Evaluation of confirmatory data following the Article 12 MRL review for pyraflufen-ethyl

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Abstract

The applicant, Nichino Europe Co. Ltd., submitted application request to the competent national authority in the Netherlands to evaluate confirmatory data that were identified for pyraflufen-ethyl in the framework of the maximum residue level (MRL) review under Article 12 of Regulation (EC) No 396/2005 as not available. The submitted data were sufficient to confirm the MRLs for citrus fruits, tree nuts, pome fruits, stone fruits, table and wine grapes, currants, gooseberries, table olives, potatoes, rapeseeds/canola seeds, olives for oil production, barley, oat, rye, and wheat. Furthermore, the submitted data were sufficient to propose an MRL for cotton seeds. The confirmatory data requirement for an analytical method in hops has not been addressed satisfactorily; as regards the existing MRL for hops, further risk management decisions need to be taken. Based on the risk assessment results, EFSA concluded that the short-term and long-term intake of residues resulting from the use of pyraflufen-ethyl according to the reported agricultural practices is unlikely to present a risk to consumer health.

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Summary

In 2013, the European Food Safety Authority (EFSA) reviewed the maximum residue levels (MRLs) for the active substance pyraflufen-ethyl in accordance with Article 12 of Regulation (EC) No 396/2005. EFSA identified some information as unavailable during the MRL review (data gaps) and derived tentative MRL proposals for those uses not fully supported by data but for which no risk to consumers was identified. The following data gaps were identified by EFSA:

1) a validated analytical method for enforcement of residues in hops;
2) an independent laboratory validation (ILV) and a confirmatory method for enforcement of residues in dry commodities;
3) a confirmatory method for enforcement of residues in acidic, high oil content and high water content commodities;
4) further information on the magnitude of residues in cotton;
5) a storage stability study investigating a period of at least 18 months in dry commodities.

The tentative MRL proposals have been implemented in the MRL legislation by Commission Regulation (EU) No 703/2014, including footnotes indicating the type of confirmatory data related to data gaps Nos (1), (2), (3) and (5) that should be provided by any party having an interest in maintaining the tentative MRL by 26 June 2016. Data gap No 4 has not been implemented in the MRL regulation, and Commission Regulation (EU) No 703/2014 set the MRL for cotton seeds at the specific limit of quantification (LOQ).

In accordance with the procedure set out in the Working Document SANTE/10235/2016, the applicant, Nichino Europe Co. Ltd., submitted an application to the competent national authority in the Netherlands (rapporteur Member State (RMS)) to evaluate confirmatory data identified during the MRL review. The application also included new information for the setting of an MRL in cotton seeds. The RMS assessed the new information in an evaluation report, which was submitted to the European Commission and forwarded to EFSA on 1 June 2017. When assessing the evaluation report, EFSA identified points which needed further clarification. On 22 June 2018, the RMS submitted a revised evaluation report which addressed the points for clarification.

The summary table below provides an overview of the assessment of confirmatory data and the recommended MRL modifications to Regulation (EU) No 396/2005.

| Code(a) | Commodity                  | Existing EU MRL(b) (mg/kg) | Proposed EU MRL (mg/kg) | Conclusion/recommendation                                      |
|---------|----------------------------|----------------------------|-------------------------|---------------------------------------------------------------|
| 110000  | Citrus fruits              | 0.02* (ft 1)               | 0.02*                   | The confirmatory data requirement for information on analytical methods has been addressed. The available data are sufficient to confirm the existing MRLs. A consumer health risk was not identified |
| 120000  | Tree nuts                  | 0.02* (ft 1)               | 0.02*                   |                                                              |
| 130000  | Pome fruits                | 0.02* (ft 1)               | 0.02*                   |                                                              |
| 140000  | Stone fruits               | 0.02* (ft 1)               | 0.02*                   |                                                              |
| 151000  | Grapes (table and wine grapes) | 0.02* (ft 1)               | 0.02*                   |                                                              |
| 154030  | Currants (black, red and white) | 0.02* (ft 1)               | 0.02*                   |                                                              |
| 154040  | Gooseberries (green, red and yellow) | 0.02* (ft 1)               | 0.02*                   |                                                              |
| 154080  | Elderberries               | 0.02* (ft 1)               | 0.02*                   |                                                              |
| 161030  | Table olives               | 0.02* (ft 1)               | 0.02*                   |                                                              |
| 211000  | Potatoes                   | 0.02* (ft 1)               | 0.02*                   |                                                              |
| 401060  | Rapeseeds/canola seeds     | 0.02* (ft 1)               | 0.02*                   |                                                              |
| 401090  | Cotton seeds               | 0.02*                      | 0.02*                   | The submitted data are sufficient to derive an MRL proposal. No MRL change is required. A consumer health risk was not identified |

Enforcement residue definition: Sum of pyraflufen-ethyl and pyraflufen, expressed as pyraflufen-ethyl

(a) Code: Reference code used for reporting purposes.
(b) MRL: Maximum residue level.
| Code<sup>(a)</sup> | Commodity        | Existing EU MRL<sup>(b)</sup> (mg/kg) | Proposed EU MRL (mg/kg) | Conclusion/recommendation                                                                 |
|-----------------|------------------|-------------------------------------|-------------------------|------------------------------------------------------------------------------------------|
| 402010          | Olives for oil production | 0.02* (ft 1)                        | 0.02*                   | The confirmatory data requirement for information on analytical methods has been addressed. The available data are sufficient to confirm the existing MRL. A consumer health risk was not identified. |
| 500010          | Barley           | 0.02* (ft 2)                         | 0.02*                   | The confirmatory data requirement for information on storage stability and analytical methods has been addressed. The available data are sufficient to confirm the existing MRLs. A consumer health risk was not identified. |
| 500050          | Oat              | 0.02* (ft 2)                         | 0.02*                   |                                                                                         |
| 500070          | Rye              | 0.02* (ft 2)                         | 0.02*                   |                                                                                         |
| 500090          | Wheat            | 0.02* (ft 2)                         | 0.02*                   |                                                                                         |
| 700000          | Hops             | 0.1* (ft 3)                          |                         | The available data are not sufficient to address the confirmatory data requirement for information on analytical methods; a fully validated analytical method for enforcement of residues in hops is still required. A consumer health risk was not identified for the existing MRL. A risk management decision is required to follow up on the identified data gap. |

MRL: maximum residue level.

