Review of the existing maximum residue levels for fluometuron 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 fluometuron. To assess the occurrence of fluometuron residues in plants, processed commodities, rotational crops and livestock, EFSA considered the conclusions derived in the framework of Commission Regulation (EC) No 33/2008 as well as the European authorisations reported by Member States (including the supporting residues data). Based on the assessment of the available data, an MRL proposal was derived and a consumer risk assessment was carried out. All information required by the regulatory framework was present and a risk to consumers was not identified. In addition, EFSA identified some data gaps which are not expected to impact on the validity of the MRL derived but which might have an impact on national authorisations.

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Keywords: Fluometuron, MRL review, Regulation (EC) No 396/2005, consumer risk assessment, phenylurea, herbicide, trifluoroacetic acid (TFA)

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Question number: EFSA-Q-2009-00054
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Acknowledgement: EFSA wishes to thank the rapporteur Member State Greece for the preparatory work on this scientific output.

Suggested citation: EFSA (European Food Safety Authority), Abdourahime H, Anastassiadou M, Brancato A, Brocca D, Carrasco Cabrera L, De Lentdecker C, Ferreira L, Greco L, Jarrah S, Kardassi D, Leuschner R, Lostia A, Lythgo C, Medina P, Miron I, Molnar T, Nave S, Pedersen R, Raczyk M, Reich H, Ruocco S, Sacchi A, Santos M, Stanek A, Sturma J, Tarazona J, Theobald A, Vagenende B, Verani A and Villamar-Bouza L, 2019. Reasoned opinion on the review of the existing maximum residue levels for fluometuron according to Article 12 of Regulation (EC) No 396/2005. EFSA Journal 2019;17(1):5560, 27 pp. https://doi.org/10.2903/j.efsajournal.2019.5560

ISSN: 1831-4732

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Summary

Fluometuron was initially not included in Annex I to Directive 91/414/EEC by Commission Decision 2008/934/EC. Following a resubmission application Fluometuron was subsequently approved by Commission Implementing Regulation (EU) No 540/2011 of 25 May 2011 as an active substance, in accordance with the provision of Regulation (EC) No 1107/2009.

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 15 September 2017 EFSA initiated the collection of data for this active substance. In a first step, Member States were invited to submit by 15 October 2017 their national Good Agricultural Practices (GAPs) in a standardised way, in the format of specific GAP forms, allowing the designated rapporteur Member State (RMS) Greece to identify the critical GAPs in the format of a specific GAP overview file. Subsequently, Member States were requested to provide residue data supporting the critical GAPs, within a period of 1 month, by 15 January 2018. On the basis of all the data submitted by Member States and by the EURLs, EFSA asked the RMS to complete the Pesticide Residues Overview File (PROFile) and to prepare a supporting evaluation report. The PROFile and evaluation report, together with Pesticide Residues Intake Model (PRIMo) calculations and updated GAP overview file were provided by the RMS to EFSA on 3 May 2018. Subsequently, EFSA performed the completeness check of these documents with the RMS. The outcome of this exercise including the clarifications provided by the RMS, if any, was compiled in the completeness check report.

Based on the information provided by the RMS, Member States and the EU Reference Laboratories for Pesticides Residues (EURL), and taking into account the conclusions derived by EFSA in the framework of Commission Regulation (EC) No 33/2008, EFSA prepared in September 2018 a draft reasoned opinion, which was circulated to Member States for consultation via a written procedure. Comments received by 7 November 2018 were considered during the finalisation of this reasoned opinion. The following conclusions are derived.

The metabolism of fluometuron in plants was investigated in primary and rotational crops. The residue definition for enforcement can be proposed as sum of fluometuron and all metabolites determined as trifluoromethylaniline (TFMA), expressed as fluometuron. Fully validated analytical methods are available for the enforcement of the proposed residue definition in oilseeds at the limit of quantification (LOQ) of 0.01 mg/kg. According to the metabolism study and considering the toxicological information on trifluoroacetic acid (TFA), the residue definition for risk assessment is proposed as sum of fluometuron and all metabolites containing the TFMA moiety, expressed as fluometuron.

Available residue trials data were considered sufficient to derive MRL proposals as well as risk assessment values for the only commodity under evaluation. It is noted that information was missing regarding the magnitude of residues in leafy crops when grown in rotation (data gap). EFSA notes this data gap is not expected to impact on the validity of the MRLs derived but might have an impact on national authorisations.

Fluometuron is authorised for use on cotton that might be fed to livestock. Since the calculated dietary burdens for all groups of livestock were found to be below the trigger value of 0.1 mg/kg dry matter (DM), further investigation of residues as well as the setting of MRLs in commodities of animal origin is unnecessary.

Chronic and acute consumer exposure resulting from the authorised uses reported in the framework of this review was calculated using revision 2 of the EFSA PRIMO. The highest chronic exposure was calculated for the Dutch children representing 0.01% of the acceptable daily intake (ADI). There was no consumption data in PRIMO rev. 2.0 allowing to perform an acute risk assessment for cotton seeds, however when considering the total oilseed group the highest acute exposure calculated represented 0.7% of the acute reference dose (ARFD). Although some uncertainties remain due to the data gaps identified, this indicative exposure calculation did not indicate a risk to consumer’s health. A risk assessment regarding the overall exposure to metabolite TFA was performed in a previous EFSA reasoned opinion. The potential contribution of TFA resulting from the application of fluometuron in primary crops is deemed covered by this previous assessment.
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.

Fluometuron was evaluated in the framework of Directive 91/414/EEC with Greece designated as a rapporteur Member State (RMS). In 2008, a decision on the non-inclusion of the active substance was taken by Commission Decision 2008/934/EC\(^3\) following the voluntary withdrawal of the support for the active substance by the applicant. The applicant submitted a new application requesting the accelerated procedure, regarding the inclusion of the active substance in Annex I of Directive 91/414/EEC. Based on the EFSA conclusion which was issued on 13 January 2011 (EFSA, 2011), the decision to approve the active substance in accordance with the provision of Regulation (EC) 1107/2009\(^4\), repealing the provisions of Directive 91/414/EEC, was taken.

As fluometuron was included in Annex I to Council Directive 91/414/EEC on 1 June 2011 Commission Implementing Directive 2011/57/EU\(^5\) which has been deemed to be approved under Regulation (EC) No 1107/2009\(^6\), in accordance with Commission Implementing Regulation (EU) No 540/2011\(^7\), as amended by Commission Implementing Regulation (EU) No 541/2011\(^8\). Therefore, EFSA initiated the review of all existing MRLs for that active substance.

By way of background information, in the framework of Commission Regulation (EC) No 33/2008\(^9\) fluometuron was evaluated by Greece, designated as rapporteur Member State (RMS). Subsequently, a peer review on the initial evaluation of the RMS was conducted by EFSA, leading to the conclusions set out in the EFSA scientific report (EFSA, 2011). The approval of fluometuron is restricted to uses as a herbicide on cotton.

