REASONED OPINION

Reasoned opinion on the modification of the existing MRLs for flonicamid in several crops[1]

European Food Safety Authority[2]

European Food Safety Authority (EFSA), Parma, Italy

ABSTRACT

In accordance with Article 6 of Regulation (EC) No 396/2005, both France, hereafter referred to as the evaluating Member State (EMS-FR), and the Netherlands, hereafter referred to as the evaluating Member State (EMS-NL) received an application from ISK Biosciences Europe N.V. to modify the existing maximum residue levels (MRLs) for the active substance flonicamid in peas without pods, cotton seeds and rye (EMS-FR) and peppers, Brussels sprouts, barley and oat (EMS-NL). France and the Netherlands drafted an evaluation report in accordance with Article 8 of Regulation (EC) No 396/2005 which was submitted to the European Commission and forwarded to EFSA. According to EFSA the data are sufficient to derive MRL proposals of 0.3 mg/kg for peppers (indoor uses), 0.6 mg/kg for Brussels sprouts, 0.7 mg/kg for peas without pods, 0.2 mg/kg for cotton seeds, 0.4 mg/kg for barley and oat. The extrapolation to rye of the current MRL of 2 mg/kg set on wheat in the EU legislation and recommended during the Article 12 review of the existing MRLs is confirmed. Sufficient data were not provided to support the outdoor use of flonicamid on peppers. Adequate analytical methods are available to control the residues of flonicamid and its metabolites TFNG and TFNA in the crops under consideration. Based on the risk assessment results, EFSA concludes that the proposed uses of flonicamid on the crops under consideration will not result in a consumer exposure exceeding the toxicological reference values and therefore are unlikely to pose a consumer health risk.

KEY WORDS

flonicamid, vegetables, cotton and cereals, MRL application, Regulation (EC) No 396/2005, consumer risk assessment, insecticide

[1] On request from the European Commission, Question No EFSA-Q-2014-00397 and EFSA-Q-2014-00788, approved on 28 April 2015.

[2] Correspondence: pesticides.mrl@efsa.europa.eu

Suggested citation: EFSA (European Food Safety Authority), 2015. Reasoned opinion on the modification of the existing MRLs for flonicamid in several crops. EFSA Journal 2015;13(5):4103, 26 pp. doi:10.2903/j.efsa.2015.4103

Available online: www.efsa.europa.eu/efsajournal

SUMMARY

In accordance with Article 6 of Regulation (EC) No 396/2005, France, hereafter referred to as the evaluating Member State (EMS-FR), received an application from ISK Biosciences Europe N.V. to modify the existing maximum residue levels (MRLs) for the active substance flonicamid in peas without pods, cotton seeds and rye. In addition, the Netherlands, hereafter referred to as the evaluating Member State (EMS-NL), received an application from ISK Biosciences Europe N.V. to modify the existing MRLs for the active substance flonicamid in peppers, Brussels sprouts, barley and oat. France and the Netherlands drafted an evaluation report in accordance with Article 8 of Regulation (EC) No 396/2005 which was submitted to the European Commission (EC) and forwarded to EFSA on 27 May 2014 and 31 October 2014, respectively.

For reasons of efficiency EFSA combined both applications in a single reasoned opinion. EFSA bases its assessment on the evaluation reports, the Draft Assessment Report (DAR) and its addendum prepared under Council Directive 91/414/EEC, the Commission Review Report on flonicamid, the conclusion on the peer review of the pesticide risk assessment of the active substance flonicamid as well as the conclusions from previous EFSA opinions on flonicamid.

The toxicological profile of flonicamid was assessed in the framework of the peer review under Council Directive 91/414/EEC and the data were sufficient to derive an acceptable daily intake (ADI) of 0.025 mg/kg bw per day and an acute reference dose (ARfD) of 0.025 mg/kg bw.

The metabolism of flonicamid in primary crops was investigated in the fruit, root/tuber and cereal crop groups following foliar applications. EFSA proposed to maintain the existing residue definition for enforcement in plants as the sum of flonicamid and the metabolites TFNG and TFNA, but with the information that total residues are expressed as flonicamid equivalents. The same residue definition was established for risk assessment. For the use on the crops under consideration, EFSA concludes that the metabolism in primary crops is sufficiently addressed and that the derived residue definitions are applicable.

EFSA concludes that the submitted residue trials are sufficient to derive MRL proposals of 0.3 mg/kg for peppers (indoor uses), 0.6 mg/kg for Brussels sprouts, 0.7 mg/kg for peas without pods, 0.2 mg/kg for cotton seeds, 0.4 mg/kg for barley and oat. The extrapolation to rye of the current MRL of 2 mg/kg set on wheat in the EU legislation and recommended during the Article 12 review of the existing MRLs is confirmed. Sufficient data were not provided to support the outdoor use of flonicamid on peppers. Adequate analytical methods are available to control the residues of flonicamid and its metabolites TFNG and TFNA in the crops under consideration at the validated combined the limit of quantification (LOQ) of 0.03 mg/kg.

Flonicamid showed to be hydrolytically stable under standard hydrolysis conditions, but no data were provided on the stability of the metabolites TFNG and TFNA and additional information was required during the Article 12 review. Processing studies on peas and barley were reported in the framework of these MRL applications. Pending the submission of additional data on peas and information on the stability of the TFNG and TFNA under hydrolysis conditions, the inclusion of the derived processing factors in Annex VI of Regulation (EC) 396/2005 is not recommended by EFSA.

The occurrence of flonicamid residues in rotational crops was investigated in the framework of the peer review. Based on the available information, the degradation of flonicamid and its metabolites is extremely rapid in soil and significant residue levels are unlikely to occur in rotational crops.

Since the intended uses on cereals do not have an impact on the livestock dietary burden obtained from the existing uses, no changes are proposed to the MRLs for commodities of animal origin recommended during the Article 12 MRL review.

The consumer risk assessment was performed with revision 2 of the EFSA Pesticide Residues Intake Model (PRIMo). EFSA updated the chronic consumer risk assessment performed the framework of the

review of the existing MRLs according to Article 12 of Regulation (EC) No 396/2005 with the supervised trials median residue levels (STMRs) derived from the submitted residue trials for the crops under consideration. The acute exposure assessment was performed only with regard to the commodities under consideration.

Under the assumption that the MRLs will be amended as proposed in the Article 12 review, no long-term consumer intake concerns were identified for any of the European diets incorporated in the EFSA PRIMo. The total calculated chronic intake accounted for up to 17 % of the ADI (Danish child). The maximum acute intake was calculated to be 38 % of the ARfD (German child) for peppers and therefore, no acute consumer intake concern was identified in relation to the MRL proposals.

EFSA concludes that the proposed uses of flonicamid on the crops under consideration will not result in a consumer exposure exceeding the toxicological reference values and therefore are unlikely to pose a consumer health risk.

Thus, EFSA proposes to amend the existing MRLs as reported in the summary table.

SUMMARY TABLE

Code[(a)]	**Commodity**	**Existing EU MRL** (mg/kg)	**Proposed MRL** (mg/kg)		**Comment/Justification**
			Art. 12[(b)]	**Art. 10**[(c)]	
Enforcement residue definition: Sum of flonicamid, TNFG and TNFA expressed as flonicamid[(d)]					
0231020	Sweet peppers/bell peppers	0.15	0.2	0.3	Indoor use only. Outdoor NEU use not sufficiently supported by data.
0242010	Brussels sprouts	0.05*	0.03*	0.6	Supported by NEU trials (with adjuvant).
0260040	Peas (without pods)	0.05*	0.03*	0.7	Supported by NEU trials.
0401090	Cotton seeds	0.05*	0.06*	0.2	Supported by SEU trials.
0500010	Barley	0.05*	0.03*	0.4	Supported by NEU trials.
0500050	Oat	0.05*	0.03*	0.4	Extrapolated from barley.
0500070	Rye	0.05*	2	2	Extrapolation from wheat.

(*): Indicates that the MRL is set at the limit of analytical quantification.
(a): According to Annex I of Regulation (EC) No 396/2005.
(b): MRL proposals made in the framework of the Article 12 review (SANCO/11481/2014 Rev. 1) not yet discussed for adoption in the EU legislation.
(c): MRL proposal made in the framework of these MRL applications.
(d): Residue definition as proposed in the framework of the Article 12 MRL review (EFSA, 2014).