*: Indicates that the MRL is set at the limit of analytical quantification (LOQ).

(a): Commodity code number according to Annex I of Regulation (EC) No 396/2005.

(b): Existing EU MRL and corresponding footnote on confirmatory data in accordance with Commission Regulation (EU) No 703/2014.

(ft 1): The European Food Safety Authority identified some information on analytical methods as unavailable. When reviewing the MRL, the Commission will take into account the information referred to in the first sentence, if it is submitted by 26 June 2016, or, if that information is not submitted by that date, the lack of it. (Footnote related to data gap No 3.)

(ft 2): Commission Regulation (EU) No 703/2014: The European Food Safety Authority identified some information on storage stability and analytical methods as unavailable. When reviewing the MRL, the Commission will take into account the information referred to in the first sentence, if it is submitted by 26 June 2016, or, if that information is not submitted by that date, the lack of it. (Footnote related to data gaps Nos 2 and 5.)

(ft 3): The European Food Safety Authority identified some information on analytical methods as unavailable. When re-viewing the MRL, the Commission will take into account the information referred to in the first sentence, if it is submitted by 26 June 2016, or, if that information is not submitted by that date, the lack of it. (Footnote related to data gap No 1.)
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The maximum residue levels (MRLs) for the active substance pyraflufen-ethyl have been reviewed by the European Food Safety Authority (EFSA) in 2013 (MRL review) (EFSA, 2013), according to Article 12 of Regulation (EC) No 396/2005. During the MRL review, EFSA identified some information as unavailable (data gaps) and derived tentative MRL proposals for those uses not fully supported by data but for which no risk to consumers was identified. The list of Good Agricultural Practices (GAPs) assessed in the framework of the MRL review that were not fully supported by data and for which confirmatory data were requested are listed in Appendix A.

The MRL modifications proposed following the MRL review have been implemented in the MRL legislation by Commission Regulation (EU) No 703/2014 that specified for the relevant MRLs the type of information that was identified as missing. Any party having an interest in maintaining the proposed tentative MRL was requested to address the confirmatory data by 26 June 2016. In accordance with the specific provisions set out in the working document of the European Commission SANTE/10235/2016 (European Commission, 2016) the applicant, Nichino Europe Co. Ltd., submitted an application to the competent national authority in the Netherlands (rapporteur Member State (RMS)) for the evaluation of confirmatory data, which was received by the RMS on the 22 June 2016. In response to the data gaps identified by EFSA, the applicant submitted:

- an analytical method for hops following pre-registration guidance;
- an analytical method and independent laboratory validation (ILV) for enforcement of residues in high water content, dry, high acid content and high oil content commodities;
- information indicating that the requested data to demonstrate frozen storage stability of pyraflufen-ethyl in dry commodities for a period of 18 months is not available. In order to support the use of pyraflufen-ethyl in cereals which is affected by the lack of data on storage stability, the applicant provided information on residue trials performed in cereals according to the critical GAP in which the samples were analysed within the demonstrated acceptable frozen storage stability period.
- residue trials performed in cotton seeds.

The RMS assessed the new information in an evaluation report, which was submitted to the European Commission and forwarded to EFSA on 1 June 2017 (Netherlands, 2017). EFSA assessed the application as requested by the European Commission in accordance with Article 9 of Regulation (EC) No 396/2005. During the detailed assessment, EFSA identified points which needed further clarifications. On 22 June 2018, the RMS submitted a revised evaluation report which addressed the points for clarification.

It is highlighted that the application received covered not only the confirmatory data requirements implemented in the MRL legislation, but also included residue trials performed in cotton and a proposal for the setting of MRLs for pyraflufen-ethyl in cotton seeds; which is related to data gap in point (4) that has not been implemented as a confirmatory data requirement in the MRL legislation.

EFSA based its assessment on the revised evaluation report submitted by the RMS (Netherlands, 2017), the reasoned opinion on the MRL review according to Article 12 of Regulation (EC) No 396/2005 (EFSA, 2013), the draft assessment report (DAR) prepared under Council Directive 91/414/EEC (Belgium, 1999), the renewal assessment report (RAR) and its addendum prepared under Regulation (EC) 1107/2009 (Netherlands, 2013, 2014) and the EFSA conclusion on the peer review of the pesticide risk assessment of the active substance pyraflufen-ethyl (EFSA, 2015).

For this application, the data requirements established in Regulation (EU) No 544/2011 and the relevant guidance documents at the date of implementation of the confirmatory data requirements by Commission Regulation (EU) No 703/2014 are applicable. The assessment is performed in accordance

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1 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, 16.3.2005, p. 1–16.
2 Commission Regulation (EU) No 703/2014 of 19 June 2014 amending Annexes II, III and V to Regulation (EC) No 396/2005 of the European Parliament and of the Council as regards maximum residue levels for acibenzolar-S-methyl, ethoxyquin, flusilazole, isoxaflutole, molinate, propoxycarbazone, pyraflufen-ethyl, quinclorac and warfarin in or on certain products. OJ L 186, 26.6.2014, p. 1–48.
3 Commission Regulation (EU) No 544/2011 of 10 June 2011 implementing Regulation (EC) No 1107/2009 of the European Parliament and of the Council as regards the data requirements for active substances. OJ L 155, 11.6.2011, p. 1–66.
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. A detailed description of the GAPs for the uses of pyraflufen-ethyl, which are relevant to the current confirmatory data evaluation, is reported in Appendix A.