According to the legal provisions, EFSA shall base its reasoned opinion in particular on the relevant assessment report prepared under Directive 91/414/EEC repealed by Regulation (EC) No 1107/2009. It should be noted, however, that, in the framework of Regulation (EC) No 1107/2009, 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 Regulation (EC) No 1107/2009 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 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.

\(^1\) 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 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.

\(^4\) 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 Directive 2011/57/EU of 27 April 2011 amending Council Directive 91/414/EEC to include fluometuron as active substance and amending Commission Decision 2008/934/EC. OJ L 108, 28.4.2011, p. 34–37.

\(^6\) 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.

\(^7\) 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.

\(^8\) 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 9(2) of that Directive but have not been included into its Annex I. OJ L 15, 18.1.2008, p. 5–12.
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 15 September 2017 EFSA initiated the collection of data for this active substance. In a first step, Member States were invited to submit by 15 October 2017 their Good Agricultural Practices (GAPs) that are authorised nationally, in a standardised way, in the format of specific GAP forms. In the framework of this consultation eight Member States provided feedback on their national authorisations of fluometuron. Based on the GAP data submitted, the designated RMS Greece was asked to identify the critical GAPs to be further considered in the assessment, in the format of a specific GAP overview file. Subsequently, in a second step, Member States were requested to provide residue data supporting the critical GAPs by 15 January 2018.

On the basis of all the data submitted by Member States and the EU Reference Laboratories for Pesticides Residues (EURL), EFSA asked Greece to complete the PROFile and to prepare a supporting evaluation report. The PROFile and the supporting evaluation report, together with the Pesticide Residues Intake Model (PRIMo) calculations and updated GAP overview file, were submitted to EFSA on 3 May 2018. Subsequently, EFSA performed the completeness check of these documents with the RMS. The outcome of this exercise including the clarifications provided by the RMS, if any, was compiled in the completeness check report. A GAP on sesame seeds was reported by Greece as being authorised in its country. However, since according with Commission Implementing Directive 2011/57/EU, fluometuron is restricted for use only as a herbicide on cotton, the GAP for sesame seeds was disregarded from this review.

Considering all the available information, EFSA prepared in September 2018 a draft reasoned opinion, which was circulated to Member States for commenting via a written procedure. All comments received by 7 November 2018 were considered by EFSA during the finalisation of the reasoned opinion.

The evaluation report submitted by the RMS (Greece, 2018), taking into account also the information provided by Member States during the collection of data, and the EURL report on analytical methods (EURL, 2018) are considered as main supporting documents to this reasoned opinion and, thus, made publicly available.

In addition, further supporting documents to this reasoned opinion are the completeness check report (EFSA, 2018a) and the Member States consultation report (EFSA, 2018b). These reports are developed to address all issues raised in the course of the review, from the initial completeness check to the reasoned opinion. Furthermore, the exposure calculations for all crops reported in the framework of this review performed using the PRIMo and the PROFile as well as the GAP overview file listing all authorised uses are key supporting documents and made publicly available as background documents to this reasoned opinion. A screenshot of the report sheet of the 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

Fluometuron is the ISO common name for 1,1-dimethyl-3-(α,α,α-trifluoro-m-tolyl)urea (IUPAC).

The chemical structure of the active substance and its main metabolites are reported in Appendix F.

The EU MRLs for fluometuron are established in Annexes IIIA of Regulation (EC) No 396/2005. Codex maximum residue limits (CXLs) for fluometuron are not available. There are no MRL changes occurred since the entry into force of the Regulation mentioned above.

For the purpose of this MRL review, all the uses of fluometuron currently authorised within the EU as submitted by the Member States during the GAP collection, have been reported by the RMS in the GAP overview file. The critical GAPs identified in the GAP overview file were then summarised in the
PROFile and considered in the assessment. The details of the authorised critical GAPs for fluometuron are given in Appendix A. The RMS did not report any use authorised in third countries that might have a significant impact on international trade.

Assessment

EFSA has based its assessment on the following documents:

- the PROFile submitted by the RMS;
- the evaluation report accompanying the PROFile (Greece, 2018);
- the draft assessment report (DAR) and its addenda prepared under Council Directive 91/414/EEC (Greece, 2007);
- the additional report (AR) and its addenda prepared under Commission Regulation (EC) No 33/2008 (Greece, 2010);
- the conclusion on the peer review of the pesticide risk assessment of the active substance fluometuron (EFSA, 2011);

The assessment is performed in accordance with the legal provisions of the uniform principles for evaluation and authorisation of plant protection products as set out in Commission Regulation (EU) No 546/2011 and the currently applicable guidance documents relevant for the consumer risk assessment of pesticide residues (European Commission, 1997a–g, 2000, 2010a,b, 2017; OECD, 2011, 2013).

More detailed information on the available data and on the conclusions derived by EFSA can be retrieved from the list of end points reported in Appendix B.

1. Residues in plants

1.1. Nature of residues and methods of analysis in plants

1.1.1. Nature of residues in primary crops

The metabolism of fluometuron, labelled uniformly in the phenyl ring, was investigated in pulses and oilseeds (Greece, 2010), and assessed in the framework of the peer-review (EFSA, 2011).

After two applications (one pre-emergence application of 2.6 kg a.s./ha and one post-emergence application 35 days later of 2.6 kg a.s./ha), fluometuron was not detected either in cotton stalks or cotton seeds. The metabolite trifluoroacetic acid (TFA) metabolite was recovered in significant amounts in mature stalks and cotton seed (31% and 21.5% total radioactive residue (TRR), accounting to 0.084 mg eq./kg and 0.0155 mg eq./kg, respectively). Multiple structurally related metabolites containing the trifluoromethylaniline (TFMA) moiety were mainly identified in immature cotton stalks accounting for approximately 42% of the TRR, and to a minor extent in mature stalks and seeds, present at 14% and 4% of the TRR, respectively (EFSA, 2011). In mature cotton seeds, the TRR was 0.022 mg eq./kg, and TFA was the only metabolite observed at significant amounts (0.0155 mg eq./kg), while no other single metabolite accounted for more than 0.01 mg/kg (Greece, 2010).

The metabolic pathway of fluometuron depicted on cotton was sufficient to illustrate the behaviour of fluometuron in pulses and oilseeds.

1.1.2. Nature of residues in rotational crops

Fluometuron is authorised on cotton that may be grown in rotation. The field DT₅₀ reported in the soil degradation studies evaluated in the framework of the peer review was more than 100 days (EFSA, 2011).

