Review of the existing maximum residue levels for fluquinconazole according to Article 12 of Regulation (EC) No 396/2005

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Abstract

According to Article 12 of Regulation (EC) No 396/2005, EFSA has reviewed the maximum residue levels (MRLs) currently established at European level for the pesticide active substance fluquinconazole. Considering the information provided by Member States, neither EU uses nor import tolerances are currently authorised for fluquinconazole within the European Union. Furthermore, no MRLs are established by the Codex Alimentarius Commission (codex maximum residue limits) for this active substance. Therefore, residues of fluquinconazole are not expected to occur in any plant or animal commodity. Nevertheless, available data allowed EFSA to propose a marker residue and limit of quantifications (LOQs) for enforcement against potential illegal uses.

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Keywords: fluquinconazole, MRL review, Regulation (EC) No 396/2005, consumer risk assessment, fungicide, triazole derivative metabolites

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Summary

Fluquinconazole was approved on 1 January 2012 by means of Commission Implementing Regulation (EU) No 806/2011 under Regulation (EC) No 1107/2009 as amended by Commission Implementing Regulations (EU) No 540/2011 and 541/2011. As the active substance was approved after the entry into force of Regulation (EC) No 396/2005 on 2 September 2008, the European Food Safety Authority (EFSA) is required to provide a reasoned opinion on the review of the existing maximum residue levels (MRLs) for that active substance in compliance with Article 12(1) of the aforementioned regulation.

As the basis for the MRL review, on 16 August 2017, EFSA initiated the collection of data for this active substance. In a first step, Member States were invited to submit their national Good Agricultural Practices (GAPs) by 15 September 2017, in a standardised way, in the format of specific GAP forms, in the format of specific GAP overview file. According to the information provided in the GAP forms no uses are currently authorised for fluquinconazole in the Member States. Moreover, the rapporteur Member State (RMS) did not report any uses authorised in third countries that might have a significant impact on international trade.

On the basis of all the data submitted by Member States, EFSA, according to the process, should in principle ask Ireland as the designated RMS, to complete the Pesticide Residues Overview File (PROFile) and to prepare a supporting evaluation report. The evaluation report was provided by the RMS to EFSA on 21 December 2017. Nevertheless, since neither European Union (EU) uses nor import tolerances are currently authorised for fluquinconazole, a GAP overview file and a PROFile were not considered relevant and were not submitted.

Following a scientific check on the data submitted undertaken by EFSA, no additional clarification/amendment were needed and, on 9 February 2018, the RMS was directly informed of the completeness of the information received.

Based on the information provided by the RMS, Member States and the EU Reference Laboratories for Pesticides Residues and taking into account the conclusions derived by EFSA in the framework of Directive 91/414/EEC, EFSA prepared in June 2018 a draft reasoned opinion, which was circulated to Member States for consultation via a written procedure. Comments received by 30 July 2018 were considered during the finalisation of this reasoned opinion. The following conclusions are derived.

Residues of fluquinconazole are not expected to occur in any plant commodity or in any animal product because no uses or import tolerances are currently authorised for fluquinconazole in the EU and no codex maximum residue limits (CXLs) are available for this active substance. A risk assessment is therefore in principle not required.

Nevertheless, in order to assist risk managers in applying the most appropriate enforcement measures (against potential illegal uses), EFSA assessed the available data with particular attention to the analytical methods and the nature of residues in plants and livestock.

According to the results from the available metabolism studies in primary, rotational crops and in animals, parent compound is considered to be the most adequate marker for enforcement against the potential illegal use of fluquinconazole. It is expected that this compound can be enforced with an limit of quantification (LOQ) of 0.01 mg/kg in all animal and plant commodities, except in complex matrices (e.g. tea, herbal infusions, cocoa, hops and spices). For these plant commodities, in the absence of fully validated analytical method, a higher LOQ of 0.05 mg/kg is tentatively proposed.

Since in the metabolism studies performed with dichlorophenyl-labelled fluquinconazole, residues present in fat and in milk were almost exclusively represented by the parent molecule, this residue is to be considered as fat soluble.

Considering that the enforcement against potential illegal uses falls under the remit of risk managers, EFSA is not in a position to recommend whether the default MRL of 0.01 mg/kg, as defined by Regulation (EC) No 396/2005, or whether the setting of specific LOQ values for plant and animal commodities should apply. It is noted however that for fluquinconazole, LOQ values of 0.05 mg/kg in complex matrices of plant origin and of 0.01 mg/kg in all other plant commodities and in animal commodities, would provide a satisfactory level of protection for European consumers.
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Background

Regulation (EC) No 396/2005\(^1\) (hereinafter referred to as ‘the Regulation’) establishes the rules governing the setting and the review of pesticide maximum residue levels (MRLs) at European level. Article 12(1) of that Regulation stipulates that the European Food Safety Authority (EFSA) shall provide within 12 months from the date of the inclusion or non-inclusion of an active substance in Annex I to Directive 91/414/EEC\(^2\) a reasoned opinion on the review of the existing MRLs for that active substance. As fluquinconazole was approved on 1 January 2012 by means of Commission Implementing Regulation (EU) No 806/2011\(^3\) under Regulation (EC) No 1107/2009\(^4\) as amended by Commission Implementing Regulations (EU) No 540/2011\(^5\) and 541/2011\(^6\), EFSA initiated the review of all existing MRLs for that active substance.