An updated list of end points, including the end points of relevant studies assessed previously and the confirmatory data evaluated in this application, is presented in Appendix B.

The revised evaluation report submitted by the RMS (Netherlands, 2017) is considered a supporting document to this reasoned opinion and, thus, is made publicly available as a background document.

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 nature of residues in primary crops is not relevant to the evaluation of the confirmatory data submitted. However, for the proposed setting of an MRL in cotton seeds, the metabolism of pyraflufen-ethyl has been investigated for foliar application as a preharvest desiccant in cotton in the framework of the EU pesticides peer review (EFSA, 2015). For the intended use on cotton, the metabolic behaviour in primary crops is sufficiently addressed.

1.1.2. Nature of residues in rotational crops

The nature of residues in rotational crops is not relevant to the evaluation of the confirmatory data submitted. Pyraflufen-ethyl is proposed to be used on cotton, which can be grown in rotation with other crops. The metabolism of pyraflufen-ethyl in rotational crops has been investigated in the framework of the EU pesticides peer review (EFSA, 2015) and, for the proposed setting of an MRL in cotton seeds; no further information on the nature of residues in rotational crops is required.

1.1.3. Nature of residues in processed commodities

The nature of residues in processed commodities is not relevant to the evaluation of the confirmatory data submitted. Processing studies addressing the nature and the magnitude of the residues in processed commodities are not triggered for the proposed setting of an MRL in cotton seeds.

1.1.4. Methods of analysis in plants

The MRL review identified a data gap for a validated analytical method for enforcement of residues in hops, which was implemented as a confirmatory data requirement by Commission Regulation (EU) No 703/2014. The applicant submitted a study with validation data for an analytical method for hops following the pre-registration guidance SANCO/3029/99 rev. 4 (European Commission, 2000). However, the analytical method does not fully meet the requirements of the guidance for post-registration control and enforcement analytical methods SANCO/825/00 rev. 8.1 (European Commission, 2010b) because the analytical method uses the hazardous reagent diazomethane, and, inter alia, further data is required on the efficiency of the derivatisation step and the recovery for the qualifier ion. The data gap for a validated analytical method for enforcement of residues in hops remains open because a suitable analytical method with additional validation data is required to meet the guidance for post-registration control and enforcement.

The MRL review identified data gaps for an ILV and a confirmatory method for enforcement of residues in dry commodities, and for a confirmatory method for enforcement of residues in acidic, high oil content and high water content commodities, which were implemented as confirmatory data requirements by Commission Regulation (EU) No 703/2014. The applicant referred to the multi-residue high-performance liquid chromatography with tandem mass spectrometry (HPLC–MS/MS) method DFG-S19 (also reported as method L 00.00-34), which was assessed by the RMS and peer reviewed by EFSA in the framework of the renewal of the approval of pyraflufen-ethyl under Regulation (EC) No 1107/2009 (AIR II). The EFSA Conclusion on the pesticide peer review determined that the HPLC–MS/MS multi-residue method DFG-S19
is appropriate to analyse for pyraflufen-ethyl and the metabolite pyraflufen in products of plant origin (EFSA, 2015). The method was validated for determination of pyraflufen-ethyl and the metabolite pyraflufen in high water content (cucumber), dry (wheat grain), high acid content (orange fruit) and high oil content (sunflower seeds) commodities with a limit of quantification (LOQ) of 0.01 mg/kg for each analyte (Netherlands, 2013). The HPLC-MS/MS multi-residue method uses two separate mass transitions for determination of pyraflufen-ethyl and pyraflufen which allows for simultaneous primary detection and confirmation, in accordance with the guidance SANCO/825/00 rev. 8.1 (European Commission, 2010b). The independent laboratory validation of the multi-residue method DFG-S19 was reported in the RAR (Netherlands, 2013). Therefore the data gaps for an ILV and a confirmatory method for enforcement of residues in dry commodities, and for a confirmatory method for enforcement of residues in acidic, high oil content and high water content commodities are sufficiently addressed. Furthermore it is concluded that sufficiently validated methods are available to enforce an MRL in cotton seeds.

1.1.5. Stability of residues in plants

The MRL review identified a data gap for a storage stability study investigating a period of at least 18 months in dry commodities; this study was required to verify the validity of the residue trials submitted in support of the uses in barley, oats, rye and wheat (crops classified as dry/high starch commodities). In the peer review, storage stability of residues of pyraflufen-ethyl was demonstrated in dry commodities (wheat grain) for up to 12 months while residues of the metabolite pyraflufen were shown to be stable for 18 months (EFSA, 2015).

In the context of the present confirmatory data application, the applicant referred to a freezer storage stability study which had been previously evaluated in the DAR prepared in the context of the inclusion of the active substance pyraflufen-ethyl in Annex I of the Council Directive 91/414/EEC (Belgium, 1999). In this study, residues of pyraflufen-ethyl in wheat matrices (grain, straw and shoot) were found to be not acceptably stable for periods greater than 12 months, and degradation of pyraflufen-ethyl to pyraflufen was observed. However, it was reported that the total of pyraflufen-ethyl and pyraflufen residues in wheat matrices (grain, straw and shoot) expressed as pyraflufen-ethyl equivalents (in accordance with the residue definitions for monitoring and risk assessment) were stable for at least 18 months when stored frozen at or below −18°C. Although storage stability for pyraflufen-ethyl in dry commodities for a period of 18 months could not be demonstrated, there is evidence that total residues (sum of pyraflufen-ethyl and pyraflufen, expressed as pyraflufen-ethyl) are stable for at least 18 months in dry commodities (Netherlands, 2017).