Confined rotational crop studies (in greenhouse and field conditions) with radiolabelled fluometuron were assessed by the RMS (Greece, 2010), and reviewed in the framework of the peer-review (EFSA, 2011). In the greenhouse study, fluometuron was applied as a pre-emergence treatment of 1.96 kg a.s./ha followed after 35 days by a post-emergence application of 2.24 kg a.s./ha to cotton, which was allowed to grow to maturity. After harvesting the cotton, crops were planted at nominal plant-back intervals (PBI) of 194 days after the second and last treatment (DAT). Crops planted at each interval...
consisted of leafy vegetable (lettuce), cereals (spring wheat) and pulses and oilseeds (soyabean). The two major metabolites present at significant percentages of the TRR in all plants were TFA and TFMA. The TRR in mature lettuce was 0.59 mg eq./kg, while in spring wheat was 0.14 mg eq./kg and in soyabees accounted to 0.44 mg eq./kg. Metabolite TFA was present in spring wheat (grain), lettuce (head) and soyabees (beans) at 0.14, 0.45 and 0.18 mg eq./kg, respectively, whereas TFMA was present at 0.04, 0.43 and 0.31 mg eq./kg in these same crop parts, respectively. These metabolites were also observed in the primary crop metabolism study.

In addition, five confined studies conducted under field/outdoor conditions were carried out with lettuce, spring wheat, corn, soyabees and carrots. Fluometuron was applied as a pre-emergence treatment of 1.96 kg a.s./ha followed by a second application to soil of 2.24 kg a.s./ha, 35 days later. After harvesting the cotton, crops were planted at nominal PBI of 41-46 weeks after the second and last treatment (DAT). As in the greenhouse studies the two major metabolites found in these confined field studies were TFA and TFMA. The TRR in mature lettuce was 0.13 mg/kg, with TFMA accounting to 26.8% and TFA to 15.9% of the TRR. In spring wheat, TRR was 0.30 mg/kg in grain, with TFMA accounting to 28.6%, while no TFA was characterised in wheat. The TRR in corn stalks was 0.14 mg/kg with TFMA accounting to 4.3% and TFA to 107.5%. In soyabees, the TRR was 0.11 mg/kg with TFMA present at 37.9% while no TFA was characterised in beans, whereas in soyabees stalks TRR was 0.15 mg/kg with TFA accounting to 99.6% whereas no TFMA was characterised in stalks. In carrots, TRR was 0.42 mg/kg in roots (no metabolites were characterised in roots), while in carrot tops TRR was 0.37 mg/kg and TFA was present at 86.9% while no TFMA was characterised in carrot tops. The metabolism was the same as the pathway depicted in greenhouse studies.

The metabolism and distribution of fluometuron in rotational crops is similar to the metabolic pathway observed in primary crops (EFSA, 2011).

1.1.3. Nature of residues in processed commodities

There were no studies investigating the nature of residues of fluometuron in processed commodities available for this review. In all commodities, residues were below 0.1 mg/kg and the total theoretical maximum daily intake is below 10% of the acceptable daily intake (ADI). Therefore, the investigation of the nature of residues in processed commodities is not required.

1.1.4. Methods of analysis in plants

During the peer-review a hyphenated analytical method based on liquid chromatography (LC) coupled to tandem mass spectrometry (MS/MS) detection was validated in high water (sugar beet), high oil (cotton seed) and dry (maize) content commodities with a limit of quantification (LOQ) of 0.01 mg/kg for the sum of fluometuron and all metabolites containing the TFMA moiety, expressed as fluometuron (EFSA, 2011). This primary method is supported by an independent laboratory validation (ILV) (EFSA, 2011). According to the EURLs report, no validation data for the proposed residue definition for monitoring is available (EURL, 2018). In addition, the EURLs reported that analytical standards of the parent fluometuron and the metabolite TFMA are commercially available (EFSA, 2018b).

1.1.5. Stability of residues in plants

The storage stability of fluometuron was investigated in the framework of the peer review (EFSA, 2011). The storage stability of the sum of fluometuron and all metabolites containing the trifluoromethylaniline moiety was investigated in high oil (cotton seed), dry high starch (maize) and high water (sugar beet) content matrices (Greece, 2010). Fluometuron residues are stable in cotton seed, cotton fodder and cotton oil for a minimum of 576 days (approx. 19 months) when stored at −15°C. The stability in sugar beet leaves/roots and whole maize plants could only be demonstrated for 3 months when stored at −18°C (EFSA, 2011). No conclusion on the stability of maize grain could be drawn and a data gap was identified (EFSA, 2011; see also Section 1.2.2).

1.1.6. Proposed residue definitions

The metabolism of fluometuron was assessed in pulses and oilseeds. The metabolism in rotational crops is similar to the metabolism observed in primary crops. The investigation of the nature of residues in processed commodities is not required.

The parent compound alone is not a sufficient marker; it is considered needed to include all metabolites containing the common moiety TFMA to enforce fluometuron residues (EFSA, 2011).
Residue definition for enforcement and risk assessment is therefore proposed as sum of fluometuron and all metabolites containing the TFMA moiety, expressed as fluometuron. An analytical method for the enforcement of the proposed residue definition at the LOQ of 0.01 mg/kg in high water, high oil and dry content matrices is available (EFSA, 2011). This residue definition is restricted to the pulses and oilseeds group only.

Although the extensive metabolism observed might lead to the significant presence of TFA, a separate residue definition for monitoring including TFA was not considered because this compound is not specific to the use of fluometuron.

In the peer-review, it was noted that information on the toxicological properties of metabolite TFA was not sufficient to derive a proper toxicological characterisation of TFA (EFSA, 2011). However, in the peer review conclusion on flurtamone (another active substance that produces TFA metabolite), toxicological studies have been provided to address these concerns on TFA and an ADI for TFA of 0.05 mg/kg body weight (bw) per day has been derived, while no acute reference dose (ARfD) was needed (EFSA, 2017). Therefore, TFA is less toxic that the parent compound as its ADI is 100 times higher than that of fluometuron. A separate residue definition for risk assessment for this metabolite is not deemed required. It is noted that a risk assessment regarding the overall exposure to TFA was performed in a previous EFSA reasoned opinion (EFSA, 2014; see Section 3.2).

1.2. Magnitude of residues in plants

1.2.1. Magnitude of residues in primary crops

To assess the magnitude of fluometuron residues resulting from the reported GAPs, EFSA considered all residue trials reported by the RMS in the DAR (Greece, 2010) and evaluated in the framework of the peer review (EFSA, 2011). All residue trial samples considered in this framework were stored in compliance with the conditions for which storage stability of residues was demonstrated. Decline of residues during storage of the trial samples is therefore not expected.

The number of residue trials and extrapolations were evaluated in accordance with the European guidelines on comparability, extrapolation, group tolerances and data requirements for setting MRLs (European Commission, 2017).

For all crops, available residue trials are sufficient to derive MRL and risk assessment values, taking note of the following considerations:

- Cotton seeds: The number of residue trials supporting the southern outdoor GAPs is not compliant with the data requirements for this crop. However, according to the metabolism studies performed with 2.6N rate, residues in mature cotton seed are expected to be below 0.01 mg/kg. It is also noted that additional residue trials performed with two split applications (pre- and post-emergence) up to approx. 2 kg a.s./ha total rate showed no quantifiable residues in cotton seeds (Greece, 2010). Therefore, the reduced number of residue trials is considered acceptable in this case because all results were below the LOQ and a no residues situation is expected. Further residue trials are therefore not required.

