolite is considered as toxic as fluquinconazole with regard to the long-term exposure.

Residue Data B.7				
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			metabolite. Only the residue trials submitted as part of the confirmatory data submission analysed for the dione metabolite. Residue definition for risk assessment (2): UK evaluation of the triazole metabolites to be consider before agreeing to a residue definition for risk assessment of Triazole Derivative Metabolites (TDMs).	
3(2)	Confirmatory data July 2014 – Residues of TDMs in primary crops (wheat)	EFSA: 4 residue trials covering respectively the NEU and SEU GAPs were submitted and determined the magnitude of residues of 1,2,4-triazole, triazole alanine, triazole acetic acid and triazole lactic acid in wheat grain and straw. The triazole alanine metabolite was by far the predominant compound of the total residues in wheat grain and reflects the outcome of the metabolism study on spring wheat. The triazole acetic acid compound was also recovered in wheat grain and straw whilst 1, 2, 4-triazole was never detected (<LOQ). It is noted that the storage stability of TDMs residues in cereal grain and straw and covering the storage period of the trials samples was not provided.	**BASF (11 Dec 2014)** Storage stability of TDMs residues in cereals straw and grain are reported and are part of TDM data package submitted to RMS UK. (The CRD reference is COP 2011/00502: 'TRIAZOLE DERIVATIVE METABOLITES CONSUMER RISK DATA' and COP 2012/01449 for the additional residue data submitted on 3rd July 2012.). **RMS Response December 2014:** Agree that a storage stability study for the dione metabolite and the triazole metabolites in cereal grain and straw was not provided to the RMS Ireland. However, the Applicant has provided this information to the RMS UK for their	4 NEU and SEU GAP-compliant residue trials conducted respectively on wheat and barley were submitted to determine the magnitude of metabolite dione and TDMs (1,2,4-triazole, triazolyl alanine, triazolyl acetic acid and triazole lactic acid) residues in grain and straw. However, residue storage stability data on TDMs and metabolite dione in cereals were not provided to cover the maximum storage time period of the residue samples. No conclusion can therefore be drawn on the validity of these residue trials as the storage stability data on the TDMs are currently under assessment by the United Kingdom and storage stability data on metabolite dione are required.

Residue Data B.7				
No.	**Column 1** **Reference to addendum to assessment report**	**Column 2** **Comments from Member States / applicant / EFSA**	**Column 3** **Evaluation by rapporteur Member State** /comments by the applicant	**Column 4** **EFSA's scientific views on the specific points raised in the commenting phase conducted on the RMS's assessment of confirmatory data**
			evaluation of TDMs. UK's evaluation to be considered at product evaluation.	
3(3)	Confirmatory data July 2014 – Residues of TDMs in rotational crops	EFSA: Rotational crops field trials were conducted on wheat, lettuce/spinach, carrot/radish and cauliflower after one bare soil application at a rate of 250 g a.s./ha and with 30d and 120d plant back intervals. It is noted that during the peer review, the plateau concentration of 1,2,4-triazole was calculated considering a DT_{50} of 6.3-12.3 d. However, updated end points* for this compound were agreed upon by EFSA. EFSA is therefore of the opinion that for the representative use, a recalculation of the plateau concentration of 1,2,4-triazole compound over a soil layer depth of 20 cm and using the updated DT_{50} should be required. Furthermore, it should also be demonstrated whether the submitted rotational crops field trials analysing the TDMs were carried out at a rate covering the recalculated plateau concentration. Finally, it is noted that the storage stability of TDMs residues in these crop categories and covering the storage period of the trials samples was not	**BASF (11 Dec 2014)** When recalculating plateau concentration for 20 cm soil layer depth the amended DT_{50} value for degradation of 1,2,4-Triazole in soil will be used and can be provided till end of year. **BASF (11 Dec 2014)** Storage stability of TDMs residues in cereals straw and grain are reported and are part of TDM data package submitted to RMS UK. (The CRD reference is COP 2011/00502: 'TRIAZOLE DERIVATIVE METABOLITES CONSUMER RISK DATA' and COP 2012/01449 for the additional residue data submitted on 3rd July 2012.). **RMS Response December 2014:** The final background concentration in total soil for 1,2,4,-triazole over 20 cm is 0.0030 mg/kg. This is estimated to occur after 10 years of application without crop rotation. The plateau concentration was reached after 10 years. This calculation is considered conservative as it ignores best	Although the rotational crops field trials analysing the TDMs can be considered as sufficiently dosed to cover the calculated plateau concentration for 1,2,4-triazole (0.003 mg/kg), residue storage stability data on TDMs in the relevant crop matrices were not provided and therefore no conclusion can be drawn on the acceptability of these trials. It is noted that the storage stability data on the TDMs are currently under assessment by the United Kingdom.