According to the legal provisions, EFSA shall base its reasoned opinion in particular on the relevant assessment report prepared under Directive 91/414/EEC. It should be noted, however, that, in the framework of Directive 91/414/EEC, only a few representative uses are evaluated, whereas MRLs set out in Regulation (EC) No 396/2005 should accommodate all uses authorised within the European Union (EU), and uses authorised in third countries that have a significant impact on international trade. The information included in the assessment report prepared under Directive 91/414/EEC is therefore insufficient for the assessment of all existing MRLs for a given active substance.

To gain an overview of the pesticide residues data that have been considered for the setting of the existing MRLs, EFSA developed the Pesticide Residues Overview File (PROFile). The PROFile is an inventory of all pesticide residues data relevant to the risk assessment and MRL setting for a given active substance. This includes data on:

- the nature and magnitude of residues in primary crops;
- the nature and magnitude of residues in processed commodities;
- the nature and magnitude of residues in rotational crops;
- the nature and magnitude of residues in livestock commodities;
- the analytical methods for enforcement of the proposed MRLs.

As the basis for the MRL review, on 16 August 2017, EFSA initiated the collection of data for this active substance. In a first step, Member States were invited to submit their national Good Agricultural Practices (GAPs) that are authorised in different Member States by 15 September 2017, in a standardised way in the format of specific GAP forms. In the framework of this consultation four Member States (the Czech Republic, Ireland, Germany and Poland) provided feedback on their national authorisations. An evaluation report was also submitted by the European Union Reference Laboratories for Pesticides Residues (EURLs, 2018). According to the information provided in the GAP forms, uses are no currently authorised for fluquinconazole in the Member States. Moreover, the rapporteur Member State (RMS) did not report any uses authorised in third countries that might have a significant impact on international trade.

On the basis of all the data submitted by Member States, EFSA, according to the process, should in principle ask Ireland as the designated RMS, to complete the Pesticide Residues Overview File (PROFile) and to prepare a supporting evaluation report. The evaluation report was provided by the RMS to EFSA on 21 December 2017. Nevertheless, since neither EU uses nor import tolerances are currently authorised for fluquinconazole, a GAP overview file and a PROFile were not considered relevant and were not submitted.

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\(^1\) Regulation (EC) No 396/2005 of the European Parliament and of the Council of 23 February 2005 on maximum residue levels of pesticides in or on food and feed of plant and animal origin and amending Council Directive 91/414/EEC. OJ L 70, 16.3.2005, p. 1–16.

\(^2\) Council Directive 91/414/EEC of 15 July 1991 concerning the placing of plant protection products on the market. OJ L 230, 19.8.1991, p. 1–32. Repealed by Regulation (EC) No 1107/2009.

\(^3\) 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.

\(^4\) 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.

\(^5\) Commission Implementing Regulation (EU) No 540/2011 of 25 May 2011 implementing Regulation (EC) No 1107/2009 of the European Parliament and of the Council as regards the list of approved active substances. OJ L 153, 11.6.2011, p. 1–186.

\(^6\) Commission Implementing Regulation (EU) No 541/2011 of 1 June 2011 amending Implementing Regulation (EU) No 540/2011 implementing Regulation (EC) No 1107/2009 of the European Parliament and of the Council as regards the list of approved active substances. OJ L 153, 11.6.2011, p. 187–188.
Following a scientific check on the data submitted undertaken by EFSA, no additional clarification/amendment were needed and, on 9 February 2018, the RMS was directly informed of the completeness of the information received.

Based on the information provided by the RMS, Member States and the EURels and taking into account the conclusions derived by EFSA in the framework of Directive 91/414/EEC, EFSA prepared in June 2018 a draft reasoned opinion, which was circulated to Member States for consultation via a written procedure. Comments received by 30 July 2018 were considered during the finalisation of this reasoned opinion.

The evaluation report submitted by the RMS (Ireland, 2017) and the Member States consultation report (EFSA, 2018) are considered as supporting documents to this reasoned opinion and, thus, are made publicly available.

Furthermore, a screenshot of the Report sheet of the EFSA Pesticide Residues Intake Model (PRIMo) is presented in Appendix C.

**Terms of Reference**

According to Article 12 of Regulation (EC) No 396/2005, EFSA shall provide a reasoned opinion on:

- the inclusion of the active substance in Annex IV to the Regulation, when appropriate;
- the necessity of setting new MRLs for the active substance or deleting/modifying existing MRLs set out in Annex II or III of the Regulation;
- the inclusion of the recommended MRLs in Annex II or III to the Regulation;
- the setting of specific processing factors as referred to in Article 20(2) of the Regulation.

**The active substance and its use pattern**

Fluquinconazole is the common name for 3-(2,4-dichlorophenyl)-6-fluoro-2-(1H-1,2,4-triazol-1-yl)quinazolin-4(3H)-one (IUPAC).