In order to address the data gap, the applicant referred to residue trials performed in cereals, in which the samples were stored for a shorter period and thus, the possible degradation of residues during storage is not expected to have an impact on the individual substances included in the residue definition (see Section 1.2.1, below).

For cotton seeds, storage stability of pyraflufen-ethyl and pyraflufen was demonstrated for at least 6 months, covering the storage period of the cotton seeds samples derived from the residue trials reported under Section 1.2.1.

1.1.6. Proposed residue definitions

Based on the metabolic pattern identified in metabolism studies, the results of hydrolysis studies, the toxicological significance of metabolites and/or degradation products, and the capabilities of enforcement analytical methods, the following residue definition was proposed in the EFSA Conclusion on the EU pesticides peer review (EFSA, 2015):

- Residue for risk assessment and enforcement: Sum of pyraflufen-ethyl and pyraflufen, expressed as pyraflufen-ethyl.

The same residue definitions are applicable to rotational crops and processed products.

The residue definition for enforcement set in Regulation (EC) No 396/2005 is identical with the above mentioned residue definition. Taking into account the additional information provided in the present confirmatory data evaluation, EFSA concluded that these residue definitions are appropriate and no modification is required. The residue definitions are also appropriate for cotton seeds.
1.2. Magnitude of residues in plants

1.2.1. Magnitude of residues in primary crops

A summary of residues data from the supervised residue trials is presented in Appendix B.1.2.1.

Cotton seeds

The critical GAP for cotton assessed in the framework of the MRL review (1 \times 26.5 g a.s./ha with a preharvest interval (PHI) of 14 days in Spain) \(^5\) was not supported by residue trials and consequently the MRL review identified a data gap for further information on the magnitude of residues in cotton seeds. This data gap has not been implemented as a confirmatory data requirement in the MRL legislation and Commission Regulation (EU) No 703/2014 set the MRL for cotton seeds at the specific limit of determination or at the default MRL as set out in Article 18(1)(b) of Regulation (EC) No 396/2005.

The critical GAP for cotton proposed by the applicant in the context of the confirmatory data evaluation (1 \times 9.28 g a.s./ha at BBCH 87–88 with a PHI of 14 days) is not yet authorised, with a new product authorisation procedure ongoing in Italy (Netherlands, 2017).

The applicant submitted four residue trials performed in cotton during 2011 (study 1). The trials were conducted with three varieties of cotton at four geographically independent sites located in Spain. Trials were performed with one application of an emulsion formulation at BBCH 83–88 with application rates ranging from 9.78 to 10.57 g a.s./ha. Samples of cotton seeds were collected (harvest) immediately after application (day 0) and at 14 \pm 2 days after application. Samples were dried overnight at ambient temperature, ginned the following day and frozen for storage under the conditions for which integrity of residues has been demonstrated. Samples of cotton seeds were analysed for pyraflufen-ethyl and pyraflufen, in accordance with the residue definition for risk assessment and enforcement. According to the assessment of the RMS, the liquid chromatography with tandem mass spectrometry (LC–MS/MS) analytical method used in the residue trials was sufficiently validated and fit for purpose, with individual LOQs of 0.01 mg/kg for each component of the residue definition (overall LOQ of 0.02 mg/kg for the residue definition). The residue levels of pyraflufen-ethyl and pyraflufen in cotton seeds were below the LOQ in all submitted trials.

A further four trials in cotton seeds submitted by the applicant with application rates ranging from 5.07 to 5.28 g a.s./ha (study 2) are not compliant with the critical GAP; since no quantifiable residues of pyraflufen-ethyl and pyraflufen were detected, the trials could not be scaled up to the nominal application rate. Thus, the trials have not been assessed in the evaluation.

Cotton seeds are a major crop in the southern Europe (SEU) zone and normally a minimum of eight GAP-compliant residue trials are required. However, four trials are considered acceptable because the available trials provide sufficient evidence of a no-residue situation (European Commission, 2017). This finding is supported by information from the metabolism study, where residues in undelinted cotton seeds following foliar application at BBCH 86–87 with 6 g a.s./ha and harvest at 7 day PHI were at a level of 0.0004 mg eq/kg (pyrazole label) and 0.0006 mg eq/kg (phenyl label); because of the low residues in seeds, no further identification the residues was attempted (EFSA, 2013).

Cereals

In order to support the use of pyraflufen-ethyl in cereals, the applicant referred to residue trials performed in cereals in which the samples were analysed within the demonstrated acceptable frozen storage stability period (see Section 1.1.5, above). The RMS evaluated data from a total of 17 trials in wheat, rye and barley performed during the 1995–1996 growing season in northern Europe (NEU) (barley, rye and wheat) and SEU (barley and wheat) (Netherlands, 2017), which have been previously assessed in the DAR prepared in the context of the inclusion of the active substance pyraflufen-ethyl in Annex I of the Council Directive 91/414/EEC (Belgium, 1999). In 15 of the submitted residue trials in wheat, rye and barley, the samples of grain and straw were stored frozen for less than the 12 months period for which integrity of residues has been demonstrated. In two of the submitted residue trials on wheat (NEU), the samples of grain were reported to be stored frozen for up to 13 months until analysis, slightly exceeding the demonstrated acceptable storage stability time period of 12 months for pyraflufen-ethyl in dry/high starch category commodities (wheat grain). However, it has been demonstrated that the total residues of pyraflufen-ethyl and pyraflufen expressed as pyraflufen-ethyl

\(^5\) The applicant claimed that the GAP for cotton seeds assessed in the MRL review was incorrect since the approved use in Spain was 1 \times 2.65 g a.s./ha with a PHI of 14 days (Netherlands, 2017).
equivalents are stable when stored frozen for up to 18 months in dry/high starch category commodities (wheat grain; see Section 1.1.5, above). Therefore, when considering the total residues of pyraflufen-ethyl and pyraflufen, the storage period for samples of grain in two residue trials reported to be up to 13 months can be considered a minor deviation.