Residue Data B.7				
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		provided.	agricultural practices such as crop rotation. **The maximum total soil concentration for triazole over 5 cm considering accumulation* is 0.0071 mg/kg**. It was assumed the parent substance fluquinconaozle was applied at a rate of 2 x 125 g a.s./ha with an interval between applications of 21 days, to cereals (FOMC kinetics for multiple applications, 2011 EFSA conclusion). The approach adopted for multiple applications involving the metabolite follows the same approach used in the EFSA conclusion, except the calculations incorporate the new EFSA kinetic endpoints for the triazole metabolite (k1=0.0632 d^{-1}, k2=0.0020 d^{-1}, g=0.5732). In the rotational crop study the triazole metabolite was <LOQ (0.01 mg/kg) in all crop commodities. The recalculated plateau concentration of 1,2,4-triazole compound over a soil layer depth of 20 cm and using the updated kinetic endpoints was 0.003 mg/kg after 10 years and the maximum total soil concentration for triazole over 5 cm considering accumulation* was 0.0071 mg/kg. In the rotational crop study	

Residue Data B.7				
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			1,2,4-triazole was not found at or above the LOQ (0.01 mg/kg). Therefore the RMS considers that this shows that the submitted rotational crop study analysing the TDMs was carried out at a rate covering the recalculated plateau concentration. (* a tillage depth of 20 cm was considered for calculating the background concentration) Agree that a storage stability study for the TDMs in the rotational crops, covering the storage period of the trials samples was not carried out.	
3(4)	Confirmatory data July 2014 – Contribution of the potential residues of the dione metabolite in rotational crops in rotational crops to the overall consumer exposure.	EFSA: Rotational crops field trials conducted after one bare soil application of fluquinconazole on wheat, lettuce/spinach, carrot/radish and cauliflower at a rate of 250 g a.s./ha showed that the dione metabolite was not detected (<0.01 mg/kg) in any of the edible parts of the rotational crops at 30d and 120d PBIs, except in wheat straw (0.02-0.071 mg/kg at 30d PBI) and in carrot/radish tops (0.014 mg/kg at 120d PBI). These field trials also cover the plateau concentration	**BASF (11 Dec 2014)** Storage stability data of Dione residues in cereals grain are not available. But as outlined under 3(1) Dione metabolite is considered stable in the respective matrices (s.a. Appendix 1). **RMS Response December 2014:** Agree that the contribution of the dione metabolite to the overall consumer exposure is negligible. Agree that a storage stability study for	The submitted rotational crop field trials demonstrated that the contribution of metabolite dione to the consumer exposure is negligible. The acceptability of these trials is however pending on the submission of residue storage stability data on metabolite dione in the plant matrices of concern and covering the maximum storage time period of the residue samples.

Residue Data B.7				
No.	**Column 1** **Reference to addendum to assessment report**	**Column 2** **Comments from Member States / applicant / EFSA**	**Column 3** **Evaluation by rapporteur Member State** /comments by the applicant	**Column 4** **EFSA's scientific views on the specific points raised in the commenting phase conducted on the RMS's assessment of confirmatory data**
		of dione metabolite in soil. EFSA therefore concludes that the contribution of this compound to the overall consumer exposure is considered as negligible. The storage stability of dione metabolite in these crop categories and covering the storage period of the trials samples was however not provided.	the dione metabolite in the rotaional crops, covering the storage period of the trials samples was not carried out.	
3(5)	Overall consumer exposure assessment considering the contribution of the TDMs in primary crops, processed products, rotational crops and animal products of animal origin	EFSA: A sound consumer exposure assessment considering the contribution of the TDMs in primary crops, processed commodities, rotational crops and animal commodities is missing and should be conducted.	**BASF (11 Dec 2014)** Consumer RA for TDMs residues in cereals grain are reported and are part of TDM data package submitted to RMS UK. (The CRD reference is COP 2011/00502: 'TRIAZOLE DERIVATIVE METABOLITES CONSUMER RISK DATA' and COP 2012/01449 for the additional residue data submitted on 3rd July 2012.). **RMS Response December 2014:** UK evaluation of triazoles to be considered at product evaluation.	Toxicological reference values for the triazole derivative metabolites (1,2,4-triazole, triazolyl alanine, triazolyl acetic acid and triazole lactic acid) cannot be currently proposed as toxicological information on these metabolites was not provided. The overall consumer exposure assessment with regard to TDMs residues therefore cannot be conducted and will be reconsidered based on the outcome of the on-going UK assessment. EFSA also highlights that the change in the originally proposed representative use on wheat (BBCH 30-59 instead of BBCH 25-59) will not impact significantly the outcome of the overall consumer exposure assessment.