1.2.2. Magnitude of residues in rotational crops

Field rotational crop studies performed with roots (sugar beet) and cereals (maize) were available for this review (Greece, 2010; EFSA, 2011); however, no studies on leafy crops were available. Two applications of fluometuron were done at presowing (broadcast) and pre-emergence (banded), resulting in a nominal total application rate of 1.78 kg g a.s./ha to cotton. Maize was sowed 1 year after the second application of fluometuron and samples of whole maize plants (including cobs) and grain were taken from plots at BBCH 75 and BBCH 99 (3 and 5 months after sowing of maize plants, respectively). Sugar beet was sowed 29 weeks after the second application of fluometuron, and samples of sugar beet tops and roots were taken at BBCH 49 approximately (7 months after sowing). In both maize and sugar beet samples, residues at plant back intervals of 6 months and 1 year showed no quantifiable residues above 0.01 mg/kg at harvest (EFSA, 2011). However, as no reliable data were provided to cover the storage stability or residues in maize grain, the results obtained for maize grain should be considered as indicative only. A data gap was identified for additional storage stability data on maize grain (EFSA, 2011).

In the framework of the peer-review, a data gap was also identified to address the magnitude of the residues in rotated leafy crops, since non-negligible total radioactive residues were recovered in
rotational leafy crops in the confined metabolism study (EFSA, 2011). The RMS presented an argumentation addressing the data gap on the magnitude of the residues in rotated leafy crops in its evaluation report, stating that the application of fluometuron to cotton seeds will not result in significant uptake to succeeding crops, including leafy vegetables (Greece, 2018). The main reasons presented by the RMS were the exaggerated dose in the rotational crop metabolism studies leading to all crops having measurable residues. The RMS also pointed out that those leafy crops had lower TRR than roots and cereals, and since there were no major differences in metabolic pathways between the different crops, maize (cereals) and sugar beet (roots) were chosen for the field rotational crop studies. As no residues were detected in these crops under field conditions, the RMS concluded that no residues would have occurred in leafy crops, also assuming sugar beet leaves analysed in the field study can be considered as a surrogate for leafy crops (Greece, 2018).

EFSA still considers that the data gaps identified in the peer-review (EFSA, 2011) were not addressed in the MRL review. In the confined rotational metabolism studies that were done at 2.1N, residues in leafy crops were observed at significant amounts (see Section 1.1.2). Therefore, a study investigating the magnitude of the residues in rotated leafy crops is required (data gap).

1.2.3. Magnitude of residues in processed commodities

The effect of industrial processing and/or household preparation was not assessed. Further processing studies are not required as they are not expected to affect the outcome of the risk assessment. However, if processing factors were to be required by risk managers, in particular for enforcement purposes, processing studies would be needed.

1.2.4. Proposed MRLs

The available data are considered sufficient to derive MRL proposals as well as risk assessment values for both commodities under evaluation.

2. Residues in livestock

Fluometuron is authorised for use on cotton seeds that might be fed to livestock. Livestock dietary burden calculations were therefore performed for different groups of livestock according to OECD guidance (OECD, 2013), which has now also been agreed upon at European level. The input values for all relevant commodities are summarised in Appendix D. Since the calculated dietary burdens for all groups of livestock were found to be below the trigger value of 0.1 mg/kg dry matter (DM), further investigation of residues as well as the setting of MRLs in commodities of animal origin is unnecessary.

Although not necessary, the metabolism of fluometuron residues in livestock was investigated in lactating goats and laying hens (Greece, 2010) at dose rates covering the maximum dietary burdens calculated in this review, but these studies were not peer-reviewed.

Studies were conducted with fluometuron radiolabelled in the phenyl ring of the molecule. The study performed on lactating goats, fed with 5 ppm (equivalent to 0.14 mg/kg bw per day) for 10 consecutive days, indicated that fluometuron is extensively metabolised in urine and faeces, whereas radioactive levels in individual tissues were below 0.01 mg/kg, except in the kidney and liver where they were detected at 0.049 and 0.109 mg/kg, respectively. The plateau in milk was reached on the second day of the study. The study performed on laying hens, fed with 5 ppm (equivalent to 0.32 mg/kg bw per day) for 20 consecutive days, showed that fluometuron is extensively degraded, and over 97% of the total radioactivity was eliminated via the excreta. Accumulation of radioactivity in all tissues was low. The radioactive residues in egg yolks reached a plateau by day 8.

No storage stability studies and/or analytical methods for livestock products were provided for this review. These are not necessary since MRLs for livestock products are not required because livestock is not expected to be exposed to significant levels of fluometuron residues.

3. Consumer risk assessment

3.1. Risk assessment of fluometuron and all metabolites containing the trifluoromethylaniline moiety, expressed as fluometuron

Chronic and acute exposure calculations for all crops reported in the framework of this review were performed using revision 2 of the EFSA PRIMo (EFSA, 2007). Input values for the exposure
calculations were derived in compliance with the decision tree reported in Appendix E. Hence, for those commodities where a MRL could be derived by EFSA in the framework of this review, input values were derived according to the internationally agreed methodologies (FAO, 2009). All input values included in the exposure calculations are summarised in Appendix D.

The exposure values calculated were compared with the toxicological reference values for fluometuron, derived by EFSA (2011). The highest chronic exposure was calculated for the Dutch children representing 0.01% of the ADI. There was no consumption data in PRIMo rev. 2.0 allowing to perform an acute risk assessment for cotton seeds; however, when considering the total oilseed group the highest acute exposure calculated represented 0.7% of the ARfD (EFSA, 2011). It should be noted that this calculation did not account for potential uptake of residues in leafy crops when grown in rotation, since quantitative information on residue levels in leafy crops is not available (see also Section 1.2.2). This indicative exposure calculation did not indicate a risk to consumer’s health.

3.2. Risk assessment of trifluoroacetic acid

A separate residue definition for TFA or its inclusion in the risk assessment residue definition for fluometuron was not deemed necessary (see Section 1.1.6). TFA is a ubiquitous compound which can occur from different sources. The risk assessment regarding the overall exposure to metabolite TFA was performed in a previous EFSA reasoned opinion (EFSA, 2014). In this opinion, the exposure calculations were performed by taking into account the TFA concentration resulting from the use of pesticides which are possible sources of TFA and all environmental contaminations. In these calculations, the highest chronic exposure was calculated for German children, representing 5% of the ADI (EFSA, 2014). It should be noted that currently there is no need to conduct the acute exposure calculations for TFA as no ARfD is deemed necessary (EFSA, 2017).

In the framework of the present review, EFSA still relies on the calculations and conclusions of this previous assessment. For cotton seeds, TFA residue level arising from the use of saflufenacil (0.165 mg TFA/kg) was considered as the most critical input value (EFSA, 2014). As such, the potential contribution of TFA resulting from the application of fluometuron in primary crops is deemed covered by the previous assessment (EFSA, 2014) and no specific calculations for TFA resulting from the application of fluometuron on cotton seeds are considered necessary for this MRL review.