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BACKGROUND

Regulation (EC) No 396/2005[3] establishes the rules governing the setting of pesticide MRLs at European Union level. Article 6 of that Regulation lays down that any party having a legitimate interest or requesting an authorisation for the use of a plant protection product in accordance with Council Directive 91/414/EEC,[4] repealed by Regulation (EC) No 1107/2009,[5] shall submit to a Member State, when appropriate, an application to set or modify a MRL in accordance with the provisions of Article 7 of that Regulation.

France, hereafter referred to as the EMS-FR, received an application from the company ISK Biosciences Europe N.V.[6] to modify the existing MRLs for the active substance flonicamid in peas without pods, cotton and rye. The Netherlands, hereafter referred to as the EMS-NL, received an application from the company ISK Biosciences Europe N.V. to modify the existing MRLs for the active substance flonicamid in peppers, Brussels sprouts, barley and oat. These applications were notified to the European Commission and EFSA and were subsequently evaluated in accordance with Article 8 of the Regulation.

After completion, the evaluation reports were submitted to the European Commission who forwarded the applications, the evaluation reports and the supporting dossiers to EFSA on 27 May 2014 and 31 October 2014, respectively.

These applications were included in the EFSA Register of Questions with the reference number EFSA-Q-2014-00397 and EFSA-Q-2014-00788 and the following subjects:

Flonicamid - *Application to set new MRLs in peas (without pods), cotton seeds and rye*

Flonicamid - *Application to modify the existing MRLs in peppers (chili peppers), Brussels sprouts, barley and oats*

The EMS-FR proposed to raise the existing MRLs of flonicamid from the LOQ of 0.05 mg/kg to 0.7 mg/kg, 0.2 mg/kg and 2 mg/kg in peas without pods, cotton seeds and rye, respectively. Clarifications on residue trials on cotton and processing study on peas were provided in an updated Evaluation Report (France, 2015).

The EMS-NL proposed to raise the existing MRLs from the LOQ of 0.05 mg/kg to 0.4 mg/kg in barley and oat grains, 0.6 mg/kg in Brussels sprouts and from 0.15 mg/kg to 0.4 mg/kg in peppers. EFSA identified some data requirements, which prevented EFSA to conclude on the consumer risk assessment, which was then suspended. An updated evaluation report with the reply (Netherlands, 2015) was submitted by the EMS-NL on 22 January 2015 and taken into consideration by EFSA for the finalization of this reasoned opinion. In addition, the Netherlands confirmed that the formulation under concern is a water dispersible granule (WG).

EFSA proceeded with the assessment of the applications and the evaluation reports as required by Article 10 of the Regulation. For reasons of efficiency EFSA combined both applications in one reasoned opinion.

[3] Regulation (EC) No 396/2005 of the 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, 16.03.2005, p. 1–16.

[4] Council Directive 91/414/EEC of 15 July 1991 concerning the placing of plant protection products on the market. OJ L 230, 19.08.1991, p. 1–32.

[5] 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.

[6] ISK Biosciences Europe N.V., Pegasus Park De Kleetlaan 12B, 1831 Diegem, Belgium.

TERMS OF REFERENCE

In accordance with Article 10 of Regulation (EC) No 396/2005, EFSA shall, based on the evaluation report provided by the evaluating Member State, provide a reasoned opinion on the risks to the consumer associated with the application.

In accordance with Article 11 of that Regulation, the reasoned opinion shall be provided as soon as possible and at the latest within three months (which may be extended to six months where more detailed evaluations need to be carried out) from the date of receipt of the application. Where EFSA requests supplementary information, the time limit laid down shall be suspended until that information has been provided.

In this particular case the deadlines for providing the reasoned opinion are 27 August 2014 and 19 March 2015, respectively.

THE ACTIVE SUBSTANCE AND ITS USE PATTERN

Flonicamid is the ISO common name for *N*-cyanomethyl-4-(trifluoromethyl)nicotinamide (IUPAC). The chemical structure of the compound is reported below.

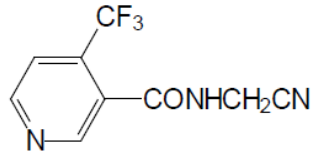


Figure 1: Structure of flonicamid. Molecular weight: 229.16 g/mol

Flonicamid is a systemic insecticide belonging to the pyridinecarboxamide chemical family. Flonicamid is effective against aphids and other sucking insects of plants. It acts by blocking type-A potassium channels, leading to loss of direct movement and suppression of aphid feeding.

Flonicamid was evaluated in the framework of Council Directive 91/414/EEC with France designated as rapporteur Member State (RMS). It was included in Annex I of this Directive by Commission Directive 2010/29/EU[7] which entered into force on 01 September 2010 for use as insecticide. In accordance with Commission Implementing Regulation (EU) No 540/2011[8] flonicamid is approved under Regulation (EC) No 1107/2009, repealing Council Directive 91/414/EEC. The representative uses evaluated in the peer review were foliar applications on apples, pears, peaches, potatoes and wheat. The Draft Assessment Report (DAR) of flonicamid has been peer reviewed by EFSA (EFSA, 2010a).

The EU MRLs for flonicamid are established in Annex IIIA of Regulation (EC) No 396/2005. MRL proposals on citrus fruits, cherries, peppers and aubergines were evaluated by EFSA and new temporary MRLs were established through Regulation (EU) No 893/2010;[9] a request for the modification of the MRL for peas (without pods) was not upheld due to a lack of a sufficient number of residue trials (EFSA, 2010b). EFSA recently issued a reasoned opinion for flonicamid which reviewed all uses authorised at EU level according to Article 12 of Regulation (EC) No 396/2005 (EFSA, 2014). Modifications of the existing MRLs were proposed for several crops, including peppers

[7] Commission Directive 2010/29/EU of 27 April 2010 amending Council Directive 91/414/EEC to include flonicamid (IKI-200) as active substance. OJ L 106, 28.04.2010, p. 9–11.

[8] Commission Implementing Regulation (EU) No 540/2011 of 23 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, 11.06.2011, p. 1–186.

[9] Commission Regulation (EU) No 893/2010 of 8 October 2010 amending Annexes II and III to Regulation (EC) No 396/2005 of the European Parliament and of the Council as regards maximum residue levels for acequinocyl, bentazone, carbendazim, cyfluthrin, fenamidone, fenazaquin, flonicamid, flutriafol, imidacloprid, ioxynil, metconazole, prothioconazole, tebufenozide and thiophanate-methyl in or on certain products. OJ L 266, 09.10.2010, p. 10–38.

and rye. A draft Regulation on MRL proposals (SANCO/11481/2014 Rev. 1) is under discussion but not yet adopted by the Standing Committee on Plants, Animals, Food and Feed (SCPAFF). The existing EU MRLs for flonicamid (established as sum of flonicamid, TFNG and TFNA) on the crops under consideration are set at the LOQ of 0.05 mg/kg except peppers (0.15 mg/kg). No Codex maximum residue limits (CXLs) are established for flonicamid.

The details of the intended GAPs for flonicamid are given in Appendix A. EFSA notes that the GAP proposed for rye in France has been reported as authorised in Slovenia and already assessed by EFSA during the review of the existing MRLs according to Article 12 of Regulation (EC) No 396/2005 (EFSA, 2014).

ASSESSMENT

EFSA bases its assessment on the revised evaluation reports (France, 2015; Netherlands, 2015), the Draft Assessment Report (DAR) and its addendum prepared under Council Directive 91/414/EEC (France, 2005, 2009), the Commission Review Report on flonicamid (EC, 2010a), the conclusion on the peer review of the pesticide risk assessment of the active substance flonicamid (EFSA, 2010a) as well as the conclusions from previous EFSA opinions on flonicamid, including the EFSA reasoned opinion on the review of the existing MRLs according to Article 12 of Regulation (EC) No 396/2005 (EFSA, 2010b, 2014). The assessment is performed in accordance with the legal provisions of the Uniform Principles for the Evaluation and the Authorisation of Plant Protection Products adopted by Commission Regulation (EU) No 546/2011[10] and the currently applicable guidance documents relevant for the consumer risk assessment of pesticide residues (EC, 1996, 1997a–g, 2000, 2010b, 2010c, 2011; OECD, 2011).

1. Method of analysis

1.1. Methods for enforcement of residues in food of plant origin

Analytical methods for the determination of residues in commodities of plant origin were assessed in the framework of the peer review and the review of the existing MRLs under Article 12 of Regulation (EC) No 396/2005. EFSA concluded that validated methods are available to enforce flonicamid and its metabolites TFNG and TFNA in high water, high acid and high oil content and in dry commodities at the LOQ of 0.01 mg/kg for each analyte (combined LOQ of 0.03 mg/kg) (EFSA, 2014).