Fluquinconazole belongs to the group of triazole compounds which are used as fungicides. It has a systemic activity by inhibiting ergosterol biosynthesis.

The chemical structures of fluquinconazole and its main metabolites are reported in Appendix D.

Fluquinconazole was evaluated in the framework of Directive 91/414/EEC with Ireland designated as RMS (Ireland, 2005). The peer review process terminated following the notifier’s decision to withdraw, in accordance with Article 11(e) of Commission Regulation (EC) No 1490/2002, their support and fluquinconazole was not included in the Annex I to Directive 91/414/EEC through Commission Decision 2008/934/EC. The applicant made a resubmission of the application under an accelerated procedure (Regulation (EC) No 33/2008), the RMS evaluation of the additional data in the format of an Additional Report (Ireland, 2010) has been peer-reviewed by EFSA (EFSA, 2011). The representative use supported for the peer review, was as fungicide on wheat. Following the peer-review carried out by EFSA, a decision on inclusion of the active substance in Annex I to Directive 91/414/EEC was published by means of Commission Implementing Regulation (EU) No 806/2011, which entered into force on 1 January 2012. This approval is restricted to uses only as a fungicide.

According to the Annex to the approval Regulation (EU) No 806/2011, the applicant was required to submit to the European Commission further studies in the area of residues and ecotoxicology by 31 December 2013. The confirmatory data relevant for the residue area were assessed in the EFSA technical Report on confirmatory data (EFSA, 2015)

The EU MRLs for fluquinconazole are established in Annex IIIA of Regulation (EC) No 396/2005 and codex maximum residue limits (CXLs) for this active substance are not available. For the purpose of this MRL review, no uses were reported. The RMS did not report any uses authorised in third countries that might have a significant impact on international trade.

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7 Commission Regulation (EC) No 1490/2002 of 14 August 2002 laying down further detailed rules for the implementation of the third stage of the programme of work referred to in Article 8(2) of Council Directive 91/414/EEC and amending Regulation (EC) No 451/2000. OJ L 224, 21.8.2002, p. 23–48.
8 Commission Decision 2008/934/EC of 5 December 2008 concerning the non-inclusion of certain active substances in Annex I to Council Directive 91/414/EEC and the withdrawal of authorisations for plant protection products containing these substances (notified under document number C(2008) 7637). OJ L 333, 11.12.2008, p. 11–14.
9 Commission Regulation (EC) No 33/2008 of 17 January 2008 laying down detailed rules for the application of Council Directive 91/414/EEC as regards a regular and an accelerated procedure for the assessment of active substances which were part of the programme of work referred to in Article 8(2) of that Directive but have not been included into its Annex I. OJ L 15, 18.1.2008, p. 5–12.
Assessment

Considering that no uses are currently authorised for fluquinconazole within the EU, that no CXLs are available for this active substance and that no uses authorised in third countries were notified to the RMS, European consumers are not expected to be exposed to residues of this active substance and a consumer risk assessment is, in principle, not required. Risk managers might have interest, however, to enforce against the potential illegal use of fluquinconazole within the EU, as well as the presence of illegitimate residue levels in imported products.

Therefore, in order to assist risk managers in applying the most appropriate enforcement measures, EFSA assessed the available data with particular attention to the analytical methods, the toxicological reference values and the nature of residues in plants and livestock.

EFSA has based its assessment on the draft assessment report (DAR) and its addenda prepared under Council Directive 91/414/EEC (Ireland, 2005, 2010), the conclusion on the peer review of the pesticide risk assessment of the active substance fluquinconazole (EFSA, 2011) and the confirmatory data assessed following approval (Ireland, 2014; EFSA, 2015). The evaluation report submitted by the RMS in the framework of this review (Ireland, 2017) was considered as additional supporting information.

Primary crop metabolism of fluquinconazole was investigated in fruit crops (apple, grapes), root crops (carrots) and cereals (wheat) following foliar application, while rotational crop metabolism was investigated in cereals (wheat), leafy crops (lettuce) and root crops (radishes) (Ireland, 2005, 2010). Although triazole derivative metabolites (TDMs) were found at significant levels in the metabolism studies performed with the triazolyl label (especially in wheat grain and in rotational crops), parent fluquinconazole remained the predominant compound in all crops investigated, representing up to 95% total radioactive residue (TRR). Therefore, based on the available data and considering that TDMs are not specific for the active substance under assessment, parent compound only is considered to be the most adequate marker for enforcement against the potential illegal use of fluquinconazole in plants.