Field rotational crops showed that residues are not to be expected in roots and cereals when planted after cotton; however, no information was available for leafy crops (see Section 1.2.2). Therefore, it is not possible to assess the exposure of TFA resulting from rotational crops. However, according to the confined rotational study the highest value of TFA in mature lettuce is 0.45 mg eq./kg. If this value were to be used in the PRIMo for all leafy crops, it is not expected a significant increase of the chronic exposure calculated in the previous EFSA reasoned opinion (EFSA, 2014).

Conclusions

The metabolism of fluometuron in plants was investigated in primary and rotational crops. The residue definition for enforcement can be proposed as sum of fluometuron and all metabolites determined as TFMA, expressed as fluometuron. Fully validated analytical methods are available for the enforcement of the proposed residue definition in oilseeds at the LOQ of 0.01 mg/kg. According to the metabolism study and considering the toxicological information on TFA, the residue definition for risk assessment is proposed as sum of fluometuron and all metabolites containing the TFMA moiety, expressed as fluometuron.

Available residue trials data were considered sufficient to derive a MRL proposal as well as risk assessment values for the only commodity under evaluation. It is noted that information was missing regarding the magnitude of residues in leafy crops when grown in rotation (data gap). EFSA notes this data gap is not expected to impact on the validity of the MRL derived but might have an impact on national authorisations.

Fluometuron is authorised for use on cotton that might be fed to livestock. Since the calculated dietary burdens for all groups of livestock were found to be below the trigger value of 0.1 mg/kg DM, further investigation of residues as well as the setting of MRLs in commodities of animal origin is unnecessary.

Chronic and acute consumer exposure resulting from the authorised uses reported in the framework of this review was calculated using revision 2 of the EFSA PRIMo. The highest chronic exposure was calculated for the Dutch children representing 0.01% of the ADI. There was no
consumption data in PRIMo rev. 2.0 allowing to perform an acute risk assessment for cotton seeds; however, when considering the total oilseed group, the highest acute exposure calculated represented 0.7% of the ARfD (EFSA, 2011). Although some uncertainties remain due to the data gaps identified, this indicative exposure calculation did not indicate a risk to consumer’s health. A risk assessment regarding the overall exposure to metabolite TFA was performed in a previous EFSA reasoned opinion. The potential contribution of TFA resulting from the application of fluometuron in primary crops is deemed covered by this previous assessment.

**Recommendations**

MRL recommendations were derived in compliance with the decision tree reported in Appendix E of the reasoned opinion (see Table 1). The MRL value listed as ‘Recommended’ in the table is sufficiently supported by data and is therefore proposed for inclusion in Annex II to the Regulation.

However, it is noted that information was missing regarding the magnitude of residues in rotational crops. Therefore, EFSA identified the following data gaps which are not expected to impact on the validity of the MRL derived but which might have an impact on national authorisations:

- a representative study investigating the magnitude of the residues in rotated leafy vegetables;
- a representative study investigating the storage stability of fluometuron and all metabolites containing the TFMA moiety in maize grain.

If the above reported data gaps are not addressed or if appropriate mitigation measures to restrict the potential uptake of residue from rotational crops are not implemented (e.g. prohibit the rotation of leafy crops following fluometuron application), Member States are recommended to modify the relevant authorisations at the national level.

**Table 1**: Summary table

| Code number | Commodity                     | Existing EU MRL (mg/kg) | Outcome of the review | Comment               |
|-------------|-------------------------------|-------------------------|-----------------------|-----------------------|
|             | Enforcement residue definition (existing): Sum of fluometuron and all metabolites containing the trifluoromethylaniline (TFMA) moiety, expressed as fluometuron | 0.01*                  | Recommended(a)       |                       |
|             | Enforcement residue definition (proposed): Sum of fluometuron and all metabolites containing the trifluoromethylaniline (TFMA) moiety, expressed as fluometuron | 0.01*                  |                       |                       |
| 401090      | Cotton seed                   |                         | 0.01*                 | Recommended(a)       |
| –           | Other commodities of plant and/or animal origin | See Reg. 839/2008 | –                     | Further consideration needed(b) |

MRL: maximum residue level; CXL: codex maximum residue limit.

*Indicates that the MRL is set at the limit of quantification.

(a): MRL is derived from a GAP evaluated at EU level, which is fully supported by data and for which no risk to consumers was identified (assuming the existing residue definition); no CXL is available (combination E-I in Appendix E).

(b): There are no relevant authorisations or import tolerances reported at EU level; no CXL is available. Either a specific LOQ or the default MRL of 0.01 mg/kg may be considered (combination A-I in Appendix E).

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**Abbreviations**

| Abbreviation | Description                  |
|--------------|------------------------------|
| a.i.          | active ingredient            |
| a.s.          | active substance             |
| ADI           | acceptable daily intake      |
| AR            | additional report            |
| ARFD          | acute reference dose         |
| BBCH          | growth stages of mono- and dicotyledonous plants |
| bw            | body weight                  |
| Acronym | Definition |
|---------|------------|
| CXL     | codex maximum residue limit |
| DAR     | draft assessment report |
| DAT     | days after treatment |
| DB      | dietary burden |
| DM      | dry matter |
| EMS     | evaluating Member State |
| eq.     | residue expressed as a.s. equivalent |
| EURLs   | European Union Reference Laboratories for Pesticide Residues (former CRLs) |
| FAO     | Food and Agriculture Organization of the United Nations |
| GAP     | Good Agricultural Practice |
| HR      | highest residue |
| InChiKey| International Chemical Identifier Key |
| 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      | liquid chromatography |
| LC-MS/MS| liquid chromatography with tandem mass spectrometry |
| LOQ     | limit of quantification |
| Mo      | monitoring |
| MRL     | maximum residue level |
| MS      | Member States |
| MS/MS   | tandem mass spectrometry detector |
| NEDI    | national estimated daily intake |
| NESTI   | national estimated short-term intake |
| NEU     | northern European Union |
| NTMDI   | national theoretical maximum daily intake |
| OECD    | Organisation for Economic Co-operation and Development |
| PBI     | plant-back interval |
| PF      | processing factor |
| PHI     | preharvest interval |
| PRIMO   | (EFSA) Pesticide Residues Intake Model |
| PROFile | (EFSA) Pesticide Residues Overview File |
| RA      | risk assessment |
| RD      | residue definition |
| RMS     | rapporteur Member State |
| SANCO   | Directorate-General for Health and Consumers |
| SC      | suspension concentrate |
| SEU     | southern European Union |
| SMILES  | simplified molecular-input line-entry system |
| STMR    | supervised trials median residue |
| TAR     | total applied radioactivity |
| TFA     | trifluoroacetic acid |
| TFMA    | trifluoromethylaniline |
| TMDI    | theoretical maximum daily intake |
| TRR     | total radioactive residue |
# Appendix A – Summary of authorised uses considered for the review of MRLs

## A.1. Authorised outdoor uses in southern EU

| Crop and/or situation | MS or country | F G or I(a) | Pests or Group of pests controlled | Preparation | Application | Application rate per treatment | PHI (days)(d) | Remarks |
|-----------------------|--------------|------------|-----------------------------------|-------------|-------------|-------------------------------|--------------|---------|
| Cotton seeds EL F     |              | F          | Annual broad leaf weeds and grasses| SC Conc. a.s. | 500 g/L | Soil treatment – spraying | 01–09 | 1 | – | – | 2 kg a.i./ha | n.a | Pre-emergence, incorporation via rain or irrigation |

MRL: maximum residue level; MS: Member State; a.s.: active substance; a.i.: active ingredient; SC: suspension concentrate.