Additionally, an analytical method using high performance liquid chromatography with tandem mass spectrometry (HPLC-MS/MS) was validated for the determination of flonicamid and its metabolites TFNG, TFNA and TFNA-AM in wheat straw with an LOQ of 0.02 mg/kg for each analyte, but no confirmatory method and ILV was available (France, 2009). This data may be required when the setting of MRLs in feed items will be in place (EFSA, 2014).

Since the commodities under consideration belong to the group of high water, high oil content commodities and dry commodities, EFSA concludes that sufficiently validated analytical methods for enforcing the proposed MRLs for flonicamid according to the residue definition for enforcement are available.

1.2. Methods for enforcement of residues in food of animal origin

Analytical methods for the determination of residues in commodities of animal origin were assessed in the framework of the peer review and the review of the existing MRLs under Article 12 of Regulation (EC) No 396/2005. EFSA concluded that validated analytical methods are available to enforce flonicamid and its metabolite TFNA-AM in milk, eggs, bovine muscle, fat, kidney and liver with an LOQ of 0.01 mg/kg for each analyte (combined LOQ of 0.02 mg/kg) (EFSA, 2014).

[10] Commission Regulation (EU) No 546/2011 of 10 June 2011 implementing Regulation (EC) No 1107/2009 of the European Parliament and of the Council as regards uniform principles for evaluation and authorisation of plant protection products. OJ L 155, 11.06.2011, p. 127–175.

EFSA concludes that sufficiently validated analytical methods for enforcing the proposed MRLs for flonicamid according to the residue definition for enforcement in food of animal origin are available.

2. Mammalian toxicology

The toxicological profile of the active substance flonicamid was assessed in the framework of the peer review under Council Directive 91/414/EEC (EFSA, 2010a; EC, 2010a). The data were sufficient to derive toxicological reference values for flonicamid which are compiled in Table 2-1.

Table 2-1: Overview of the toxicological reference values

	Source	Year	Value	Study relied upon	Safety factor
Flonicamid					
ADI	EC	2010	0.025 mg/kg bw per day	Rabbit, developmental	100
ARfD	EC	2010	0.025 mg/kg bw	Rabbit, developmental	100

The toxicological endpoints set for flonicamid are also applicable to its metabolites TFNA, TFNG and TFNA-AM, which have been included in the residue definition for risk assessment of plant and animal origin commodities (EFSA, 2010a; 2014).

3. Residues

3.1. Nature and magnitude of residues in plant

3.1.1. Primary crops

3.1.1.1. Nature of residues

During the peer review and in the framework of the Article 12 review of the existing MRLs, the metabolism of flonicamid in plants was investigated in the fruit (peach, pepper), root/tuber (potato) and cereal (wheat) crop groups, following foliar applications (France, 2005, 2009; EFSA, 2010a, 2014). The available metabolism studies are summarised in Table 3-1 below.

Table 3-1: Summary of available metabolism studies in plants

Crop group	Crop	Application details			Sampling[(a)]	Remarks
		Method	Rate (g/ha)	Number		
Fruit	Peach	Foliar	100 500	2 2	21 21	-
	Pepper	Foliar	100	1	7, 14	-
Root/tuber	Potato	Foliar	100 500	2 2	14 14	-
Cereals	Wheat	Foliar	100 500	1 1	21 21	-

(a): Days after last application

For risk assessment, the peer review agreed to define the residue as the sum of flonicamid and its metabolites TFNG and TFNA expressed as flonicamid (EFSA 2010a). For monitoring, a clear marker for the residues could not be identified from these metabolism studies. Flonicamid was the major component of the residues in peach fruits and peppers (30 to 91 % TRR), while TFNG was major in cereal grains (39 to 44 % TRR) and TFNG and TFNA in potato tubers (33 to 39 % TRR). Therefore, a single residue definition could not be concluded on and two options were proposed to define the residue for monitoring:

1) sum of flonicamid, TFNG and TFNA expressed as flonicamid (as for risk assessment)
2) flonicamid only (considering that the setting of conversion factors for risk assessment could be problematic for some crops where flonicamid residue levels are expected to be <LOQ)

The residue definitions were reconsidered in the framework of the Article 12 review, where EFSA opted to define the residues as the sum of flonicamid, TFNG and TFNA expressed as flonicamid for both, enforcement and risk assessment. The residue definition for monitoring currently set in Regulation (EC) No 396/2005 is similar to this proposal (sum of flonicamid, TFNG and TFNA), but without the information that total residue should be expressed as flonicamid equivalents. In addition, EFSA confirmed that further clarification on whether the TFNA metabolite could be a metabolite common to other compounds is desirable, as this may have an impact on the residue definition (EFSA, 2014).

For the uses on the crops under consideration in this MRL application, EFSA concludes that the metabolism of flonicamid is sufficiently addressed. The residue definition as concluded after the Article 12 review will be considered for the MRL proposed in this reasoned opinion.

3.1.1.2. Magnitude of residues

All samples from the submitted residue trials were analysed for flonicamid, TFNG and TFNA. When requested and in order to express the total residue as flonicamid equivalent, levels of each metabolite were adjusted with their molecular weights (MW) using the following formula: flonicamid + 0.92 × TFNG + 1.2 × TFNA.[11]

a. Peppers (Indoor GAP: 2 × 60 g/ha, PHI 1 day; NEU GAP: 2 × 60 g/ha, PHI 3 days)

Indoor: Eight GAP-compliant trials conducted on peppers under greenhouse conditions in 2012 were submitted. Trials on protected crops from one growing season are acceptable (EC, 1997b). All trials were designed as decline up to PHI 3 or 7 days. Two trials involving different crop varieties were conducted at the same timing and rate of applications and treatment operations. Since the EMS-NL confirmed that the two greenhouses of these trials were located in different geographical areas of the same Greek location, these trials were considered as independent (Netherlands, 2015). The data are sufficient to derive a MRL of 0.3 mg/kg.

NEU: Trials were conducted in four Hungarian locations. In each location the active substance was applied on two different pepper varieties at the same timing, same rate of applications and treatment operations, same harvest dates. Since the experimental conditions are similar, EFSA is of the opinion that different varieties are not a sufficient parameter to consider these two experimental conditions as independent trials as proposed by the EMS-NL (Netherlands, 2015). Therefore, EFSA concludes that only four independent values are available to support the use of flonicamid in the NEU. The highest value from the two different varieties experimented in each location should be considered for MRL calculation. Since pepper is a major crop, a MRL is not proposed to cover the outdoor use of flonicamid in NEU and four additional trials are requested.

Moreover, as the residues levels observed under outdoor conditions at a 3-day PHI are not significantly lower than the residues levels observed in the indoor trials at 1-day PHI, it cannot be concluded that the MRL derived from the indoor dataset covers the outdoor NEU uses of flonicamid on peppers.

It is highlighted that in peppers (indoor trials), residues are composed of the parent flonicamid (0.02 to 0.13 mg/kg), while the TFNG and TFNA metabolites were almost not present (below or at the LOQ of 0.01 mg/kg or 0.02 mg/kg)

[11] MW flonicamid (229.16)/MW TFNA (191.10); MW flonicamid (229.16)/MW TFNG (248.2).

b. Brussels sprouts (NEU GAP: 2 × 70 g/ha, PHI 7 days)

Eight decline residue trials conducted on Brussels sprouts in the NEU (Germany and United Kingdom) over two seasons were provided. Each trial was conducted with two side-by-side experimental conditions, with and without the addition of an adjuvant (esterified rapeseed oil). All trials are compliant with the GAP except that a longer interval between applications is noted in one location (14 days instead of 7 to 10 days). This deviation was assumed to have a limited impact on the final residue level.

Higher residue levels were observed in the plots conducted with the adjunction of the adjuvant and, therefore, these data were selected to derive a MRL proposal of 0.6 mg/kg.

It is noted that in Brussels sprouts, parent flonicamid is almost not present (below or at the LOQ of 0.01 mg/kg or 0.03 mg/kg) and the residues are mainly composed of the TFNG and TFNA metabolites (<0.01 to 0.14 mg/kg and <0.01 to 0.15 mg/kg, respectively).

c. Peas without pods (NEU GAP: 1 × 70 g/ha, PHI 14 days)

Eight GAP-compliant residue trials conducted on peas without pods in the NEU (Belgium and France) over more than two seasons are available. None of the trials was designed as decline and the most part of the pea samples was separated manually from the pods. Six trials were already assessed in a previous EFSA reasoned opinion (EFSA, 2010b). Total residue levels were in the range of 0.10 to 0.43 mg/kg, resulting in a MRL proposal of 0.7 mg/kg.