Samples of cereal grains and straw were analysed for pyraflufen-ethyl and pyraflufen, in accordance with the residue definition for risk assessment and enforcement. According to the assessment of the RMS, the analytical methods used in the residue trials were sufficiently validated and fit for purpose, with individual LOQs for each component of the residue definition of 0.01 mg/kg in grain (overall LOQ of 0.02 mg/kg in grain) and with individual LOQs of 0.02 mg/kg in straw (overall LOQ of 0.04 mg/kg in straw).

The residue levels of pyraflufen-ethyl and pyraflufen in wheat, rye and barley grain were below the LOQ in all submitted GAP compliant trials. The submitted residue trials on cereals are sufficient and confirm the MRL proposal and risk assessment values for barley, oat, rye and wheat derived in the framework of the MRL review.

In 11 GAP-compliant trials in barley and wheat, residues were also measured in straw, where residue levels of pyraflufen-ethyl and pyraflufen were low or were below the LOQ. The calculated highest residue (HR) value for straw is slightly higher than the HR value derived in the framework of the MRL review and therefore should be taken into account in a revised dietary burden calculation for livestock, together with the residues in cotton by-products used for feed purpose (see Section 2 and Appendix D.1).

1.2.2. Magnitude of residues in rotational crops

The magnitude of residues in rotational crops is not relevant to the evaluation of the confirmatory data submitted. With regard to the proposed setting of an MRL in cotton seeds, the possible transfer of pyraflufen-ethyl residues to crops that are grown in crop rotation has been assessed in EU pesticides peer review (EFSA, 2015). The available studies demonstrated that no significant residues (residues below 0.01 mg/kg) are expected in succeeding crops (lettuce, spring barley, sugar beet, cabbage and maize) planted in soil treated at 42.3 g a.s./ha. Since the maximum annual application rate for the proposed use in cotton (i.e. 9.28 g a.s./ha) is lower than the application rate tested in the rotational crop studies, it is concluded that no residues are expected, provided that the active substance is applied according to the proposed GAP.

1.2.3. Magnitude of residues in processed commodities

The magnitude of residues in processed commodities is not relevant to the evaluation of the confirmatory data submitted. Studies addressing the magnitude of the residues in processed commodities are not triggered for the proposed setting of an MRL in cotton seed.

2. Residues in livestock

The present confirmatory data evaluation included an assessment of residue data for cereals (barley, oat, rye and wheat grains and straws) and the evaluation of new residue trial data for cotton seeds, which may be used for feed purposes and therefore may have an impact on pesticide residues expected in livestock. Hence, it was necessary to update the previous dietary burden calculation for livestock to estimate whether the intended use of pyraflufen-ethyl would have an impact on the residues expected in food of animal origin. The calculations were performed in accordance with the OECD guidance document on residues in livestock (OECD, 2013) using the input values for the exposure calculations for livestock presented in Appendix D.1.

The results of the updated dietary burden calculation are presented in Section B.2, and demonstrated that the estimated exposure of livestock did not exceed the trigger values defined in the relevant guidance document. Consequently further investigation of residues in livestock, as well as the setting on MRLs in commodities of animal origin, is not necessary.

3. Consumer risk assessment

EFSA updated the previous risk assessment, taking into account the new residue data submitted under this application, in order to assess whether the residues on crops that are expected to result from the authorised uses are likely to pose a consumer health risk. The dietary risk assessment was performed using revision 2 of the EFSA PRIMo (EFSA, 2007). This exposure assessment model contains food consumption data for different sub-groups of the EU population and allows the acute
and chronic exposure assessment to be performed in accordance with the internationally agreed methodology for pesticide residues (FAO, 2016).

The toxicological reference values for pyraflufen-ethyl used in the risk assessment (i.e. acceptable daily intake (ADI) and acute reference dose (ARfD) values) were derived in the framework of the EU pesticides peer review (EFSA, 2015). For the purposes of the consumer risk assessment, the metabolite pyraflufen, included in the risk assessment residue definition, was considered to be of similar toxicity to the parent compound (EFSA, 2013, 2015).

3.1. Short-term (acute) dietary risk assessment

The short-term exposure assessment was performed in accordance with the internationally agreed methodology (FAO, 2016) for the commodities for which new residue data were provided in the framework of the present confirmatory data evaluation. The complete list of input values is presented in Appendix D.2. For the remaining crops, the short-term risk assessment presented in the MRL review (EFSA, 2013) is still valid.

The short-term exposure estimates did not exceed the ARfD for any the crops assessed in this confirmatory data evaluation (see Appendix B.3).

3.2. Long-term (chronic) dietary risk assessment

In the framework of the MRL review, a comprehensive long-term exposure assessment was performed, taking into account the existing uses at EU level (EFSA, 2013). EFSA updated the calculation with the supervised trials median residue (STMR) value for cotton seeds (at the LOQ) derived from the residue trials submitted in the present confirmatory data evaluation. The relevant STMR values for barley, oat, rye and wheat grains derived in the present confirmatory data evaluation are identical to the values derived in the framework of the MRL review. The input values used in the exposure calculations are summarised in Appendix D.2.

The use on hops reported by the RMS in the framework of the MRL review is not fully supported by data; however, hops was included in the risk assessment for indicative exposure calculations (EFSA, 2013).