(a): Outdoor or field use (F), greenhouse application (G) or indoor application (I).

(b): CropLife International Technical Monograph no 2, 6th Edition. Revised May 2008. Catalogue of pesticide.

(c): Growth stage range from first to last treatment (BBCH Monograph, Growth Stages of Plants, 1997, Blackwell, ISBN 3-8263-3152-4), including, where relevant, information on season at time of application.

(d): PHI: minimum preharvest interval.
### 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 | Application(s) | Sampling (DAT) | Comment/Source |
|-----------------------------------|-------------|------|----------------|----------------|----------------|
| Pulses/ oilseeds                 | Cotton      | Two applications: Pre-emergence 2.6 kg a.s./ha and post-emergence 35 days after of 2.6 kg a.s./ha | 35, 73, 149, 162 (after first application) | Stalks (immature and mature) and seed (Greece, 2010; EFSA, 2011) |

| Rotational crops (available studies) | Crop groups | Crop(s) | Application(s) | PBI | Comment/Source |
|--------------------------------------|-------------|---------|----------------|-----|----------------|
| Leafy crops                          | Lettuce     | Two applications: Pre-emergence 1.96 kg a.s./ha and post-emergence 35 days after of 2.24 kg a.s./ha | 194 DAT | Greenhouse studies (Greece, 2010; EFSA, 2011) |
| Cereal (small grain)                 | Spring wheat| Pre-emergence 1.96 kg a.s./ha and post-emergence 35 days after of 2.24 kg a.s./ha | 41 months | Field studies (Greece, 2010; EFSA, 2011) |
| Oilseeds                            | Soyabean    | 46 months | 46 months |

| Processed commodities (hydrolysis study) | Conditions | Stable? | Comment/Source |
|------------------------------------------|------------|---------|----------------|
| Pasteurisation (20 min, 90°C, pH 4)      | Not triggered | –       |
| Baking, brewing and boiling (60 min, 100°C, pH 5) | Not triggered | –       |
| Sterilisation (20 min, 120°C, pH 6)      | Not triggered | –       |
| Other processing conditions             | Not triggered | –       |
Can a general residue definition be proposed for primary crops?

|                | No | Yes |                |
|----------------|----|-----|----------------|
| Only available metabolism study is on cotton |                |

Rotational crop and primary crop metabolism similar?

|                | No | Yes |                |
|----------------|----|-----|----------------|
|                | Not applicable | No study available and not required |

Residue pattern in processed commodities similar to residue pattern in raw commodities?

| Plant residue definition for monitoring (RD-Mo) |                |
|------------------------------------------------|----------------|
| Pulses and oilseeds: sum of fluometuron and all metabolites containing the trifluoromethylaniline (TFMA) moiety, expressed as fluometuron |

Plant residue definition for risk assessment (RD-RA)

| Plant residue definition for risk assessment (RD-RA) |                |
|-----------------------------------------------------|----------------|
| Pulses and oilseeds: sum of fluometuron and all metabolites containing the trifluoromethylaniline (TFMA) moiety, expressed as fluometuron |

Methods of analysis for monitoring of residues (analytical technique, matrix groups, LOQs)

| Matrices with high water content, high oil content and dry matrices (Greece, 2010; EFSA, 2011): |                |
|----------------------------------------------------------------------------------|----------------|
| LC–MS/MS                                                                         |                |
| LOQ: 0.01 mg/kg                                                                 |                |
| Confirmatory method available                                                    |                |
| ILV available                                                                    |                |

a.s.: active substance; DAT: days after treatment; PBI: plant-back interval; LC–MS/MS: liquid chromatography with tandem mass spectrometry; LOQ: limit of quantification; ILV: independent laboratory validation.

B.1.1.2. Stability of residues in plants

| Plant products (available studies) | Category               | Commodity          | T (°C) | Stability period | Value Unit | Compounds covered | Comment/Source |
|------------------------------------|------------------------|--------------------|--------|-----------------|------------|-------------------|----------------|
|                                    | High water content     | Sugar beet roots/tops | −18    | 3 Months        |            | sum of fluometuron and all metabolites containing the trifluoromethylaniline moiety | No conclusion on the stability of maize grain could be drawn and a data gap was identified in EFSA, 2011 |
|                                    | High oil content       | Cotton seed        | −15    | 19 Months       |            |                   |                |
|                                    | Dry/high starch content| Maize grain        | −      | − Months        |            |                   |                |

B.1.2. Magnitude of residues in plants

B.1.2.1. Summary of residues data from the supervised residue trials – Primary crops

| Commodity | Region/Indoor (a) | Residue levels observed in the supervised residue trials (mg/kg) | Comments/Source | Calculated MRL (mg/kg) | HR(b) (mg/kg) | STMR(c) (mg/kg) |
|-----------|-------------------|-----------------------------------------------------------------|-----------------|------------------------|--------------|-----------------|
| Cotton seed | SEU               | 3 × < 0.01                                                       | Residue trials on cotton seed compliant with GAP. Reduced number of trials is sufficient since a zero residue situation is expected | 0.01*       | < 0.01       | < 0.01         |

GAP: Good Agricultural Practice; OECD: Organisation for Economic Co-operation and Development; MRL: maximum residue level. *: Indicates that the MRL is proposed at the limit of quantification. Mo: residue levels expressed according to the monitoring residue definition; RA: residue levels expressed according to risk assessment residue definition.

(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.
(b): Highest residue. The highest residue for risk assessment (RA) refers to the whole commodity and not to the edible portion.
(c): Supervised trials median residue. The median residue for risk assessment (RA) refers to the whole commodity and not to the edible portion.

### B.1.2.2. Residues in rotational crops

| Residues in rotational and succeeding crops expected based on confined rotational crop study? | Yes | Significant TRR in roots, cereals and leafy crops (Greece, 2010):
| | | 0.14 mg eq./kg spring wheat grain
| | | 0.59 mg eq./kg in mature lettuce (head)
| | | 0.44 mg eq./kg in soyabean (beans)
| | Residues in rotational and succeeding crops expected based on field rotational crop study? | Inconclusive | Significant TFA residues in roots, cereals and leafy crops (Greece, 2010):
| | | 0.14 mg eq./kg in wheat grain
| | | 0.45 mg eq./kg in mature lettuce (head)
| | | 0.18 mg eq./kg in soyabean (beans)

TRR: total radioactive residue; TFA: trifluoroacetic acid; LOQ: limit of quantification.