Livestock metabolism of fluquinconazole was investigated in lactating goat and in laying hens dosed with dichlorophenyl-labelled fluquinconazole (Ireland, 2005). In ruminants, the parent constituted the predominant compound of the total residues in milk and in all tissues (accounting for up to 99% of the TRR). These results were partially confirmed by an additional metabolism study on goats performed with triazolyl-labelled fluquinconazole and assessed as confirmatory data (Ireland, 2014). According to the results of this additional study, although 1,2,4-triazole represented the main component of the TRR in milk (57% TRR) and kidney (62% of the TRR), parent fluquinconazole was always present at significant levels in milk and ruminant tissues ranging from 11% TRR (kidney) to 53% TRR (muscle). In poultry, parent fluquinconazole constituted the predominant compound of the total residues in eggs and in all tissues, accounting for up to 99.6% of the TRR. Since the metabolism in rats and ruminants was found to be similar, the main findings of the ruminants study can be extrapolated to pigs. Therefore, based on the available data and considering that 1,2,4-triazole is not specific for the active substance under assessment, the parent compound is considered to be a valid marker for enforcement in all animal commodities against the potential illegal use of fluquinconazole. Since in the metabolism studies performed with dichlorophenyl-labelled fluquinconazole, residues present in fat and in milk were almost exclusively represented by the parent molecule, this residue is to be considered as fat soluble.

Multi-residues methods by using gas chromatography with electron capture detection (GC-ECD) or liquid chromatography with tandem mass spectrometry (LC-MS/MS) were evaluated during the peer review and found to be sufficiently validated for the enforcement of fluquinconazole residues in plant commodities (high water, high acid, high fat content and dry matrices) at the limit of quantification (LOQ) of 0.01 mg/kg and in animal commodities at the LOQs of 0.02 mg/kg (muscle, fat, milk, eggs) and 0.05 mg/kg (liver and kidney) (EFSA, 2011). Analytical methods for enforcement in complex matrices were not assessed in the framework of the peer review.

During the completeness check, information on the availability of analytical methods for the enforcement of fluquinconazole was received by the EURLs (EURLs, 2018). On the basis of the information provided, QuEChERS (LC-MS/MS or gas chromatography with tandem mass spectrometry (GC-MS/MS)) multi-residues methods are sufficiently validated in plant commodities (high water, high acid, high fat content and dry matrices), in eggs and in liver, at the LOQs of 0.01, 0.001 and 0.002 mg/kg, respectively. According to the EURLs, given the successful validation at such very low levels in liver and eggs it is supposed that an LOQ of 0.01 mg/kg will also be easily achieved in the remaining commodity groups of animal origin (muscle, kidney, milk) (EFSA, 2018; EURLs, 2018). Therefore, it is expected that fluquinconazole can be enforced with an LOQ of 0.01 mg/kg in all animal
and plant commodities, except in complex matrices (e.g. tea, herbal infusions, cocoa, hops and spices). For these plant commodities, in the absence of fully validated analytical method, a higher LOQ of 0.05 mg/kg is tentatively proposed.

The toxicological assessment of fluquinconazole was peer reviewed under Directive 91/414/EEC, which resulted in an acceptable daily intake (ADI) and an acute reference dose (ARfD) being established at 0.002 mg/kg body weight (bw) per day and 0.02 mg/kg bw, respectively (EFSA, 2011). In order to assess whether the reported LOQ values are sufficiently protective for European consumers, chronic and acute intake calculations were performed using revision 2 of the EFSA PRIMo (EFSA, 2007). These calculations were carried out assuming residues present at the LOQs of 0.05 mg/kg in complex matrices of plant origin and 0.01 mg/kg in all other plant commodities and in all commodities of animal origin.

The calculated exposures were compared with the toxicological reference values for fluquinconazole. The highest chronic exposure was calculated for French toddlers, representing 38% of the ADI, and the highest acute exposure was calculated for potatoes, representing 7.7% of the ARfD. EFSA highlights that this calculation does not reflect real exposure of consumers to fluquinconazole residues. This theoretical calculation only indicates that the above reported LOQ values would provide a satisfactory level of protection for European consumers.

**Conclusions and recommendations**

Residues of fluquinconazole are not expected to occur in any plant commodity or in any animal product because no uses or import tolerances are currently authorised for fluquinconazole in the EU and no CXLs are available for this active substance. A risk assessment is therefore in principle not required.

Nevertheless, in order to assist risk managers in applying the most appropriate enforcement measures (against potential illegal uses), EFSA assessed the available data with particular attention to the analytical methods and the nature of residues in plants and livestock.

According to the results from the available metabolism studies in primary, rotational crops and in animals, parent compound is considered to be the most adequate marker for enforcement against the potential illegal use of fluquinconazole. It is expected that this compound can be enforced with an LOQ of 0.01 mg/kg in all animal and plant commodities, except in complex matrices (e.g. tea, herbal infusions, cocoa, hops and spices). For these plant commodities, in the absence of fully validated analytical method, a higher LOQ of 0.05 mg/kg is tentatively proposed.

Since in the metabolism studies performed with dichlorophenyl-labelled fluquinconazole, residues present in fat and in milk were almost exclusively represented by the parent molecule, this residue is to be considered as fat soluble.

Considering that the enforcement against potential illegal uses falls under the remit of risk managers, EFSA is not in a position to recommend whether the default MRL of 0.01 mg/kg, as defined by Regulation (EC) No 396/2005, or whether the setting of specific LOQ values for plant and animal commodities should apply. It is noted however that for fluquinconazole, LOQ values of 0.05 mg/kg in complex matrices of plant origin and of 0.01 mg/kg in all other plant commodities and in animal commodities, would provide a satisfactory level of protection for the European consumers.