The highest estimated long-term dietary intake was 0.3% of the ADI (DE child). The contribution of residues expected in the commodities assessed in this application to the overall long-term exposure is presented in more detail in Appendix B.3. EFSA concluded that the long-term intake of residues of pyraflufen-ethyl resulting from the existing uses reported in the MRL review and the new use proposed in cotton seeds is unlikely to present a risk to consumer health. The contribution of hops to the total long-term exposure was insignificant (less than 0.001% of the ADI).

4. Conclusion and Recommendations

To address data gaps identified in the framework of the MRL review (EFSA, 2013), the applicant submitted an analytical method and ILV for enforcement of residues in high water content, dry, high acid content and high oil content commodities; residue trials performed in cotton. Instead of providing information on storage stability of pyraflufen-ethyl in dry commodities for a period of 18 months to demonstrate validity of the residue trials in cereals, the applicant provided residue trials performed in cereals, in which the samples were analysed within the demonstrated acceptable frozen storage stability period.

The data submitted by the applicant in support of this confirmatory data assessment were found to be sufficient to address the data gaps Nos (2), (3) and (5) that were identified by EFSA in the framework of the MRL review.

The available data are sufficient to derive risk assessment values and confirm the tentative MRL proposals for citrus fruits, tree nuts, pome fruits, stone fruits, table and wine grapes, currants, gooseberries, elderberries, table olives, potatoes, rapeseeds/canola seeds, olives for oil production, barley, oat, rye and wheat. Furthermore, the submitted data were found to be sufficient to derive risk assessment values and propose an MRL for cotton seeds. A modification of the existing MRL for cotton seeds is not required.

Adequate analytical methods for enforcement are available to control the residues of pyraflufen-ethyl on the commodities under consideration, except for the use on hops. The confirmatory data requirement for information on analytical methods in hops has not been addressed and the data gap identified by EFSA in the framework of the MRL review, for a validated analytical method for
enforcement of residues in hops remains open. Consequently, the available data are insufficient to support an MRL proposal for hops and further risk management considerations are required.

Based on the risk assessment results, EFSA concluded that the short-term and long-term intake of residues resulting from the use of pyraflufen-ethyl according to the reported agricultural practices is unlikely to present a risk to consumer health. The overview of the assessment of confirmatory data and the recommended MRL modifications are summarised in Appendix B.4.

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Abbreviations

a.s. active substance
ADI acceptable daily intake
AR applied radioactivity
ARfD acute reference dose
BBCH growth stages of mono- and dicotyledonous plants
bw body weight
CF conversion factor for enforcement to risk assessment residue definition
cGAP critical GAP
CV coefficient of variation (relative standard deviation)
DAR draft assessment report
DAT days after treatment
DM dry matter
EC emulsifiable concentrate
EMS evaluating Member State
eq residue expressed as a.s. equivalent
FAO Food and Agriculture Organization of the United Nations
GAP Good Agricultural Practice
HPLC-MS/MS high performance liquid chromatography with tandem mass spectrometry
HR highest residue
IEDI international estimated daily intake
| Acronym | Definition |
|---------|------------|
| IESTI   | international estimated short-term intake |
| InChiKey| International Chemical Identifier Key |
| ILV     | independent laboratory validation |
| ISO     | International Organisation for Standardisation |
| IUPAC   | International Union of Pure and Applied Chemistry |
| LC-MS/MS| high performance liquid chromatography with tandem mass spectrometry |
| LOQ     | limit of quantification |
| MRL     | maximum residue level |
| NEU     | northern Europe |
| OECD    | Organisation for Economic Co-operation and Development |
| PBI     | plant-back interval |
| PF      | processing factor |
| PHI     | preharvest interval |
| PRIMo   | (EFSA) Pesticide Residues Intake Model |
| RA      | risk assessment |
| RD      | residue definition |
| RMS     | rapporteur Member State |
| SANCO   | Directorate-General for Health and Consumers |
| SEU     | southern Europe |
| SMILES  | simplified molecular-input line-entry system |
| STMR    | supervised trials median residue |
| TAR     | total applied radioactivity |
| WHO     | World Health Organization |
### Appendix A – Summary of GAPs assessed in the evaluation of confirmatory data

| Crop and/or situation | NEU, SEU, MS or country | F G or I(a) | Pests or group of pests controlled | Preparation | Application | Application rate per treatment | PHI (days)(d) | Remarks |
|-----------------------|-------------------------|------------|-----------------------------------|-------------|-------------|---------------------------------|--------------|---------|
|                       |                         |            |                                   | Type(b)     | Conc a.s. g/L | Method kind | Range of growth stages and season(c) | Number min-max | Interval between application (min) | L product/ha min-max | Water L/ha min-max | Rate (g a.s./ha) | Remarks |
| Cotton                | SEU                     | F          | Desiccation                       | EC          | 26.5        | Foliar spray | BBCH 83-85                          | 1             | 0.1                               | 250-800          | 2.65                | 14          | Add an adjuvant (1 L/ha) with 30% open bolls |
| Cotton                | SEU                     | F          | Desiccation                       | EC          | 26.5        | Foliar spray | BBCH 87-88                          | 1             | 0.35                              | 250-800          | 9.28                | 14          | cGAP supported by residue trials |
| Barley                | FR                      | F          | Annual broad-leaved weeds         | EC          | 26.5        | Foliar spray | BBCH 13-29                          | 1             | 0.90                              | 100-300          | 13.50               |             |                                  |
| Oats                  | FR                      | F          | Annual broad-leaved weeds         | EC          | 26.5        | Foliar spray | BBCH 13-29                          | 1             | 0.90                              | 100-300          | 13.50               |             |                                  |
| Rye                   | FR                      | F          | Annual broad-leaved weeds         | EC          | 26.5        | Foliar spray | BBCH 13-29                          | 1             | 0.90                              | 100-300          | 13.50               |             |                                  |
| Wheat                 | FR                      | F          | Annual broad-leaved weeds         | EC          | 26.5        | Foliar spray | BBCH 13-29                          | 1             | 0.90                              | 100-300          | 13.50               |             |                                  |

GAP: Good Agricultural Practice; NEU: northern European Union; SEU: southern European Union; MS: Member State; a.s.: active substance; EC: emulsifiable concentrate; cGAP: critical Good Agricultural Practice.