Appendix 1 (response from the applicant regarding reporting table points 3(1) and 3(4)):

BASF (11 Dec 2014)

New available residue studies:
2013/1003734 Wheat, 2013/1003733 Barley, 2013/1291747 Field rotational crop (being part of submission of confirmatory data 16 Dec 2013)
2013/1291748 Wheat, 2013/1291749 Barley (cited but not submitted yet)

On basis of residue levels in wheat dion in straw was detected at 12.1 - 42.6 %.
With range of storage time of 58 – 278 days, no correlation between dion concentration and storage days exists.

On basis of residue levels in barley dion in straw was detected at 12 - 36 %.
With range of storage time of 68 – 265 days, no correlation between dion concentration and storage days exists.

The metabolism study in cow did not show the dion metabolite.
The feeding study done with different dose levels detected 0.02 mg/kg parent in milk using the lowest dose level which is higher than the feed burden based on the detected residue levels.
Taking the parent to dion ratio (worst case 42 % dion) into consideration;
42 % x 0.02 mg/kg/ 100 % = 0.008 mg/kg dion could be detected (<LOQ). Even adding 0.008 mg/kg to the concentration of parent, the result is still under the MRL of milk 0.03 mg/kg.
The findings of dion in the rotational crop samples are negligible.

5. Ecotoxicology

Ecotoxicology B.9				
No.	**Column 1** **Reference to addendum to assessment report**	**Column 2** **Comments from Member States / applicant / EFSA**	**Column 3** **Evaluation by rapporteur Member State**	**Column 4** **EFSA's scientific views on the specific points raised in the commenting phase conducted on the RMS's assessment of confirmatory data**
5(1)	Confirmatory data July 2014, B.9.1, B.9.4 and related study in Appendix 1, Refinement point 1	EFSA: Initial RUD refinement is basically not supported by the EFSA GD. This refinement is possible only if it is fully justified why new measured residue data will override the existing standard residue values. Please consult Appendix F of the GD, which clearly explains this.	IE- We will use the default residue values and not the initial RUD refinements. A risk assessment using the default initial RUD values from the ESFA Guidance Document shows that all TER values exceed the trigger values, with the exception of the long-term risk for the common vole. Some MS do not consider the common vole as the focal species in RA. See point 5(5) Therefore this can be addressed at zonal and/or MS product evaluation.	There is agreement to consider the default residue values. Currently, in the confirmatory data addendum (Ireland, 2014) for cereal shoot the default value was not used. This has negligible impact on the risk assessments for birds. However, it cannot be excluded that the risk assessments for mammals would fail. It should be noted that a quantitative risk assessment only for wood mouse as omnivore was performed. No quantitative risk assessment for herbivorous mammals was included. See also 5(11) and 5(14).