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Abbreviations

a.s. active substance
ADI acceptable daily intake
ARfD acute reference dose
BBCH growth stages of mono- and dicotyledonous plants
bw body weight
CAC Codex Alimentarius Commission
CXL codex maximum residue limit
DAR draft assessment report
DAT days after treatment
DB dietary burden
EURLs European Union Reference Laboratories for Pesticide Residues (former CRLs)
GAP Good Agricultural Practice
GC-ECD gas chromatography with electron capture detector
GC-MS/MS gas chromatography with tandem mass spectrometry
IEDI international estimated daily intake
IESTI international estimated short-term intake
ILV independent laboratory validation
ISO International Organisation for Standardization
IUPAC International Union of Pure and Applied Chemistry
LC-MS/MS liquid chromatography with tandem mass spectrometry
LOQ limit of quantification
Mo monitoring
MRL maximum residue level
OECD Organisation for Economic Co-operation and Development
PBI plant-back interval
PRIMo (EFSA) Pesticide Residues Intake Model
PROFile (EFSA) Pesticide Residues Overview File
QuEChERS Quick, Easy, Cheap, Effective, Rugged, and Safe (analytical method)
RA risk assessment
RD residue definition
RMS rapporteur Member State
SMILES simplified molecular-input line-entry system
TDM triazole derivative metabolite
TRR total radioactive residue
Appendix A – Summary of authorised uses considered for the review of MRLs

Neither EU uses nor import tolerances are currently authorised for fluquinconazole.
Appendix B – List of end points

B.1. Residues in plants

B.1.1. Nature of residues and methods of analysis in plants

B.1.1.1. Metabolism studies, methods of analysis and residue definitions in plants

| Primary crops (available studies) | Crop groups | Crop(s) | Application(s) | Sampling (DAT) |
|-----------------------------------|-------------|---------|----------------|---------------|
| Fruit crops                       | Apples      | Direct application on fruits, 3 × 10 or 100 g a.s./hl | 13 |
| | Grapevines | Direct application on fruits, 1 × 7.5 or 75 g a.s./hl | 15; 28; 38 |
| Root crops                        | Carrots | Foliar, 1 × 161 or 587 g a.s./ha | 0; 20; 36 |
| Cereals                           | Wheat | Foliar, 3 (BBCH 31; 39; 55) × 2,500 g a.s./ha | At maturity |
| | | Soil, 3 (BBCH 31; 39; 55) × 2,500 g a.s./ha | At maturity |

Studies on fruit crops and carrots performed with dichlorophenyl label only. Study on spring wheat performed with dichlorophenyl- and triazolyl-labelled fluquinconazole (Ireland, 2005)

| Rotational crops (available studies) | Crop groups | Crop(s) | Application(s) | PBI (DAT) |
|--------------------------------------|-------------|---------|----------------|-----------|
| Root/tuber crops                     | Radish | Bare soil, 750 g a.s./ha | 120 |
| | | Bare soil, 250 g a.s./ha | 32 |
| Leafy crops                          | Lettuce | Bare soil, 750 g a.s./ha | 120 |
| | | Bare soil, 250 g a.s./ha | 32 |
| Cereal (small grain)                 | Wheat | Bare soil, 750 g a.s./ha | 120 |
| | | Bare soil, 250 g a.s./ha | 32 |

Study performed with dichlorophenyl- and triazolyl-labelled fluquinconazole (Ireland, 2005, 2010)

| Processed commodities (hydrolysis study) | Conditions | Investigated? |
|-------------------------------------------|-------------|---------------|
|                                          | Pasteurisation (20 min, 90°C, pH 4) | Yes |
|                                          | Baking, brewing and boiling (60 min, 100°C, pH 5) | Yes |
|                                          | Sterilisation (20 min, 120°C, pH 6) | No |
| Metabolites dione and 1,2,4-triazole are formed during hydrolysis simulating baking, brewing and boiling but parent compound is still the predominant part of the residue. Sterilisation was not considered relevant for the representative use on wheat (Ireland, 2005, 2010; EFSA, 2011) | | |

Can a general residue definition be proposed for primary crops? Yes
Rotational crop and primary crop metabolism similar? Yes
Residue pattern in processed commodities similar to residue pattern in raw commodities? Yes
Plant residue definition for monitoring (RD-Mo) Fluquinconazole
Plant residue definition for risk assessment (RD-RA) Not relevant for enforcement against illegal uses
Conversion factor (monitoring to risk assessment) Not applicable
Methods of analysis for monitoring of residues (analytical technique, crop groups, LOQs)

| Crop Group | Analytical Technique | LOQ (mg/kg) | Sources |
|------------|----------------------|-------------|---------|
| lettuce, wheat, oilseed rape, almonds, grape and orange | QuEChERS (LC–MS/MS) | 0.01 | EFSA (2011); EURLs (2018) |
| | | | |

High water, high acid, high fat content and dry matrices:

- QuEChERS (LC–MS/MS)
- LOQ: 0.01 mg/kg
- Validated in lettuce, wheat, oilseed rape, almonds, grape and orange

B.1.2. Magnitude of residues in plants

Not relevant since neither EU uses nor import tolerances are currently authorised for fluquinconazole.