It is noted that in peas, residues are mainly composed of the TFNA metabolite, accounting from 0.07 to 0.30 mg/kg.

d. Cotton seeds (SEU GAP: 2 × 37.5 g/ha, PHI 30 days)

Eight GAP-compliant residue trials (five designed as decline) conducted on cotton in the SEU (Greece and Spain) over more than two seasons are available. Data are sufficient to propose a MRL of 0.2 mg/kg.

In cotton seeds, parent flonicamid is almost not present (7 × <0.01, 0.01 mg/kg) and residues are mostly composed of the TFNA metabolite, in the range of <0.01 to 0.08 mg/kg.

e. Barley, oat (NEU GAP: 1 × 70 g/ha, at BBCH 77)

Eight GAP-compliant residue trials, half of which designed as decline up to PHI 30-39, conducted on barley in the NEU (Denmark and Germany) over two seasons are available. In all trials the application was made at stage BBCH 77 (late milk stage) and samples collected at BBCH 89 (full ripe), 30 to 39 days after treatment. At harvest in grain, total residue levels were in the range of 0.04 to 0.19 mg/kg, leading to a MRL proposal of 0.5 mg/kg. Extrapolation from barley to oat is possible as the GAP is the same (EC, 2011).

It is noted that in barley grains, the parent flonicamid and its metabolite TFNA are almost not present (at or below the LOQ of 0.01 mg/kg) and the residues are mostly composed of the TFNG metabolite, up to 0.17 mg/kg.

f. Rye (NEU and SEU GAP: 2 × 70 g/ha, PHI 28 days)

The extrapolation to rye of the MRL of 2 mg/kg set on wheat in Regulation (EC) 396/2005 has already been assessed and recommended by EFSA in the framework of the Article 12 review (EFSA, 2014). This extrapolation is confirmed by EFSA in this MRL application.

As for barley, residues in wheat grains are mostly composed of the metabolite TFNG, accounting for 0.02 to 1.1 mg/kg, while flonicamid is almost absent and TFNG present in lower levels (<0.01 to 0.07 mg/kg).

The results of the residue trials, the related risk assessment input values (HR, STMR) and the MRL proposals are summarised in Table 3-2.

The storage stability of flonicamid and its metabolites TFNG and TFNA in plant matrices was investigated during the peer review and the Article 12 review (EFSA, 2010a, 2014). Residues of flonicamid, TFNG and TFNA were found to be stable at ≤ -18 °C for up to 18 months in matrices with high water content (apple, potato), dry/starch commodities (wheat grain) and in straw. Additionally, storage stability data were submitted in the framework of these MRL applications and showed the stability of flonicamid, TFNG and TFNA in dry/protein (dry beans) and high oil content commodities (rape seed) for up to 12 months when stored at about -20 °C (France, 2015). As the supervised residue trial samples were stored under conditions for which integrity of the samples was demonstrated, it is concluded that the residue data are valid with regard to storage stability.

According to the EMSs, the analytical methods used to analyse the supervised residue trial samples have been sufficiently validated and were proven to be fit for the purpose (France, 2015; Netherlands, 2015).

EFSA concludes that the data are sufficient to derive the following MRL proposals:

- 0.3 mg/kg for peppers (indoor). The intended NEU use on pepper is not sufficiently supported by residue data and no MRL proposal can therefore be derived.[12]
- 0.6 mg/kg for Brussels sprouts (NEU).
- 0.7 mg/kg for peas without pods (NEU).
- 0.2 mg/kg for cotton seeds (SEU).
- 0.4 mg/kg for oat (NEU) extrapolated from barley.
- 2 mg/kg for rye (NEU and SEU) as recommended during the Article 12 review is confirmed (extrapolation from NEU and SEU trials on wheat).

It should be highlighted that the submitted residue trial results confirmed the conclusion that have been drawn from the metabolism studies (see Section 3.1.1.1), that a single component could not be identified as a marker for the enforcement residue definition:

- Flonicamid is the marker of the residues in peppers (TFNG and TFNA almost absent).
- TFNA is the marker of the residues in peas (flonicamid and TFNG almost absent).
- TFNG is the marker of the residues in cereal grains (flonicamid and TFNA almost absent).
- TFNG and TFNA are the markers of the residues in Brussels sprouts and in cotton seeds (flonicamid almost absent).

[12] The EMS-NL proposed a MRL of 0.4 mg/kg based on the NEU use on peppers; the crop variety was considered as a factor which can define a trial as independent (Netherlands, 2015).

Table 3-2: Overview of the available residues trials data

Crop (Trial GAP)	**Region/ Indoor** (a)	**Residue levels** (mg/kg)[(b)] Sum: flonicamid + TFNG+ TFNA expressed as flonicamid	**Recommendations/comments** (c)	**MRL proposals** (mg/kg)	**HR** (mg/kg) (d)	**STMR** (mg/kg) (e)
Peppers (2 × 60 g/ha, PHI 1 day)	Indoor	Sum: 2 × 0.04; 0.05; 0.05; 0.06; 0.07; 0.11; 0.15 TFNG[(f)]: 5 × <0.01; 0.01; 2 × 0.02 TFNA[(f)]: 5 × <0.01; 0.01; 2 × 0.01	Dose rates within ± 25 % rule (66.8 to 74.5 g/ha). MRL_{OECD}: 0.23/0.3	0.3	0.15	0.06
(2 × 60 g/ha, PHI 3 days)	NEU	Sum: 0.04; 0.10; 0.15; 0.22 TFNA: 2 × <0.01; 2 × 0.01 TFNG: 4 × <0.01	Highest residue from two different varieties selected in each location. Four northern trials are requested.	-	-	-
Brussels sprouts (2 × 70 g/ha, PHI 7 days)	NEU	*With adjuvant (esterified rapeseed oil):* Sum: 2 × <0.03; 0.03; 0.05; 0.10; 0.14; 0.22; 0.32 TFNA[(f)]: 3 × <0.01; 0.01; 0.05; 0.03; 0.11; 0.15 TFNG[(f)]: 3 × <0.01; 2 × 0.03; 0.08; 0.10; 0.14	Higher levels observed in the plots conducted with adjunction of an adjuvant. STMR, HR and MRL derived from this dataset. MRL_{OECD}: 0.54/0.6	0.6	0.32	0.08
		Without adjuvant: Sum: 2 × <0.03; 2 × 0.03; 0.03; 0.05; 0.10; 0.15 TFNA[(f)]: 5 × <0.01; 0.01; 0.05; 0.06 TFNG[(f)]: 6 × <0.01; 0.03; 0.05		-	0.15	0.03
Peas (without pods) (1 × 70 g/ha, PHI 14 days)	NEU	Sum: 0.10; **0.11**; 0.17; 0.18; **0.21**; 0.28; 0.37; 0.43 TFNG: 2 × **<0.01**; 2 × 0.02; **0.04**; 0.03; 0.03; 0.05 TFNA: 2 × **0.07**; 0.12; 0.11; **0.10**; 0.19; 0.26; 0.30	Data, except two (**in bold**), already assessed by EFSA (EFSA, 2010b). Peas separated manually from pods. MRL_{OECD}: 0.7/0.7	0.7	0.43	0.20
Cotton seeds (2 × 37.5 g/ha, PHI 30 days)	SEU	Sum: <0.03; 3 × 0.03; 2 × 0.04; 0.07; 0.12 TFNG: 7 × <0.01; 0.01 TFNA: 4 × <0.01; 2 × 0.02; 0.04; 0.08	MRL_{OECD}: 0.17/02	0.2	0.12	0.04
Barley (grain) (1 × 70 g/ha, BBCH 77)	NEU	Sum: 0.06; 2 × 0.09; 0.13; 3 × 0.14; 0.18 TFNG[(f)]: 0.04; 0.07; 0.08; 2 × 0.12; 2 × 0.13; 0.17 TFNA[(f)]: 4 × <0.01; 4 × 0.01	Samples harvested 30 to 39 days after application at BBCH 77; **Extrapolation to oat** (EC, 2011). MRL_{OECD}: 0.36/0.4	0.4	0.18	0.14