Ecotoxicology B.9				
No.	**Column 1** **Reference to addendum to assessment report**	**Column 2** **Comments from Member States / applicant / EFSA**	**Column 3** **Evaluation by rapporteur Member State**	**Column 4** **EFSA's scientific views on the specific points raised in the commenting phase conducted on the RMS's assessment of confirmatory data**
5(2)	Confirmatory data July 2014, B.9.1, B.9.4 and related study in Appendix 1, Refinement point 2	EFSA: For the details of this residue decline study (all trials from Germany) just a reference to the study summary is available, but this summary itself is not included. The reliability of the DT50 values therefore could not be properly peer-reviewed.	IE- This study was already submitted at a previous stage and reviewed in the DAR (February 2005). Therefore, the study was already peer-reviewed and concluded to be useful to refine the DT_{50} on plant food items for wild birds and mammals.	See 5(15)
5(3)	Confirmatory data July 2014, B.9.1, B.9.4 and related study in Appendix 1, Refinement point 4	EFSA: EFSA does not consider the extrapolation from a triazol to another one to be justified. Although there are similarities between the molecules, there are also considerable differences. Degradation is a complex process and arthropods matrix is probably the least studied and understood one. Was the degradation for all the matrixes for which data are available compared? Please consider also EFSA comment No. 2, above.	IE- The RMS agrees there are differences between the triazoles, however using a pragmatic approach and observing a similar triazole with a comparable exposure and a higher DT_{50} seemed sensible to refine the risk assessment. Perhaps we should wait until the information is available from the UK triazole study to see if this is reasonable to extrapolate from these two triazoles?Risk mitigation may be used in the mean time. No the matrices were not compared. The main samples were analysed (in few cases pooled samples of main and additional samples were analysed). For residue analyses of foliage-dwelling arthropods main	There is a disagreement between the views of the RMS and EFSA/MS on the use of this refinement. This refinement affects the long-term risk assessments for birds and mammals. It is proposed to discuss this refinement option with MSs experts. This would give the opportunity to discuss the whole risk assessment for birds and mammals with all the proposed refinements in order to have an overall agreed approach. Moreover, it was indicated that an additional study is/was on-going (refer to column 3), which might be relevant for this point. In case of an expert discussion, an assessment by the RMS (i.e. updated addendum) reporting that study would be useful.

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			samples of all plots were pooled for each DAT, due to insufficient sampling matrix of single samples.	See also comment in 5(11) and 5(16).
5(4)	Confirmatory data July 2014, B.9.1, B.9.4 and related study in Appendix 1, Refinement point 5	EFSA: It is noted that the crop interception is currently under revision (harmonisation). The newest EFSA GD, which includes crop interception values (bee GD) is in line with the B&M GD rather than with the proposed values for refinement. See also EFSA comment No. 9.	IE- The interception values (FOCUS, 2000) are correct as these values are currently proposed by EFSA in Appendix E of the EFSA Guidance Document. In Appendix E the following is stated: *"The deposition factors provided for the different crops and growth stages are likely to reflect conservative estimates. In the context of a higher-tier risk assessment, the more detailed values of the FOCUS ground water report (FOCUS, 2000) may therefore be also used in line with the explanations provided by FOCUS (2005)."* The use of the FOCUS deposition factors is accepted by some Member States.	There is agreement that considering the originally proposed representative use (BBCH 25-59), another crop interception value should be used and not the one which is currently presented in the confirmatory data addendum from July 2014 (Ireland, 2014). The risk assessments for some scenarios would be valid only if the GAP was changed to BBCH 30-59 as proposed by the applicant under the confirmatory data. See also 5(9) and 5(12).
5(5)	Confirmatory data July 2014, B.9.4	EFSA: As regards to the choice of focal species (relevant for both the acute and long-term RA), EFSA disagrees that common vole is not considered a relevant in cereal habitats, especially in GS BBCH ≥ 40. The statement that it is recognised as a pest underpins that	IE - While some Member States consider the vole in their risk assessments, other Member States consider the vole scenario as irrelevant; and other Member States have lowered the trigger values for acceptable risks for the common vole. In the	There is a disagreement between the RMS and EFSA on the relevancy of focal species scenario for small herbivorous mammals. According to the RMS, common vole is not considered as a representative focal species in several areas of the EU and by some MS.

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		common vole is common in cereals at least in the central zone (probably also somewhat NEU and SEU). It is further noted that the lagomorphs scenario was identified to be further addressed in the original EFSA conclusion.	Nordic Guidance Document the vole is not a relevant focal species in cereals at any growth stage. Therefore, an adequate and pragmatic approach is to propose that the risk assessment for the vole scenario is better addressed at the Member State /zonal level. The notifier is willing to change the GAP for product registrations, starting with the first application in cereals after BBCH 30. Therefore, a deposition factor of 0.3 could be used, based on FOCUS groundwater scenarios as mentioned in the EFSA Guidance Document. Based on the proposed change in GAP (first application after BBCH 30), the lagomorph is not a relevant scenario for the risk assessment anymore, which is in line with the EFSA Guidance Document.	However, common vole is considered as a generic focal species that represents the small herbivorous mammals scenario by the EFSA guidance (EFSA, 2009). Additionally, the large herbivorous mammals scenario was not addressed, which would be considered acceptable if the GAP was changed to BBCH 30-59, as proposed under the confirmatory data. However, considering the originally proposed representative use (BBCH 25-59), this scenario should be addressed. See also 5(4), 5(9) and 5(12).