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

(b): EC: emulsifiable concentrate. CropLife International Technical Monograph no 2, 6th Edition. Revised May 2008. Catalogue of pesticide formulation types and international coding system.

(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(s)      | Application(s)                        | Sampling (DAT) | Comment/source                                      |
|-----------------------------------|-------------|--------------|---------------------------------------|----------------|-----------------------------------------------------|
| Fruit crops                       | Mandarin    | Soil treatment $1 \times 15.6$ g a.s./ha | 0, 28, 61 | Radiolabelled active substance: $^{14}$C-pyrazole (EFSA, 2013) |
| Root crops                        | Potato      | Foliar $1 \times 35$ g a.s./ha          | 7          | Radiolabelled active substance: $^{14}$C-phenyl and $^{14}$C-pyrazole (EFSA, 2013) |
| Cereals/grass                     | Wheat       | Foliar $1 \times 20$ g a.s./ha          | 23, 84     | Radiolabelled active substance: $^{14}$C-phenyl and $^{14}$C-pyrazole (EFSA, 2013) |
| Pulses/oilseeds                   | Cotton      | Foliar $1 \times 6$ g a.s./ha          | 7          | Radiolabelled active substance: $^{14}$C-phenyl and $^{14}$C-pyrazole (EFSA, 2013) |

| Rotational crops (available studies) | Crop groups         | Crop(s)      | Application(s)                        | PBI (DAT) | Comment/source                                      |
|--------------------------------------|---------------------|--------------|---------------------------------------|-----------|-----------------------------------------------------|
| Root/tuber crops                     | Radish              | Soil spraying $1 \times 14.2$ g a.s./ha | 30, 120   | Radiolabelled active substance: $^{14}$C-pyrazole (EFSA, 2013) |
| Leafy crops                          | Lettuce             | Soil spraying $1 \times 14.2$ g a.s./ha | 30(a), 120(a) | Radiolabelled active substance: $^{14}$C-pyrazole (EFSA, 2013) |
| Cereal (small grain)                 | Barley              | Soil spraying $1 \times 14.2$ g a.s./ha | 30, 150   | Radiolabelled active substance: $^{14}$C-pyrazole (EFSA, 2013) |

| Processed commodities (hydrolysis study) | Conditions                        | Stable?                     | Comment/Source |
|------------------------------------------|-----------------------------------|-----------------------------|----------------|
|                                          | Pasteurisation (20 min, 90°C, pH 4) | Not applicable, not required | EFSA (2015)    |
|                                          | Baking, brewing and boiling (60 min, 100°C, pH 5) | Not applicable, not required | EFSA (2015)    |
|                                          | Sterilisation (20 min, 120°C, pH 6) | Not applicable, not required | EFSA (2015)    |

DAT: days after treatment; PBI: plant-back interval; a.s.: active substance.
(a): Lettuce was transplanted and not sowing on treated plots.
Can a general residue definition be proposed for primary crops? Yes EFSA (2015)
Rotational crop and primary crop metabolism similar? Yes EFSA (2015)
Residue pattern in processed commodities similar to residue pattern in raw commodities? Not applicable EFSA (2015)
Plant residue definition for monitoring (RD-Mo) Sum of pyraflufen-ethyl and pyraflufen, expressed as pyraflufen-ethyl
Plant residue definition for risk assessment (RD-RA) Sum of pyraflufen-ethyl and pyraflufen, expressed as pyraflufen-ethyl
Methods of analysis for monitoring of residues (analytical technique, crop groups, LOQs) Matrices with high water content, high oil content, high acid content and dry matrices: LC–MS/MS, LOQ 0.01 mg/kg for each analyte. Method DFG-S19 HPLC–MS/MS; cucumber: module E1, wheat: E2, orange: module E3, sunflower seed: module E9 (EFSA, 2015) ILV and confirmatory method available for determination of pyraflufen-ethyl and the metabolite pyraflufen in high water content (cucumber), dry (wheat grain), high acid content (orange fruit) and high oil content (sunflower seed) commodities (Netherlands, 2017) A validated analytical method for enforcement of residues in hops is missing (EFSA, 2013; Netherlands, 2017)

LC -MS/MS: liquid chromatography with tandem mass spectrometry; HPLC -MS/MS: high-performance liquid chromatography with tandem mass spectrometry; ILV: independent laboratory validation; LOQ: limit of quantification.
### B.1.1.2. Stability of residues in plants

| Plant products (Available studies) | Category               | Commodity              | T (°C) | Stability period | Compounds covered | Comment/source |
|-------------------------------------|-------------------------|------------------------|--------|------------------|-------------------|----------------|
|                                     |                         |                        |        | Value            | Unit              |
| Potato, tubers                      | High water content      | ≥ - 18                 | 10     | Month            |                   | EFSA (2015)     |
| Cotton, seed                        | High oil content        | > 0                    | 6      | Month            |                   | Netherlands (2017) |
| Wheat, grain                        | Dry/high starch         | ≥ - 18                 | 12     | Month            |                   | EFSA (2015)     |
|                                     |                         | ≥ - 18                 | 18     | Month            |                   | EFSA (2015)     |
| Wheat, shoot                        | High acid content       | ≥ - 18                 | 12     | Month            |                   | EFSA (2015)     |
| Wheat, straw                        | Processed products      | ≥ - 18                 | 12     | Month            |                   | EFSA (2015)     |
|                                     |                         | ≥ - 18                 | 18     | Month            |                   | EFSA (2015)     |
|                                     | Others                  | ≥ - 18                 | 12     | Month            |                   | EFSA (2015)     |
|                                     |                         | ≥ - 18                 | 18     | Month            |                   | EFSA (2015)     |