Crop (Trial GAP)	**Region/ Indoor** (a)	**Residue levels** (mg/kg)[(b)] Sum: flonicamid + TFNG+ TFNA expressed as flonicamid	**Recommendations/comments** (c)	**MRL proposals** (mg/kg)	**HR** (mg/kg) (d)	**STMR** (mg/kg) (e)
Barley (straw)	NEU	Sum : <0.03; 0.03; 2× 0.04; 0.05; 0.06; 2× 0.07 TFNG[(f)]: <0.01; 0.01; 2 × 0.02; 0.03; 2 × 0.04; 0.05 TFNA[(f)]: 8 × <0.01		-	0.07	0.05
Wheat (grain) (2 × 70 g/ha, PHI 28 days)	NEU	Sum: 0.08; 0.13; 0.15; 0.23; 0.35; 0.52; 0.55; 0.59; 1.12 TFNG: 0.06; 0.12; 0.14; 0.21; 0.28; 0.49; 0.55; 0.56; 1.1 TFNA: 2 × <0.01; 0.01; 0.02; 0.03; 2 × 0.05; 2 × 0.06	Trials already assessed by EFSA during the peer review and the Article 12 MRL review (EFSA, 2010a, 2014). Northern and southern datasets not significantly different. STMR, HR and MRL derived from the merged datasets. MRL_{OECD}: 1.6/2 **Extrapolation to rye** recommended during the Article 12 review is confirmed (EFSA, 2014).	2	1.12	0.32
	SEU	Sum: 0.04; 0.09; 0.12; 0.20; 0.27; 0.47; 0.52; 0.57; 0.74 TFNG: 0.02; 0.07; 0.09; 2 × 0.16; 0.43; 0.46; 0.53; 0.70 TFNA: 2 × <0.01; 0.02; 0.03; 2 × 0.05; 0.07; 0.06; 0.07				
Wheat (straw)	NEU	Sum: 2 × <0.06; 0.11; 0.15; 0.17; 0.18; 0.42; 0.48 TFNG: 3 × <0.02; 0.08; 0.10; 0.15; 0.17; 0.07 TFNA: 7 × <0.02; 0.03		-	0.48	0.17
	SEU	Sum: 2 × 0.06; 0.10; 0.14; 0.18; 0.20; 0.27; 0.41; 0.48 TFNG: 2 × <0.02; 0.06; 0.10; 0.14; 0.17; 0.15; 0.36; 0.41 TFNA: 7 × <0.02; 0.02; 0.03				

(a): NEU: Outdoor trials conducted in northern Europe, SEU: Outdoor trials conducted in southern Europe, Indoor: indoor EU trials or Country code: if non-EU trials (EC, 2011).
(b): Individual residue levels for the sum are reported in ascending order; individual residue levels of TFNG and TFNA levels are matched with the corresponding sum.
Underlined values: residue level measured at the longer PHI than that requested in the proposed GAP.
(c): Any information/comment supporting the decision and OECD MRL calculation (unrounded/rounded value).
(d) STMR: Median value of the individual trial results according to residue definition for risk assessment.
(e): HR: Highest value of the individual trial results according to the residue definition for risk assessment.
(f). TFNG and TFNA levels expressed as flonicamid equivalents.

3.1.1.3. Effect of industrial processing and/or household preparation

The effect of processing on the nature of flonicamid was investigated under standard hydrolysis conditions in the framework of the MRL review (EFSA, 2014). EFSA concluded that the compound is hydrolytically stable under the representative processing conditions. No studies investigating the effect of processing on the nature of the metabolites TFNG and TFNA were available and they were requested during the MRL review (EFSA, 2014). Depending on the outcome of these studies a decision on the residue definition for processed commodities needs to be taken.

During the peer review and the review under Article 12 studies on the magnitude of flonicamid, TFNG and TFNA residues in processed products were reported for wheat and plums (EFSA, 2010a, 2014). One study on peas was submitted by the EMS-FR (France 2015). A processing factor (PF) for canned peas (1.0) and frozen peas (1.7) was derived but any conclusion can be drawn on the residue behaviour from a single study.

Four studies on barley (one balance and three follow-up) were submitted by the EMS-NL (Netherlands, 2014). Grains form trials conducted at 1N and 3N dose rates were cleaned and processed to beer. Residue in processed fractions where mainly composed of the TFNG metabolite (0.03 to 019 mg/kg in brewing malt and <0.01 to 0.06 mg/kg in beer), residues of the parent flonicamid being below the LOQ of 0.01 mg/kg and TFNA observed in the range of <0.01 to 0.03 mg/kg. Available data are summarised in Table 3-3.

Table 3-3: Overview of the available processing studies

Processed commodity	Number of studies	INDICATIVE Median PF[(a)]	Median CF[(b)]	Comments/Individual PFs (indicative)
Enforcement residue definition: to be established *(residues reported as sum of flonicamid, TFNG and TFNA expressed as flonicamid)*				
Barley/cleaned grain	4	0.91	n.a.	0.79; 0.81; 1.0; 1.02
Barley/brewing malt	4	0.73	n.a.	0.18; 0.65; 0.81; 0.96
Barley/beer	4	0.14	n.a.	<0.05; 0.13; 0.15; 0.19
Wheat, wholemeal bread	4	0.58	n.a.	Refer to EFSA, 2010a, 2014.

(a): The median processing factor is obtained by calculating the median of the individual processing factors of each processing study.
(b): The median conversion factor for enforcement to risk assessment is obtained by calculating the median of the individual conversion factors of each processing study.

Pending the submission of the standard hydrolysis studies requested for the metabolites TFNG and TFNA in the conclusion of the Article 12 review (EFSA, 2014), these PFs should be considered indicative (EFSA, 2010a, 2014) and are not recommended for inclusion in Annex VI of Regulation (EC) 396/2005.

As the residue levels in raw agricultural commodities (RAC) exceed the trigger value of 0.1 mg/kg and the total theoretical maximum daily intake (TMDI) for flonicamid and its metabolites is expected to exceed the 10 % of the ADI (EC, 1997d), further data on the nature and magnitude of residue in processed peas (including cooked peas), cooked Brussels sprouts and cereal processed products (i.e. bran, floor) are required. Nevertheless, these data are not expected to affect the outcome of the consumer risk assessment performed in the framework of this reasoned opinion.

3.1.2. Rotational crops

The crops under consideration can be grown in rotation with other plants and therefore the possible occurrence of residues in succeeding crops resulting from the use on primary crops has to be assessed.

According to the soil degradation laboratory studies evaluated in the framework of the peer review, DT_{90} values of flonicamid and its metabolites (TFNG, TFNA-OH and TFNG-AM) in the soil are all expected to range between 1.5 and 8.7 days, which are far below the trigger value of 100 days. Thus, further studies investigating the nature and magnitude of the compound uptake in rotational crops are not required (EC, 1997c).

3.2. Nature and magnitude of residues in livestock

The intended uses on cereals assessed in the framework of this application do not have an impact on the livestock dietary burden based on the existing uses evaluated during the Article 12 MRL review (EFSA, 2014). The expected residues on the cereal grains and straw under consideration are therefore covered by the authorised uses. Hence, no changes are proposed to the MRLs on the commodities of animal origin recommended during the Article 12 review (EFSA, 2014).

4. Consumer risk assessment

The consumer risk assessment was performed with revision 2 of the EFSA Pesticide Residues Intake Model (PRIMo). This exposure assessment model contains the relevant European food consumption data for different sub-groups of the EU population[13] (EFSA, 2007).

In the framework of the review of the existing MRLs for flonicamid according to Article 12 of Regulation (EC) No 396/2005 a comprehensive long-term exposure assessment was performed taking into account the existing uses at the EU level (EFSA, 2014). EFSA updated this risk assessment with the STMRs derived from the residue trials for the crops under consideration (see Table 3.1). Those food commodities, for which no uses were reported in the framework of the Article 12 review, were excluded from the exposure calculation, assuming that there is no use of flonicamid on these crops.

The acute exposure assessment was performed only with regard to the commodities under consideration assuming the consumption of a large portion of the food items as reported in the national food surveys and that these items contained residues at the highest level as observed in supervised field trials. A variability factor accounting for the inhomogeneous distribution on the individual items consumed was included in the calculation for peppers (EFSA, 2007). The input values used for the dietary exposure calculation are summarised in Table 4-1.