B.2. Residues in livestock

B.2.1. Nature of residues and methods of analysis in livestock

B.2.1.1. Metabolism studies, methods of analysis and residue definitions in livestock

| Livestock (available studies) | Animal | Dose (mg/kg bw per day) | Duration (days) | N rate/comment |
|-------------------------------|--------|-------------------------|-----------------|----------------|
| Laying hen                   | 10 mg/kg feed | 14 | Study performed with dichlorophenyl-labelled fluquinconazole |
| Lactating goat               | 10 mg/kg feed | 7 | Study performed with dichlorophenyl-labelled fluquinconazole |
|                              | 12 mg/kg feed | 12 | Nominal dose reported. Study performed with triazolyl-labelled fluquinconazole |

Sources: Ireland (2005, 2014)

| Time needed to reach a plateau concentration in milk and eggs (days) | Milk: 4–8 | Eggs: 12 |
|---------------------------------------------------------------------|-----------|----------|
| Metabolism in rat and ruminant similar (Yes/No)                    | Yes       |
| Animal residue definition for monitoring (RD-Mo)                   | Fluquinconazole |
| Animal residue definition for risk assessment (RD-RA)              | Not relevant for enforcement against illegal uses |
| Conversion factor (monitoring to risk assessment)                  | Not applicable |
| Fat soluble residues (Yes/No)                                     | Yes       |
| Methods of analysis for monitoring of residues (analytical technique, crop groups, LOQs) | Muscle, fat, milk and eggs: Multi-residues DFG S19 (GC-ECD) | 0.02 mg/kg | EFSA (2011) |
| | Kidney, liver: GC-ECD | 0.05 mg/kg | ILV not available |
| | Source: EFSA (2011) | | |
| | According to the EURLs, although QuEChERS (GC–MS/MS) validation data are only available for liver and eggs, an LOQ of 0.01 mg/kg is expected to be achievable in all animal commodities (EFSA, 2018; EURLs, 2018) | | |

bw: body weight; GC-ECD: gas chromatography with electron capture detector; LOQ: limit of quantification; ILV: independent laboratory validation; QuEChERS: Quick, Easy, Cheap, Effective, Rugged, and Safe; GC–MS/MS: gas chromatography with tandem mass spectrometry.

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B.2.2. Magnitude of residues in livestock

Not relevant since neither EU uses nor import tolerances are currently authorised for fluquinconazole.

B.3. Consumer risk assessment

B.3.1. Consumer risk assessment

| Parameter         | Value                                      | Source                              |
|-------------------|--------------------------------------------|-------------------------------------|
| ADI               | 0.002 mg/kg bw per day (EFSA, 2011)        |                                    |
| Highest IEDI,     | 38% ADI (FR, toddlers)                     |                                    |
| Assumptions made  | The calculation is based on the LOQs for   |                                    |
| for the calculations | enforcement according to the available    |                                    |
|                   | analytical methods                          |                                    |
| ARfD              | 0.02 mg/kg bw (EFSA, 2011)                 |                                    |
| Highest IESTI,    | 7.7% ARfD (potatoes)                       |                                    |
| Assumptions made  | The calculation is based on the LOQs for   |                                    |
| for the calculations | enforcement according to the available    |                                    |
|                   | analytical methods                          |                                    |

ADI: acceptable daily intake; bw: body weight; IEDI: international estimated daily intake; PRIMo: (EFSA) Pesticide Residues Intake Model; LOQ: limit of quantification; ARfD: acute reference dose; IESTI: international estimated short-term intake.
Appendix C – Pesticide Residue Intake Model (PRIMo)

PRIMo(EU)

Fluquinconazole

| Toxicological end points |
|--------------------------|
| ADI (mg/kg bw per day)   |
| Source of ADI:           |
| EFSA                     |
| Year of evaluation:      |
| 2011                     |
| Proposed LOQ (mg/kg bw)  |
| 0.002                    |
| Source of ARfD:          |
| EFSA                     |
| Year of evaluation:      |
| 2011                     |

| Status of the active substance |
|--------------------------------|
| Code no.                       |
| LOQ (mg/kg bw)                 |
| 0.002                          |

| ARfD (mg/kg bw) |
|-----------------|
| 0.02            |

| No of diets exceeding ADI |
|---------------------------|
| 0                          |

| Highest calculated TMDI values in % of ADI |
|-------------------------------------------|
| TMDI (range) in % of ADI                  |
| minimum – maximum                         |
|-------------------------------------------|
| Chronic risk assessment                   |
| Commodity/ group of commodities           |
| 2nd contributor to MS diet (in % of ADI)  |
| 3rd contributor to MS diet (in % of ADI)  |
| pTMRLs at LOQ (in % of ADI)               |