### B.1.2.3. Processing factors

No processing studies were available in the framework of the present review.

### B.2. Residues in livestock

| Relevant groups (subgroups) | Dietary burden expressed in mg/kg bw per day | Most critical subgroup(a) | Most critical commodity(b) | Trigger exceeded (Y/N) | Comments |
|----------------------------|---------------------------------------------|---------------------------|---------------------------|------------------------|----------|
| Cattle (all)               | Median 0.0001 | Maximum 0.0001 | < 0.01 | Cattle (dairy) | Cotton, undelinted seed | No |
| Cattle (dairy only)        | Median 0.0001 | Maximum 0.0001 | < 0.01 | Cattle (dairy) | Cotton, undelinted seed | No |
| Sheep (all)                | Median 0.0001 | Maximum 0.0001 | < 0.01 | Sheep (ram/ewe) | Cotton, meal | No |
| Sheep (ewe only)           | Median 0.0001 | Maximum 0.0001 | < 0.01 | Sheep (ram/ewe) | Cotton, meal | No |
| Swine (all)                | Median 0.0000 | Maximum 0.0000 | < 0.01 | Swine (breeding) | Cotton, meal | No |
| Poultry (all)              | Median 0.0001 | Maximum 0.0001 | < 0.01 | Poultry (turkey) | Cotton, meal | No |
| Poultry (layer only)       | Median 0.0000 | Maximum 0.0000 | < 0.01 | Poultry (layer) | Cotton, meal | No |
### Relevant groups (subgroups)

| Relevant groups (subgroups) | Dietary burden expressed in mg/kg bw per day | Most critical subgroup | Most critical commodity | Trigger exceeded (Y/N) | Comments |
|-----------------------------|---------------------------------------------|------------------------|-------------------------|------------------------|----------|
|                             | Median | Maximum   | Median | Maximum   |                         |          |
| Fish                        | 0.0001 | 0.0001    | < 0.01 | < 0.01    | Cattle (dairy)          | No       |
|                             |        |           |        |           | Cotton, undelinted seed |          |

bw: body weight; DM: dry matter.
(a): When one group of livestock includes several subgroups (e.g. poultry 'all' including broiler, layer and turkey), the result of the most critical subgroup is identified from the maximum dietary burdens expressed as ‘mg/kg bw per day’.
(b): The most critical commodity is the major contributor identified from the maximum dietary burden expressed as ‘mg/kg bw per day’.

### 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) | Comment/Source                                                                 |
|-------------------------------|------------|-------------------------|-----------------|-------------------------------------------------------------------------------|
|                               | Laying hen | 0.32                    | 20              | Dose rate recalculated assuming body weight of 1.9 kg and feed intake of 0.13 kg/day (Greece, 2010) |
|                               | Lactating goat | 0.14                 | 10              | Dose rate recalculated assuming body weight of 70 kg and feed intake of 2 kg/day (Greece, 2010) |

bw: body weight.

Time needed to reach a plateau concentration in milk and eggs (days)
- Milk: 2
  - Greece (2010)
- Eggs: 8
  - Greece (2010)

Metabolism in rat and ruminant similar
- Not applicable

Can a general residue definition be proposed for animals?
- Not applicable

Animal residue definition for monitoring (RD-Mo)
- Not applicable

Animal residue definition for risk assessment (RD-RA)
- Not applicable

Fat soluble residues
- Not applicable

Methods of analysis for monitoring of residues (analytical technique, matrix groups, LOQs)
- No methods available and not required

### B.2.1.2. Stability of residues in livestock

No studies available and not required.

### B.2.2. Magnitude of residues in livestock

#### B.2.2.1. Summary of the residue data from livestock feeding studies

No studies available and not required considering the calculated dietary burdens.
### B.3. Consumer risk assessment

| ARfD | 0.008 mg/kg bw (EFSA, 2011) |
|------|-----------------------------|
| Highest IESTI, according to EFSA PRIMo (rev.2.0) | No consumption data for cotton seeds to perform acute risk assessment using PRIMo rev. 2.0. (0.7%, considering all oilseeds group (EFSA 2011)) |
| NESTI (% ARfD) | Not assessed in this review |
| Assumptions made for the calculations | The calculation is based on the highest residue levels expected in raw agricultural commodities. The contribution of commodities where no GAP was reported in the framework of the MRL review were not included in the calculation. This calculation is based on the assumption that no residues occur in rotational crops |

ARfD: acute reference dose; bw: body weight; NESTI: national estimated short-term intake; PRIMo: (EFSA) Pesticide Residues Intake Model; IESTI: international estimated short-term intake; GAP: Good Agricultural Practice; MRL: maximum residue level.

| ADI | 0.0005 mg/kg bw (EFSA, 2011) |
|-----|-----------------------------|
| TMDI according to EFSA PRIMo | Not assessed in this review |
| NTMDI, according to (to be specified) | Not assessed in this review |
| Highest IEDI, according to EFSA PRIMo (rev.2.0) | 0.01% ADI (Dutch, children) |
| NEDI (% ADI) | Not assessed in this review |
| Assumptions made for the calculations | The calculation is based on the median residue levels derived for raw agricultural commodities. The calculation is based on the highest residue levels expected in raw agricultural commodities. The contribution of commodities where no GAP was reported in the framework of the MRL review were not included in the calculation. This calculation is based on the assumption that no residues occur in rotational crops |

ADI: acceptable daily intake; bw: body weight; NEDI: national estimated daily intake; PRIMo: (EFSA) Pesticide Residues Intake Model; IEDI: international estimated daily intake; GAP: Good Agricultural Practice; MRL: maximum residue level.

Consumer exposure assessment through drinking water resulting from groundwater metabolite(s) according to SANCO/221/2000 rev.10 Final (25/02/2003)

| Metabolite(s) | Not assessed in this review |
|---------------|-----------------------------|
| ADI (mg/kg bw per day) | Not assessed in this review |
| Intake of groundwater metabolites (% ADI) | Not assessed in this review |

ADI: acceptable daily intake; bw: body weight.
### B.4. Proposed MRLs

| Code number | Commodity | Existing EU MRL (mg/kg) | Outcome of the review | Comment |
|-------------|-----------|-------------------------|-----------------------|---------|
|             |           | **MRL** (mg/kg)         | **Comment**           |         |
| **Enforcement residue definition (existing):** Sum of fluometuron and all metabolites containing the trifluoromethylaniline (TFMA) moiety, expressed as fluometuron | | | | |
| **Enforcement residue definition (proposed):** Sum of fluometuron and all metabolites containing the trifluoromethylaniline (TFMA) moiety, expressed as fluometuron | | | | |
| 401090      | Cotton seed | 0.01* | 0.01* | Recommended*(a) |
| –           | Other commodities of plant and/or animal origin | See Reg. 839/2008 | – | Further consideration needed*(b) |

**MRL:** maximum residue level; **CXL:** codex maximum residue limit.

*(a): MRL is derived from a GAP evaluated at EU level, which is fully supported by data and for which no risk to consumers was identified (assuming the existing residue definition); no CXL is available (combination E-I in Appendix E).