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5(6)	Confirmatory data July 2014, B.9.3	EFSA: It is just noted that in the original calculation by EFSA, the PECplateau was used instead of PECtwa (resulting in a TER of 4.77 vs. 4.29). However the calculations presented in Table B.9.3.1-1 (and Table B.9.3.1-3) uses a higher PECsoil, thus more conservative.	IE- RMS notes that both TER's trigger a Tier 2 assessment. The refined risk assessment Tier 2 is just above the trigger and results in no risk to earthworm eating mammals as shown.	Noted
5(7)	Confirmatory data July 2014, B.9.3	EFSA: The refinement of the earthworm-eating mammal scenario was done by assuming a PT of 0.85 considering shrew as a focal specie (TER=5.03). Assumptions for PT of 0.85 were supported by some data from the literature. The followings has to be noted: - the EFSA GD does not particularly suggest to use a focal specie concept for this kind of assessments - even if it is done, it is not known whether shrew is the worst case representative mammal for this scenario. The used literature data suggests that shrew is rather a too optimistic choice - The presented calculation and the TER above the trigger is valid only if there is always at least 15% dilution in food consumption of any kind of	IE- Use of PT: On pages 72 and 73 of the EFSA GD it is mentioned that if the TER < 5 further refinement is required and reference is made to Section 6 of the EFSA GD, in which the use of PT is mentioned as one possible refinement option. Shrew as worst case species: In the EFSA GD it is stated that the shrew (b.w. 10 g) should be addressed as relevant species for earthworm eating mammal. The shrews are the smallest earthworm eating mammals potentially occurring in fields. 15% dilution earthworms: An acceptable risk was shown by assuming a relatively low reduction (15%) of the worst case exposure. This conclusion can be supported by the refinement of either PT or PD.	A rather unusual risk assessment was performed for earthworm-eating mammals. A low risk could be concluded only if there is at least 15% dilution in food consumption of the vermivorous mammals living in the agricultural area treated with fluquinconazole. There are however uncertainties concerning this assumption. A peer review is proposed for this point.

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		vermivorous mammal living in agricultural area for cereals (i.e. 15% of the collected worms are not contaminated). Supporting information for this assumption is however missing.	The submitted study (Barfknecht, 2006, BASF DocID 2007/1042674) shows that a PT value > 0.85 is highly unlikely under field conditions. The proportion of contaminated diet (PD) can also support the 15% exposure reduction. It is highly unlikely that shrews (even assuming that they spent 100% of the time in the crop, i.e. PT=1) will exclusively consume contaminated earthworms (PD=100%) due to the different ecology of earthworm species (shallow and deep burrowers) it is unlikely that the shrews only feed on contaminated earthworms exclusively living in the treated soil.	
5(8)	Confirmatory data July 2014, B.9.2	EFSA: During the previous peer-review the ED issue was addressed by a risk assessment based approach by an additional factor of 5 to the trigger value. TERs at FOCUS step 3 passed the trigger of 50 using the fish endpoint of 154 µg/L (NOEC from a 35 d ELS study). The FFLC study submitted as confirmatory data concluded a NOEC of 16.3 µg/L. The	IE- RMS agrees, low risk of ED based on NOEC 16.3 µg/L from FFLC study submitted as confirmatory data. We agree that there are some biological deviations but agree with EFSA conclusion that the choice of NOEC is reasonable. The deviations in the study that the NOEC was calculated from can be mentioned	A FFLC test was provided, which considered potential ED properties of fluquinconazole in fish. There is agreement that the risk assessment using this study (confirmatory data addendum; Ireland, 2014) indicates a low risk. However, MSs would wish some more statistical analyses to be provided for this study in order to confirm this conclusion.