Table 4-1: Input values for the consumer dietary exposure assessment

Commodity	Chronic exposure assessment		Acute exposure assessment	
	Input value (mg/kg)	**Comment**	**Input value** (mg/kg)	**Comment**
Risk assessment residue definition: sum of flonicamid, TFNA and TFNG expressed as flonicamid (products of plant origin)				
Peppers	0.06	STMR (indoor)	0.15	HR (indoor)
Brussels sprouts	0.07	STMR (with adjuvant)	0.32	HR (with adjuvant)
Peas with pods	0.2	STMR	0.43	HR
Cotton seeds	0.04	STMR	0.04	STMR
Barley, oat grain	0.17	STMR	0.17	STMR
Rye grain	0.32[(a)]	STMR	0.32	STMR

[13] The calculation of the long-term exposure (chronic exposure) is based on the mean consumption data representative for 22 national diets collected from MS surveys plus 1 regional and 4 cluster diets from the WHO GEMS Food database; for the acute exposure assessment the most critical large portion consumption data from 19 national diets collected from MS surveys is used. The complete list of diets incorporated in EFSA PRIMo is given in its reference section (EFSA, 2007).

Commodity	Chronic exposure assessment		Acute exposure assessment	
	Input value (mg/kg)	Comment	Input value (mg/kg)	Comment
Other plant origin commodities	STMR, STMR-P, MRL	See Table 4.1 in EFSA Reasoned opinion on Article 12 review (EFSA, 2014)	Acute risk assessment was undertaken only with regard to the crops under consideration.	
Risk assessment residue definition: sum of flonicamid and TFNA-AM expressed as flonicamid (products of animal origin)				
Animal origin commodities	STMR	See Table 4.1 in EFSA Reasoned opinion on Article 12 review (EFSA, 2014)	Acute risk assessment was undertaken only with regard to the crops under consideration.	

(a): In the updated chronic risk assessment EFSA replace the STMR derived from the single set of NEU trials (0.35 mg/kg) used in the Article 12 review with the STMR derived from the combined dataset of NEU and SEU trials (see Table 3-2).

The estimated exposure was then compared with the toxicological reference values derived for flonicamid (see Table 2-1). The results of the intake calculation are presented in Appendix B to this reasoned opinion.

Under the assumption that the MRLs will be amended as proposed in the Article 12 review, no long-term consumer intake concerns were identified for any of the European diets incorporated in the EFSA PRIMo. The total calculated intake accounted for 17 % of the ADI (Danish child). The contribution of residues to the total consumer exposure accounted for a maximum of 6 % of the ADI for rye (Danish child), 0.7 % for barley, 0.5 % for peas without pods and less than 0.3 % for the remaining commodities.

No acute consumer risk was identified in relation to the MRL proposals for the crops under consideration. The calculated maximum exposure in percentage was 38 % of the ARfD for peppers (German child), 14 % for peas without pods, 11 % for Brussels sprouts, 8 % for rye, 3 % for oats and 1 % for barley (no consumption data on cotton seeds in EFSA PRIMo).

EFSA concludes that the intended uses of flonicamid on the crops under consideration will not result in a consumer exposure exceeding the toxicological reference values and therefore are unlikely to pose a public health concern.

CONCLUSIONS AND RECOMMENDATIONS

CONCLUSIONS

The toxicological profile of flonicamid was assessed in the framework of the peer review under Council Directive 91/414/EEC and the data were sufficient to derive an acceptable daily intake (ADI) of 0.025 mg/kg bw per day and an acute reference dose (ARfD) of 0.025 mg/kg bw.

The metabolism of flonicamid in primary crops was investigated in the fruit, root/tuber and cereal crop groups following foliar applications. EFSA proposed to maintain the existing residue definition for enforcement in plants as the sum of flonicamid and the metabolites TFNG and TFNA, but with the information that total residues are expressed as flonicamid equivalents. The same residue definition was established for risk assessment. For the use on the crops under consideration, EFSA concludes that the metabolism in primary crops is sufficiently addressed and that the derived residue definitions are applicable.

EFSA concludes that the submitted residue trials are sufficient to derive MRL proposals of 0.3 mg/kg for peppers (indoor uses), 0.6 mg/kg for Brussels sprouts, 0.7 mg/kg for peas without pods, 0.2 mg/kg for cotton seeds, 0.4 mg/kg for barley and oat. The extrapolation to rye of the current MRL of 2 mg/kg set on wheat in the EU legislation and recommended during the Article 12 review of the existing MRLs is confirmed. Sufficient data were not provided to support the outdoor use of flonicamid on

peppers. Adequate analytical methods are available to control the residues of flonicamid and its metabolites TFNG and TFNA in the crops under consideration at the validated combined the limit of quantification (LOQ) of 0.03 mg/kg.

Flonicamid showed to be hydrolytically stable under standard hydrolysis conditions, but no data were provided on the stability of the metabolites TFNG and TFNA and additional information was required during the Article 12 review. Processing studies on peas and barley were reported in the framework of these MRL applications. Pending the submission of additional data on peas and information on the stability of the TFNG and TFNA under hydrolysis conditions, the inclusion of the derived processing factors in Annex VI of Regulation (EC) 396/2005 is not recommended by EFSA.

The occurrence of flonicamid residues in rotational crops was investigated in the framework of the peer review. Based on the available information, the degradation of flonicamid and its metabolites is extremely rapid in soil and significant residue levels are unlikely to occur in rotational crops.

Since the intended uses on cereals do not have an impact on the livestock dietary burden obtained from the existing uses, no changes are proposed to the MRLs for commodities of animal origin recommended during the Article 12 MRL review.

The consumer risk assessment was performed with revision 2 of the EFSA Pesticide Residues Intake Model (PRIMo). EFSA updated the chronic consumer risk assessment performed the framework of the review of the existing MRLs according to Article 12 of Regulation (EC) No 396/2005 with the supervised trials median residue levels (STMRs) derived from the submitted residue trials for the crops under consideration. The acute exposure assessment was performed only with regard to the commodities under consideration.

Under the assumption that the MRLs will be amended as proposed in the Article 12 review, no long-term consumer intake concerns were identified for any of the European diets incorporated in the EFSA PRIMo. The total calculated chronic intake accounted for up to 17 % of the ADI (Danish child). The maximum acute intake was calculated to be 38 % of the ARfD (German child) for peppers and therefore, no acute consumer intake concern was identified in relation to the MRL proposals.

EFSA concludes that the proposed uses of flonicamid on the crops under consideration will not result in a consumer exposure exceeding the toxicological reference values and therefore are unlikely to pose a consumer health risk.

RECOMMENDATIONS

Code[(a)]	**Commodity**	**Existing EU MRL** (mg/kg)	**Proposed MRL** (mg/kg)		**Comment/Justification**
			Art. 12[(b)]	**Art. 10**[(c)]	
Enforcement residue definition: Sum of flonicamid, TNFG and TNFA expressed as flonicamid[(d)]					
0231020	Sweet peppers/bell peppers	0.15	0.2	0.3	Indoor use only. Outdoor NEU use not sufficiently supported by data.
0242010	Brussels sprouts	0.05*	0.03*	0.6	Supported by NEU trials (with adjuvant).
0260040	Peas (without pods)	0.05*	0.03*	0.7	Supported by NEU trials.
0401090	Cotton seeds	0.05*	0.06*	0.2	Supported by SEU trials.
0500010	Barley	0.05*	0.03*	0.4	Supported by NEU trials.
0500050	Oat	0.05*	0.03*	0.4	Extrapolated from barley.
0500070	Rye	0.05*	2	2	Extrapolation from wheat.

(*): Indicates that the MRL is set at the limit of analytical quantification.
(a): According to Annex I of Regulation (EC) No 396/2005.
(b): MRL proposals made in the framework of the Article 12 review (SANCO/11481/2014 Rev. 1) not yet discussed for adoption in the EU legislation.

(c): MRL proposal made in the framework of these MRL applications.
(d). Residue definition as proposed in the framework of the Article 12 MRL review (EFSA, 2014).

REFERENCES

EC (European Commission), 1996. Appendix G. Livestock Feeding Studies. 7031/VI/95-rev.4.

EC (European Commission), 1997a. Appendix A. Metabolism and distribution in plants. 7028/IV/95-rev.3.

EC (European Commission), 1997b. Appendix B. General recommendations for the design, preparation and realisation of residue trials. Annex 2. Classification of (minor) crops not listed in the Appendix of Council Directive 90/642/EEC. 7029/VI/95-rev.6.

EC (European Commission), 1997c. Appendix C. Testing of plant protection products in rotational crops. 7524/VI/95-rev.2.