*(b): There are no relevant authorisations or import tolerances reported at EU level; no CXL is available. Either a specific LOQ or the default MRL of 0.01 mg/kg may be considered (combination A-I in Appendix E).
Appendix C – Pesticide Residue Intake Model (PRIMo)

**Fluometuron**

| Status of the active substance: | Code no.: |
|--------------------------------|-----------|
| LOQ (mg/kg bw) | Proposed LOQ |
| ADI (mg/kg bw per day): | ARfD (mg/kg bw): |
| 0.005 | 0.008 |
| Source of ADI: | Source of ARfD: |
| EFSA | EFSA |
| Year of evaluation: | Year of evaluation: |
| 2011 | 2011 |

| No of diets exceeding ADI: | --- |
|---------------------------|-----|
| Highest calculated TMDI values in % of ADI | --- |
| Commodity/group of commodities | --- |
| No of diets exceeding ADI | --- |
| 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 | --- |

**Chronic risk assessment – refined calculations**

| Commodity/group of commodities | TMDI (range) in % of ADI |
|-------------------------------|--------------------------|
| Cotton seed | 0.012 – 0.012 |
| FRUIT (FRESH OR FROZEN) | 0.003 – 0.003 |

**Conclusion:**
The estimated Theoretical Maximum Daily Intakes (TMDI), based on pTMRLs were below the ADI.

A long-term intake of residues of fluometuron 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 calculations, 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.

### Table: Acute risk assessment/children – refined calculations

| IESTI 1 | **| **| IESTI 2 | **| **| IESTI 1 | **| **| IESTI 2 | **| ** |
|---|---|---|---|---|---|---|---|---|---|---|---|
| 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): | **| ** |
| 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) | **| ** |
| 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) | **| ** |

For processed commodities, no exceedance of the ARfD/ADI was identified.

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.**

No exceedance of the ARfD/ADI was identified for any unprocessed commodity.

### Table: Acute risk assessment/adults/general population – refined calculations

| IESTI 1 | **| **| IESTI 2 | **| **| IESTI 1 | **| **| IESTI 2 | **| ** |
|---|---|---|---|---|---|---|---|---|---|---|---|
| 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): | **| ** |
| 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) | **| ** |
| 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) | **| ** |

### Conclusion:

For fluometuron, 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 D – Input values for the exposure calculations

D.1. Livestock dietary burden calculations

| Feed commodity                  | Median dietary burden | Maximum dietary burden |
|---------------------------------|-----------------------|------------------------|
|                                 | Input value (mg/kg)   | Comment                | Input value (mg/kg) | Comment |
| Cotton, undelinted seed         | 0.01* STMR            | 0.01* STMR             |
| Cotton, meal                    | 0.01* STMR (default PF not applied)\(^{(a)}\) | 0.01* STMR (default PF not applied)\(^{(a)}\) |

**Risk assessment residue definition:** Sum of fluometuron and all metabolites containing the trifluoromethylaniline (TFMA) moiety, expressed as fluometuron.

*STMR: supervised trials median residue; PF: processing factor.

*: Indicates that the input value is proposed at the limit of quantification.

\(^{(a)}\): For cotton meal, no default processing factor was applied because fluometuron applied early in the growing season and residues are expected to be below the LOQ. Concentration of residues in this commodity is therefore not expected.

D.2. Consumer risk assessment

| Commodity       | Chronic risk assessment | Acute risk assessment |
|-----------------|-------------------------|-----------------------|
|                 | Input value (mg/kg)     | Comment               | Input value (mg/kg) | Comment |
| Cotton seeds    | 0.01* STMR              |                       | 0.01* STMR          |

**Risk assessment residue definition:** Sum of fluometuron and all metabolites containing the trifluoromethylaniline (TFMA) moiety, expressed as fluometuron.

*STMR: supervised trials median residue.

*: Indicates that the input value is proposed at the limit of quantification.
Appendix E – Decision tree for deriving MRL recommendations

Evaluation of the GAPs and available residues data at EU level

Consumer risk assessment for GAPs evaluated at EU level – EU scenarios

Recommendations resulting from EU authorisations and import tolerances

(A) Specific LOQ or default MRL?
(B) Specific LOQ or default MRL?
(C) Maintain current EU MRL?
(D) Specific LOQ or default MRL?
(E) Establish tentative EU MRL?
(F) Specific LOQ or default MRL?
(G) MRL is recommended.

Comparison with CXLs.
Comparison of the EU recommendation with the existing CXL

CXL available?  
Yes  
\[ \text{RD comparable?} \]  
Yes  
CXL higher?  
Yes
No

CXL supported by data?  
Yes
No

Input values for the RA remain unchanged.

CXL is included in the RA.

Risk identified?

Yes
No

Codex median/ highest residues are included in the RA.

No
Yes

Recommendations with consideration of the existing CXL

(I) Maintain EU recommendation indicating that no CXL is available.

(II) Maintain EU recommendation indicating CXL is not compatible.

(III) Maintain EU recommendation indicating that CXL is covered.

(IV) Maintain EU recommendation; higher CXL is not safe for consumer.

(V) Maintain current CXL or EU recommendation.

(VI) Maintain EU recommendation; higher CXL is not safe for consumer.

(VII) CXL is recommended; EU recommendation is covered as well.
## Appendix F – Used compound codes

| Code/trivial name<sup>(a)</sup> | IUPAC name/SMILES notation/InChiKey<sup>(b)</sup> | Structural formula<sup>(c)</sup> |
|---------------------------------|-----------------------------------------------|---------------------------------|
| Fluometuron                     | 1,1-dimethyl-3-(α,α,α -trifluoro-m-tolyl)urea O=C(Nc1cc(ccc1)C(F)(F)F)N(C)C RZILCCWPBYDO-UHFFFAOYSA-N | ![Structural formula of Fluometuron](image1) |
| TFA (Trifluoroacetic acid)      | trifluoroacetic acid FC(F)(F)C(=O)O DTQVDTLACAAQTR-UHFFFAOYSA-N | ![Structural formula of TFA](image2) |
| TFMA (Trifluoromethylaniline)   | 3-(trifluoromethyl)aniline FC(F)(F)c1cc(N)ccc1 VIUDTWATMPPKELUHFFFAOYSA-N | ![Structural formula of TFMA](image3) |

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

<sup>(a)</sup> The metabolite name in bold is the name used in the conclusion.
<sup>(b)</sup> ACD/Name 2015 ACD/Labs 2015 Release (File version N20E41, Build 75170, 19 December 2014).
<sup>(c)</sup> ACD/ChemSketch 2015 ACD/Labs 2015 Release (File version C10H41, Build 75059, 17 December 2014).