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		factor between the two endpoints is 9.44 suggesting that the safety factor of 5 applied by the previous peer-review was too optimistic. However, if the RAs were repeated by this endpoint, a low risk could be concluded (FOCUS step 3 step 4) applying the standard trigger of 10. As regards to the submitted FFLC study, EFSA noted some deviations of some parameters (VTG levels, clutches/female/day) at the concentration which was established as NOEC from the control. However, as an overall view, the choice of the NOEC seems to be reasonable.		See comment 5(13).

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5(9)	Confirmatory data July 2014, B.9, Background	EFSA: It is noted that any change in the GAP is not allowed in this procedure. BBCH 25 vs. BBCH 30 makes the difference whether herbivorous birds like goose should or should not be considered. Large flocks of geese are not rarely seen in winter cereal fields in late autumn at least in the central zone (relevancy of this example also depends on whether BBCH 25 happens always in spring or not). This choice (BBCH 25 vs. BBCH 30) has an impact on the used crop interception (Refinement point 5), as well. It is acknowledged that the two pertinent growth stages are close to each other maybe with some overlaps.	IE- The notifier is willing to change the GAP for product registration from BBCH 25 to BBCH 30. Yes this will change the DF to 0.3.	Noted, however, considering the originally proposed representative use (BBCH 25-59), the large herbivorous birds scenario should also be addressed. See also 5(4), 5(5), 5(10) and 5(12).
5(10)	Vol. 3, B.9.1 Effects on birds, B.9.1.1 Long-term risk to omnivorous birds (skylark) and insectivorous birds (yellow wagtail)	AT: AT agrees with the RMS to address the risk for birds based on the omnivorous bird skylark and the insectivorous bird yellow wagtail. According to the EFSA GD on birds and mammals herbivorous birds are not considered relevant in cereals.	OK	Noted. EFSA also agrees with these focal species. However, EFSA notes that according to the EFSA, 2009 guidance, the large herbivorous bird scenario should also be covered. Whether this is covered by the identified focal species is questionable.
5(11)	Vol. 3, B.9.1 Effects on birds, B.9.1.1 Long-term	AT: Considering the large datasets on RUD values for cereals and grass, non-	IE- Ok will not use an initial refinement of the RUD values and use the	See 5(1), 5(14) and 5(3).

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	risk to omnivorous birds (skylark) Vol. 3, B.9.3 Effects on terrestrial vertebrates other than birds, Long-term risk to small omnivorous mammals.	grass herbs and for insects given in the EFSA GD the use of new residue data has to be well justified (new residue data mainly reflect substance- or use-specific properties rather than normal variation). In addition, the residue data were based on field studies with a difference active substance. AT is not of the opinion that the DT_{50} should be refined based on the available residue data.	default residue values instead. A risk assessment using the default RUD values from the ESFA Guidance Document shows that all TER values exceed the trigger values, with the exception of the long-term risk for the common vole.	
5(12)	Vol. 3, B.9.1 Effects on birds, B.9.1.1 Long-term risk to omnivorous birds (skylark) Vol. 3, B.9.3 Effects on terrestrial vertebrates other than birds, Long-term risk to small omnivorous mammals.	AT: We agree with the RMS to use a deposition factor to refine the risk. However, the application window of the formulation is between BBCH 25 and 59 (see EFSA Conclusion). The worst case deposition factor should be used in the refined risk assessment (DF = 0.5).	IE - As mentioned the notifier is willing to change the GAP for product registrations, starting with the first application in cereals after BBCH 30. Therefore, a deposition factor of 0.3 could be used, based on FOCUS groundwater scenarios as mentioned in the EFSA Guidance Document.	Noted See also 5(4) and 5(9).
5(13)	Vol. 3, B.9.2.1, Fish full life cycle test	SE: From the results of the fish full life cycle test, at the NOEC level there were no statistically significant effects on endocrine related parameters tested. However, from the data presented it seems that there may be an effect on male VTG levels the NOEC level although not statistically	IE- RMS agrees that at the NOEC level there were no statistically significant effects on endocrine related parameters tested. This FFLC assay is a validated sensitive and accurate GLP study which is recommended for testing all ED	See 5(8).