EC (European Commission), 1997d. Appendix E. Processing studies. 7035/VI/95-rev.5.

EC (European Commission), 1997e. Appendix F. Metabolism and distribution in domestic animals. 7030/VI/95-rev.3.

EC (European Commission), 1997f. Appendix H. Storage stability of residue samples. 7032/VI/95-rev.5.

EC (European Commission), 1997g. Appendix I. Calculation of maximum residue level and safety intervals. 7039/VI/95.

EC (European Commission), 2000. Residue analytical methods. For pre-registration data requirement for Annex II (part A, section 4) and Annex III (part A, section 5 of Directive 91/414). SANCO/3029/99-rev.4.

EC (European Commission), 2010a. Review report for the active substance flonicamid (IKI-220). Finalised in the Standing Committee on the Food Chain and Animal Health at its meeting on 12 March 2010 in view of the inclusion of flonicamid in Annex I of Council Directive 91/414/EEC. SANCO/ 10479/2010 final, 12 March 2010, 8 pp.

EC (European Commission), 2010b. Classes to be used for the setting of EU pesticide Maximum Residue Levels (MRLs). SANCO 10634/2010 Rev. 0, finalised in the Standing Committee on the Food Chain and Animal Health at its meeting of 23-24 March 2010.

EC (European Commission), 2010c. Residue analytical methods. For post-registration control. SANCO/825/00-rev.8.1.

EC (European Commission), 2011. Appendix D. Guidelines on comparability, extrapolation, group tolerances and data requirements for setting MRLs. 7525/VI/95-rev.9.

EFSA (European Food Safety Authority), 2007. Reasoned opinion on the potential chronic and acute risk to consumers health arising from proposed temporary EU MRLs. doi:10.2903/j.efsa.2007.32r

EFSA (European Food Safety Authority), 2010a. Conclusion on the peer review of the pesticide risk assessment of the active substance flonicamid. EFSA Journal 2010; 8(5) 1445, 63 pp. doi:10.2903/j.efsa.2010.1445

EFSA (European Food Safety Authority), 2010b. Modification of the existing MRLs for flonicamid in various crops. EFSA Journal 2010; 8(5):1610, 30 pp. doi:10.2903/j.efsa.2010.1610

EFSA (European Food Safety Authority), 2014. Reasoned opinion on the review of the existing maximum residue levels (MRLs) for flonicamid according to Article 12 of Regulation (EC) No 396/2005. EFSA Journal 2014;12(6):3740, 49 pp. doi:10.2903/j.efsa.2014.3740

FAO (Food and Agriculture Organization of the United Nations), 2009. Submission and evaluation of pesticide residues data for the estimation of Maximum Residue Levels in food and feed. Pesticide Residues. 2nd Ed. FAO Plant Production and Protection Paper 197, 264 pp.

France, 2005. Draft assessment report on the active substance flonicamid prepared by the rapporteur Member State France in the framework of Council Directive 91/414/EEC, February 2005.

France, 2009. Final addendum to the draft assessment report on the active substance flonicamid prepared by the rapporteur Member State France in the framework of Council Directive 91/414/EEC, compiled by EFSA, October 2009.

France, 2015. Evaluation report on the modification of MRLs for flonicamid in rye, peas and cotton prepared by the evaluating Member State France under Article 8 of Regulation (EC) No 396/2005, February 2015 (update of April, 2014), 70 pp.

Netherlands, 2015. Evaluation report on the modification of MRLs for flonicamid in peppers, barley, oats and Brussels sprouts prepared by the evaluating Member State the Netherlands under Article 8 of Regulation (EC) No 396/2005, update according to the data requirements requested by EFSA, 22 January 2015, 40 pp.

OECD (Organisation for Economic Co-operation and Development), 2011. OECD MRL Calculator: spreadsheet for single data set and spreadsheet for multiple data set, 2 March 2011. In: Pesticide Publications/Publications on Pesticide Residues.

APPENDICES

Appendix A. Good Agricultural Practice (GAPs)

Crop and/or situation (a)	Member State or Country	F G or I (b)	Pest or group of pests controlled (c)	Formulation		Application				Application rate per treatment			PHI (days) (l)	Remarks (m)
				type (d-f)	conc. a.s. (i)	Method kind (f-h)	Growth stage & season (j)	number min-max (k)	interval min-max	g a.s./hL min-max	Water L/ha min-max	g a.s./ha min-max		
Peppers	Netherlands	F	Aphids	WG	500 g/kg	Foliar spraying	BBCH 16-18 until PHI	2	7-14	12-30	200-500	60	3	
		G	Aphids	WG	500 g/kg	Foliar spraying	BBCH 16-18 until PHI	2	7-14	6-15	400-1000	60	1	
Peas without pods	France	F	Aphids	WG	500 g/kg	Foliar spraying	Development of fruits	1	-	18-47	150-400	70	14	
Brussels sprout	Netherlands	F	Aphids	WG	500 g/kg	Foliar spraying	Until BBCH 49	2	7-10	35	200	70	7	Inclusion of adjuvant not reported in the GAP.
Cotton seeds	Spain	F	Aphids	WG	500 g/kg	Foliar spraying		2	14	4.7-9.4	400-800	37.5	30	Last application during ripening (BBCH 81-89)
Rye	France	F	Aphids	WG	500 g/kg	Foliar spraying	Ears stage. (Late spring till early summer)	2	21	14-35	200-500	70	28	GAP assessed during MRL review (EFSA, 2014)
Barley, oat	Netherlands	F	Aphids	WG	500 g/kg	Foliar spraying	Until BBCH 77	1	-	35	200	70	-	PHI determined by growth stage

Remarks:

(a) For crops, EU or other classifications, e.g. Codex, should be used; where relevant, the use situation should be described (e.g. fumigation of a structure)
(b) Outdoor or field use (F), glasshouse application (G) or indoor application (I)
(c) e.g. biting and sucking insects, soil born insects, foliar fungi, weeds
(d) e.g. wettable powder (WP), emulsifiable concentrate (EC), granule (GR)
(e) GCPF Technical Monograph No 2, 4th Ed., 1999 or other codes, e.g. OECD/CIPAC, should be used
(f) All abbreviations used must be explained
(g) Method, e.g. high volume spraying, low volume spraying, spreading, dusting, drench
(h) Kind, e.g. overall, broadcast, aerial spraying, row, individual plant, between the plants - type of equipment used must be indicated
(i) g/kg or g/l
(j) Growth stage at last treatment (Growth stages of mono-and dicotyledonous plants. BBCH Monograph, 2nd Ed., 2001), including where relevant, information on season at time of application
(k) The minimum and maximum number of application possible under practical conditions of use must be provided
(l) PHI - minimum pre-harvest interval
(m) May include: Extent of use/economic importance/restrictions (i.e. feeding, grazing)

Appendix B. Pesticide Residue Intake Model (PRIMO)

Flonicamid

Status of the active substance:	**Approved**	Code no.	
LOQ (mg/kg bw):	0.03	proposed LOQ:	
Toxicological end points			
ADI (mg/kg bw/day):	**0.025**	ARfD (mg/kg bw):	**0.025**
Source of ADI:	**EC**	Source of ARfD:	**EC**
Year of evaluation:	**2010**	Year of evaluation:	**2010**