| MS Diet     | Commodity/ group of commodities | 2nd contributor to MS diet (in % of ADI) | 3rd contributor to MS diet (in % of ADI) | pTMRLs at LOQ (in % of ADI) |
|-------------|---------------------------------|------------------------------------------|------------------------------------------|---------------------------|
| 37.9 FR toddler | PRODUCTS OF ANIMAL ORIGIN | 8.7 VEGETABLES | 5.9 FRUIT (FRESH OR FROZEN) | 3.9 VEGETABLES |
| 35.4 UK infant  | PRODUCTS OF ANIMAL ORIGIN | 9.0 SUGAR PLANTS | 6.3 VEGETABLES | 3.5 VEGETABLES |
| 33.5 TK Toddler | PRODUCTS OF ANIMAL ORIGIN | 10.4 SUGAR PLANTS | 7.4 FRUIT (FRESH OR FROZEN) | 4.4 VEGETABLES |
| 33.2 NL child   | PRODUCTS OF ANIMAL ORIGIN | 11.5 FRUIT (FRESH OR FROZEN) | 8.2 VEGETABLES | 5.0 VEGETABLES |
| 32.4 FR infant  | PRODUCTS OF ANIMAL ORIGIN | 11.6 FRUIT (FRESH OR FROZEN) | 8.6 VEGETABLES | 5.3 VEGETABLES |
| 30.4 DE child   | PRODUCTS OF ANIMAL ORIGIN | 11.8 FRUIT (FRESH OR FROZEN) | 8.9 VEGETABLES | 5.3 VEGETABLES |
| 23.9 WHO Cluster diet B | VEGETABLES | 5.9 VEGETABLES | 3.6 FRUIT (FRESH OR FROZEN) | 2.4 VEGETABLES |
| 22.3 UK child    | PRODUCTS OF ANIMAL ORIGIN | 10.9 SUGAR PLANTS | 7.3 VEGETABLES | 3.7 SUGAR PLANTS |
| 19.3 SE general population 90th percentile | PRODUCTS OF ANIMAL ORIGIN | 8.8 SUGAR PLANTS | 5.9 VEGETABLES | 3.7 SUGAR PLANTS |
| 18.8 ES child    | PRODUCTS OF ANIMAL ORIGIN | 8.8 VEGETABLES | 5.5 VEGETABLES | 3.7 VEGETABLES |
| 17.1 IE adult    | FRUIT (FRESH OR FROZEN) | 7.3 SUGAR PLANTS | 4.0 VEGETABLES | 2.8 VEGETABLES |
| 15.9 WHO cluster diet E | VEGETABLES | 4.5 VEGETABLES | 3.0 CEREALS | 2.6 CEREALS |
| 14.5 WHO cluster diet O | VEGETABLES | 4.6 SUGAR PLANTS | 3.6 VEGETABLES | 2.7 SUGAR PLANTS |
| 13.9 WHO regional European diet | PRODUCTS OF ANIMAL ORIGIN | 4.7 VEGETABLES | 3.5 CEREALS | 2.7 CEREALS |
| 13.7 WHO Cluster diet F | PRODUCTS OF ANIMAL ORIGIN | 3.6 VEGETABLES | 2.9 CEREALS | 2.7 CEREALS |
| 11.1 NL general  | PRODUCTS OF ANIMAL ORIGIN | 4.1 VEGETABLES | 2.6 CEREALS | 2.3 CEREALS |
| 10.3 ES adult    | PRODUCTS OF ANIMAL ORIGIN | 3.9 SUGAR PLANTS | 2.2 CEREALS | 2.1 CEREALS |
| 9.9 UK vegetarian | SUGAR PLANTS | 1.9 VEGETABLES | 1.9 CEREALS | 2.1 CEREALS |
| 9.2 FR all population | FRUIT (FRESH OR FROZEN) | 3.1 VEGETABLES | 1.9 CEREALS | 2.1 CEREALS |
| 9.1 PT General population | FRUIT (FRESH OR FROZEN) | 3.2 VEGETABLES | 1.9 CEREALS | 2.1 CEREALS |
| 9.1 UK Adult     | PRODUCTS OF ANIMAL ORIGIN | 2.2 SUGAR PLANTS | 1.9 VEGETABLES | 2.1 SUGAR PLANTS |
| 8.7 DK adult     | PRODUCTS OF ANIMAL ORIGIN | 3.8 SUGAR PLANTS | 1.8 CEREALS | 2.1 CEREALS |
| 8.2 IT kids/toddler | CEREALS | 4.2 VEGETABLES | 1.8 VEGETABLES | 2.1 VEGETABLES |
| 8.1 LT adult     | PRODUCTS OF ANIMAL ORIGIN | 3.0 VEGETABLES | 1.8 CEREALS | 2.0 CEREALS |
| 7.6 FI adult     | PRODUCTS OF ANIMAL ORIGIN | 3.4 VEGETABLES | 1.8 CEREALS | 2.0 CEREALS |
| 6.6 FI toddler   | CEREALS | 2.5 VEGETABLES | 1.8 CEREALS | 2.0 CEREALS |
| 4.8 FI general population | VEGETABLES | 3.1 SUGAR PLANTS | 1.7 CEREALS | 2.0 SUGAR PLANTS |

Conclusion:
The estimated Theoretical Maximum Daily Intakes (TMDI), based on pTMRLs were below the ADI. A long-term intake of residues of Fluquinconazole is unlikely to present a public health concern.
The acute risk assessment is based on the ARfD. For each commodity, the calculation is based on the highest reported MS consumption per kg bw and the corresponding unit weight from the MS with the critical consumption. If no data on the unit weight was available from that MS, an average European unit weight was used for the IESTI calculation.