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		significant. From our point of view, the lack of statistical significance may often be due to a high variability of the data. We therefore propose that the standard deviations are included in the result presentation, along with an analysis of the Minimum Detectable Difference, in order to examine whether the data is sufficiently robust to draw a conclusion on the potential for endocrine disruption.	related parameters in fish. We can include the standard deviations in the table but the minimum detectable differences are unwarranted.	
5(14)	Vol. 3, B9.1.1, Long-term risk to birds, RUD	SE: A new RUD-value was used to refine the long-term risk assessment. In our view more information is needed to justify the why the new measured residue data will override the existing residue values presented in the EFSA GD for birds and mammals (2009). According to the EFSA GD a large number of GLP studies have been used to generate the generic RUD values and any additional residue study would tend to rather broaden the existing database than to replace a RUD derived from it. In addition more data will be needed to prove the representativeness of the new data based on regional climate	IE- A risk assessment using the default RUD values from the ESFA Guidance Document shows that all TER values exceed the trigger values, with the exception of the long-term risk for the common vole.	See 5(1) and 5(11).

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		differences, statistical robustness and the different crops fluquinconazole is applied for.		
5(15)	Vol. 3, B9. Long-term risk to birds, Residual decline in cereal plants	SE: To estimate the residue decline in cereal plants results from field residue trials on one crop from two sites in Germany were used. We are of the opinion that, to cover for between-site variations of the foliage degradation time, results must be available from at least 4 different sites. This is considered to be consistent with the data requirements for degradation in soil and, where relevant, residue trials. In addition the representativeness of additional new data will be needed, based on regional climate differences, statistical robustness and the different crops fluquinconazole is applied for. For further guidance the GD for higher tier risk assessments of birds and mammals in the Northern Zone (2013) (http://mst.dk/82462.aspx) can be used. According to the Nordic GD the longest DT50 value shall be used if the study includes 4-10 sites and only if more than 10 sites are included the DT50 mean can be used.	This study was already submitted and reviewed in the DAR (February 2005). Therefore, the study was already peer-reviewed and concluded to be useful to refine the DT_{50} on plant food items for wild birds and mammals. The company will suggest some risk mitigation measures at zonal /MS level.	There is a disagreement between MS and the RMS on the use of this refinement. It is proposed to discuss this refinement option with MSs experts. This would give the opportunity to discuss the whole risk assessment for birds and mammals with all the proposed refinements in order to have an overall agreed approach. See also 5(2).

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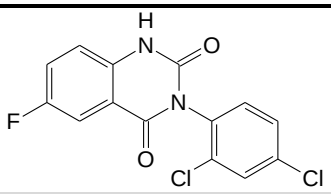
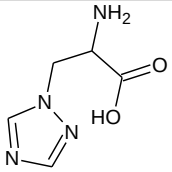
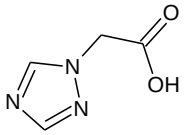
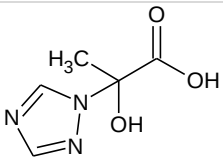
5(16)	Vol. 3, B9. Long-term risk to birds, Residues in arthropods, Use of a residue field study for epoxiconazole.	SE: In our view this part of the RA needs to be more thoroughly discussed.	IE- These sections have been discussed thoroughly, MSs can view the company studies if more detail is needed.	See 5(3) and 5(11).

Appendix B – Used compound code(s)

Code/trivial name*	Chemical name/SMILES notation**	Structural formula**
dione AE C596912 FBC 96912 SN 596912 M615F001	3-(2,4-dichlorophenyl)-6-fluoro-2,4(1*H*,3*H*)-quinazolinedione Clc1ccc(c(Cl)c1)N2C(=O)c3cc(F)ccc3NC2=O	
1,2,4-triazole AE C500859	1*H*-1,2,4-triazole c1ncnn1	
triazolyl alanine	3-(1*H*-1,2,4-triazol-1-yl)-DL-alanine NC(Cn1cncn1)C(=O)O	
triazolyl acetic acid	1*H*-1,2,4-triazol-1-ylacetic acid O=C(O)Cn1cncn1	
triazole lactic acid	(2*RS*)-2-hydroxy-2-(1*H*-1,2,4-triazol-1-yl)propanoic acid CC(O)(C(=O)O)n1cncn1	

* The compound name in bold is the name used in the report.
** ACD/ChemSketch, Advanced Chemistry Development, Inc., ACD/Labs Release: 12.00 Product version: 12.00 (Build 29305, 25 Nov 2008).