Chronic risk assessment - refined calculations

TMDI (range) in % of ADI minimum - maximum	
2	17
No of diets exceeding ADI:	---

Highest calculated TMDI values in % of ADI	MS Diet	Highest contributor to MS diet (in % of ADI)	Commodity / group of commodities	2nd contributor to MS diet (in % of ADI)	Commodity / group of commodities	3rd contributor to MS diet (in % of ADI)	Commodity / group of commodities	pTMRLs at LOQ (in % of ADI)
17.2	DK child	7.7	Wheat	5.7	Rye	1.0	Milk and cream,	1.4
16.7	WHO Cluster diet B	11.9	Wheat	1.7	Tomatoes	0.3	Potatoes	0.9
14.2	DE child	5.8	Wheat	2.8	Apples	1.1	Milk and cream,	1.7
13.9	NL child	6.6	Wheat	2.3	Milk and cream,	1.5	Apples	3.4
12.4	WHO cluster diet D	9.1	Wheat	0.6	Tomatoes	0.5	Rye	1.1
11.2	IT kids/toddler	9.3	Wheat	0.8	Tomatoes	0.2	Apples	0.1
9.9	FR toddler	3.7	Wheat	3.2	Milk and cream,	0.6	Apples	4.1
9.6	ES child	6.2	Wheat	1.0	Milk and cream,	0.5	Tomatoes	1.7
9.3	UK Toddler	5.5	Wheat	1.7	Milk and cream,	0.4	Potatoes	2.2
9.1	UK Infant	3.7	Wheat	3.1	Milk and cream,	0.5	Peas (without pods)	3.7
8.8	WHO cluster diet E	5.5	Wheat	0.6	Rye	0.5	Potatoes	1.0
8.5	WHO Cluster diet F	5.0	Wheat	1.0	Rye	0.4	Potatoes	1.0
8.1	SE general population 90th percentile	4.5	Wheat	1.0	Milk and cream,	0.5	Potatoes	1.6
7.7	PT General population	5.5	Wheat	0.6	Potatoes	0.5	Tomatoes	0.6
7.5	IT adult	5.8	Wheat	0.7	Tomatoes	0.2	Apples	0.1
7.2	WHO regional European diet	4.2	Wheat	0.6	Tomatoes	0.5	Potatoes	1.3
7.2	IE adult	3.2	Wheat	0.7	Barley	0.3	Potatoes	0.7
6.0	FR all population	4.6	Wheat	0.2	Tomatoes	0.2	Milk and cream,	0.5
5.6	ES adult	3.3	Wheat	0.4	Tomatoes	0.4	Milk and cream,	0.8
5.5	NL general	2.9	Wheat	0.5	Milk and cream,	0.3	Potatoes	1.1
5.5	FR infant	2.1	Milk and cream,	1.2	Wheat	0.6	Apples	2.7
5.3	DK adult	2.8	Wheat	0.9	Rye	0.4	Milk and cream,	0.7
5.0	LT adult	1.5	Wheat	1.4	Rye	0.4	Apples	0.9
4.4	UK vegetarian	2.9	Wheat	0.3	Tomatoes	0.3	Milk and cream,	0.5
3.6	FI adult	1.4	Wheat	0.9	Rye	0.5	Milk and cream,	0.6
3.5	UK Adult	2.3	Wheat	0.2	Tomatoes	0.2	Milk and cream,	0.4
1.7	PL general population	0.5	Tomatoes	0.5	Apples	0.4	Potatoes	0.4

Conclusion:

The estimated Theoretical Maximum Daily Intakes (TMDI), based on pTMRLs were below the ADI.
A long-term intake of residues of Flonicamid is unlikely to present a public health concern.

Acute risk assessment /children - refined calculations						Acute risk assessment / adults / general population - refined calculations					
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** calculations, the variability factors of 10 and 7 were replaced by 5. For lettuce the calculation was performed with a variabilty factor of 3. **Threshold MRL** is the calculated residue level which would leads to an exposure equivalent to 100 % of the ARfD.											
Unprocessed commodities	**No of commodities for which ARfD/ADI is exceeded (IESTI 1):**			**---**	**No of commodities for which ARfD/ADI is exceeded (IESTI 2):**			**---**	**No of commodities for which ARfD/ADI is exceeded (IESTI 1):**			**---**	**No of commodities for which ARfD/ADI is exceeded (IESTI 2):**			**---**
	IESTI 1	***)**	****)**		**IESTI 2**	***)**	****)**		**IESTI 1**	***)**	****)**		**IESTI 2**	***)**	**)	
	Highest % of ARfD/ADI	Commodities	pTMRL/ threshold MRL (mg/kg)		Highest % of ARfD/ADI	Commodities	pTMRL/ threshold MRL (mg/kg)		Highest % of ARfD/ADI	Commodities	pTMRL/ threshold MRL (mg/kg)		Highest % of ARfD/ADI	Commodities	pTMRL/ threshold MRL (mg/kg)	
	37.8	Peppers	0.15 / -		27.0	Peppers	0.15 / -		9.8	Peppers	0.15 / -		7.0	Peppers	0.15 / -	
	14.1	Peas (without pods)	0.43 / -		14.1	Peas (without	0.43 / -		6.6	Peas (without pods)	0.43 / -		6.6	Peas (without pods)	0.43 / -	
	11.2	Brussels sprouts	0.32 / -		11.2	Brussels sprouts	0.32 / -		6.5	Brussels sprouts	0.32 / -		6.5	Brussels sprouts	0.32 / -	
	8.1	Rye	0.32 / -		8.1	Rye	0.32 / -		6.2	Rye	0.32 / -		6.2	Rye	0.32 / -	
	2.7	Oats	0.17 / -		2.7	Oats	0.17 / -		4.1	Barley	0.14 / -		4.1	Barley	0.14 / -	
	1.0	Barley	0.14 / -		1.0	Barley	0.14 / -		1.0	Oats	0.17 / -		1.0	Oats	0.17 / -	
	No of critical MRLs (IESTI 1)			---					**No of critical MRLs (IESTI 2)**			---				
Processed commodities	**No of commodities for which ARfD/ADI is exceeded:**			**---**					**No of commodities for which ARfD/ADI is exceeded:**			**---**				
			*****)**								*****)**					
	Highest % of ARfD/ADI	Processed commodities	pTMRL/ threshold MRL (mg/kg)						Highest % of ARfD/ADI	Processed commodities	pTMRL/ threshold MRL (mg/kg)					

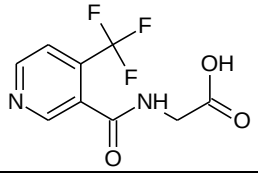
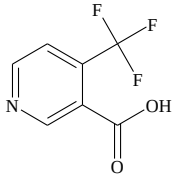
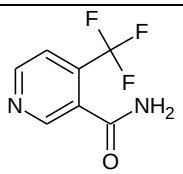
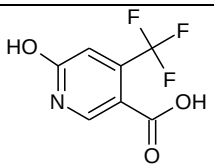
*) The results of the IESTI calculations are reported for at least 5 commodities. If the ARfD is exceeded for more than 5 commodities, all IESTI values > 90% of ARfD are reported.
**) pTMRL: provisional temporary MRL
***) pTMRL: provisional temporary MRL for unprocessed commodity

Conclusion:

For Flonicamid 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.

Appendix C. List of metabolites and related structural formula

Code/Trivial name	Chemical name*	Structural formula*
TFNG	*N*-(4-trifluoromethylnicotinoyl)glycine	
TFNA	4-trifluoromethylnicotinic acid	
TFNA-AM	4-(trifluoromethyl)pyridine-3-carboxamide	
TFNA-OH	6-hydroxy-4-(trifluoromethyl)pyridine-3-carboxylic acid	

* ACD/ChemSketch, Advanced Chemistry Development, Inc., ACD/Labs Release: 12.00 Product version: 12.00 (Build 29305, 25 Nov 2008) (EFSA, 2010a).

ABBREVIATIONS

ADI	acceptable daily intake
ARfD	acute reference dose
a.s.	active substance
BBCH	growth stages of mono- and dicotyledonous plants
bw	body weight
CXL	Codex Maximum Residue Limit (Codex MRL)
d	day
DAR	Draft Assessment Report
DT_{90}	period required for 90 % dissipation (define method of estimation)
EC	European Commission
EFSA	European Food Safety Authority
EMS	evaluating Member State
EU	European Union
FAO	Food and Agriculture Organization of the United Nations
FR	France
GAP	good agricultural practice
GCPF	Global Crop Protection Federation (former GIFAP)
ha	hectare
hL	hectolitre
HPLC	high performance liquid chromatography
HR	highest residue
i.e.	that is (id est, *Latin*)
ILV	independent laboratory validation
ISO	International Organisation for Standardisation
IUPAC	International Union of Pure and Applied Chemistry
kg	kilogram
L	litre
LOQ	limit of quantification
MRL	maximum residue level
MS-MS	tandem mass spectrometry
MW	molecular weight
NL	The Netherlands
NEU	Northern Europe
OECD	Organisation for Economic Co-operation and Development
PF	processing factor
PHI	pre-harvest interval
PRIMo	(EFSA) Pesticide Residues Intake Model
RAC	raw agricultural commodity
RMS	rapporteur Member State
SANCO	Directorate-General for Health and Consumers

SCPAFF	Standing Committee on Plants, Animals, Food and Feed, (formerly: Standing Committee on the Food Chain and Animal Health; SCFCAH)
SEU	Southern Europe
STMR	supervised trials median residue
STMR-P	supervised trials median residue, processed commodity
TMDI	theoretical maximum daily intake
TRR	total radioactive residue
WG	water dispersible granule
WHO	World Health Organization