In the IESTI 1 calculation, the variability factors were 10, 7 or 5 (according to JMPR manual 2002) for lettuce, a variability factor of 5 was used. In the IESTI 2 calculation, the variability factors of 10 and 7 were replaced by 5. For lettuce, the calculation was performed with a variability factor of 3.

Threshold MRL is the calculated residue level which would lead to an exposure equivalent to 100% of the ARfD. No exceedance of the ARfD/ADI was identified for any unprocessed commodity.

### Acute risk assessment/children

| Commodity               | pTMRL/threshold MRL (mg/kg) | ARfD/ADI exceeded |
|-------------------------|-----------------------------|-------------------|
| Potatoes                | 0.01/-                      | No                |
| Melons                  | 0.01/-                      | No                |
| Milk and milk products  | 0.01/-                      | No                |
| Watermelons             | 0.01/-                      | No                |
| Oranges                 | 0.01/-                      | No                |
| Carrot, juice           | 0.01/-                      | No                |
| Pineapples preserved    | 0.01/-                      | No                |

### Acute risk assessment/adults/general population

| Commodity               | pTMRL/threshold MRL (mg/kg) | ARfD/ADI exceeded |
|-------------------------|-----------------------------|-------------------|
| Apple juice             | 0.01/-                      | No                |
| Orange juice            | 0.01/-                      | No                |
| Carrot, juice           | 0.01/-                      | No                |
| Grape juice             | 0.01/-                      | No                |
| Peach juice             | 0.01/-                      | No                |

### Conclusion:

For Fluquinconazole, IESTI 1 and IESTI 2 were calculated for food commodities for which pTMRLs were submitted and for which consumption data are available. No exceedance of the ARfD/ADI was identified for any unprocessed commodity. For processed commodities, no exceedance of the ARfD/ADI was identified.

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**Notes:**

1. The results of the IESTI calculations are reported for at least 5 commodities. If the ARfD is exceeded for more than 5 commodities, all IESTI values > 90% of ARfD are reported.

2. pTMRL: provisional temporary MRL.

---

**Threshold MRL** is the calculated residue level which would lead to an exposure equivalent to 100% of the ARfD. No exceedance of the ARfD/ADI was identified for any unprocessed commodity.

### No of commodities for which ARfD/ADI is exceeded:

| ARfD/ADI exceeded | IESTI 1 | IESTI 2 |
|-------------------|---------|---------|
| No                | -       | -       |

### No of critical MRLs (IESTI 1):

| IESTI 1 |
|---------|
| No       | -       |

### No of critical MRLs (IESTI 2):

| IESTI 2 |
|---------|
| No       | -       |

---

**Processed commodities**

### No of commodities for which ARfD/ADI is exceeded:

| ARfD/ADI exceeded | pTMRL/threshold MRL (mg/kg) | Processed commodities |
|-------------------|-----------------------------|-----------------------|
| No                | -                           | No                    |

### No of critical MRLs (IESTI 1):

| IESTI 1 |
|---------|
| No       | -       |

### No of critical MRLs (IESTI 2):

| IESTI 2 |
|---------|
| No       | -       |
Appendix D – Used compound codes

| Code/trivial name\(^{(a)}\) | IUPAC name/SMILES notation/InChiKey\(^{(b)}\) | Structural formula\(^{(c)}\) |
|-----------------------------|-----------------------------------------------|-----------------------------|
| Fluquinconazole             | 3-(2,4-dichlorophenyl)-6-fluoro-2-(1H-1,2,4-triazol-1-yl) quinazolin-4(3H)-one Fc1ccc2N=C(n3ncnc3)N(c4ccc(Cl)cc4Cl)C(-O)c2c1 IJVMEXYNJXOJ-UHFFFAOYSA-N | ![Fluquinconazole structural formula](attachment:image) |
| 1,2,4-triazole              | 1H-1,2,4-triazole N1N=CN-C1 NSPMIYGKQJPBQR-UHFFFAOYSA-N | ![1,2,4-triazole structural formula](attachment:image) |

IUPAC: International Union of Pure and Applied Chemistry; SMILES: simplified molecular-input line-entry system; InChiKey: International Chemical Identifier Keys.

\(^{(a)}\): The metabolite name in bold is the name used in the conclusion.

\(^{(b)}\): ACD/Name 2015 ACD/Labs 2015 Release (File version N20E41, Build 75170, 19 December 2014).

\(^{(c)}\): ACD/ChemSketch 2015 ACD/Labs 2015 Release (File version C10H41, Build 75059, 17 December 2014).