Degradation of pyraflufen-ethyl to pyraflufen was observed. However, total of pyraflufen-ethyl and pyraflufen residues expressed as pyraflufen-ethyl equivalents were stable (Netherlands, 2017).
### B.1.2. Magnitude of residues in plants

#### B.1.2.1. Summary of residues data from the supervised residue trials

| Commodity       | Region/ indoor(a) | Residue levels observed in the supervised residue trials(b) (mg/kg) | Comments/source | Calculated MRL (mg/kg) | HR(c) (mg/kg) | STMR(d) (mg/kg) | CF(e) |
|-----------------|-------------------|-------------------------------------------------------------------|-----------------|------------------------|---------------|-----------------|-------|
| Cotton seed     | SEU               | Mo: 4 × 0.02*<sup>*</sup>, RA: 4 × 0.02*                           | Residue trials on cotton compliant with GAP | 0.02<sup>*</sup> | Mo: 0.02 | RA: 0.02 | 1     |
| Barley, grain   | NEU               | Mo: 2 × 0.02*, 3 × 0.02*<sup>*,(f)</sup>, RA: 2 × 0.02*, 3 × 0.02*<sup>*,(f)</sup> | Residue trials on barley compliant with GAP | – | Mo: 0.02 | RA: 0.02 | 1     |
|                 | SEU               | Mo: 2 × 0.02*<sup>,(f)</sup>, RA: 2 × 0.02*<sup>,(f)</sup> | Residue trials on barley compliant with GAP | – | Mo: 0.02 | RA: 0.02 | 1     |
| Rye, grain      | NEU               | Mo: 0.02*<sup>*</sup>, RA: 0.02*                                 | Residue trials on rye compliant with GAP | – | Mo: 0.02 | RA: 0.02 | 1     |
| Wheat, grain    | NEU               | Mo: 3 × 0.02*, 0.02*<sup>,(f)</sup>, 2 × 0.02*<sup>,(f),(f)</sup>, RA: 3 × 0.02*, 0.02*<sup>,(f)</sup>, 2 × 0.02*<sup>,(f),(f)</sup> | Residue trials on wheat compliant with GAP | – | Mo: 0.02 | RA: 0.02 | 1     |
|                 | SEU               | Mo: 3 × 0.02*<sup>*</sup>, RA: 3 × 0.02*                         | Residue trials on wheat compliant with GAP | – | Mo: 0.02 | RA: 0.02 | 1     |
| Barley, grain   | NEU + SEU         | Mo: 9 × 0.02*, 6 × 0.02*<sup>,(f)</sup>, 2 × 0.02*<sup>,(f),(f)</sup>, RA: 9 × 0.02*, 6 × 0.02*<sup>,(f)</sup>, 2 × 0.02*<sup>,(f),(f)</sup> | Combined data set. Residue trials on barley, rye and wheat compliant with GAP. Residue trials are sufficient for extrapolation to barley, oat, rye and wheat | 0.02<sup>*</sup> | Mo: 0.02 | RA: 0.02 | 1     |
| Oat, grain      |                   |                                                                  |                 |                        |               |                 |       |
| Rye, grain      |                   |                                                                  |                 |                        |               |                 |       |
| Wheat, grain    |                   |                                                                  |                 |                        |               |                 |       |
| Barley, straw   | NEU               | Mo: 3 × 0.04*<sup>,(f)</sup>, RA: 3 × 0.04*<sup>,(f)</sup> | Residue trials on barley compliant with GAP. Two trials excluded as it is reported that ‘mix-up’ had occurred with straw control samples | – | Mo: 0.04 | RA: 0.04 | 1     |
|                 | SEU               | Mo: 2 × 0.04*<sup>,(f)</sup>, RA: 2 × 0.04*<sup>,(f)</sup> | Residue trials on barley compliant with GAP | – | Mo: 0.04 | RA: 0.04 | 1     |
| Rye, straw      | NEU               | Mo: –<sup>,*</sup>, RA: –<sup>,*</sup>                          | Residue trial excluded as it is reported that ‘mix-up’ had occurred with straw control samples | – | Mo: –<sup>,*</sup> | RA: –<sup>,*</sup> |       |
## Commodity Region/indoor (a) Residue levels observed in the supervised residue trials (mg/kg) Comments/source Calculated MRL (mg/kg) HR (c) (mg/kg) STMR (d) (mg/kg) CF (e)

| Commodity                  | Region/indoor (a) | Residue levels observed in the supervised residue trials (mg/kg) | Comments/source | Calculated MRL (mg/kg) | HR (c) (mg/kg) | STMR (d) (mg/kg) | CF (e) |
|----------------------------|-------------------|-----------------------------------------------------------------|-----------------|------------------------|----------------|-----------------|--------|
| Wheat, straw               | NEU               | Mo: 3 × 0.04*,(f) RA: 3 × 0.04*.(f)                              | Residue trials on wheat compliant with GAP. Three trials excluded due to low procedural recoveries for straw matrix | –                      | Mo: 0.04        | RA: 0.04         | 1      |
|                            | SEU               | Mo: 2 × 0.053, 0.057 RA: 2 × 0.053, 0.057                        | Residue trials on wheat compliant with GAP | –                      | Mo: 0.057       | RA: 0.057        | 1      |
| Barley, straw              | NEU + SEU         | Mo: 8 × 0.04*,(f), 2 × 0.053, 0.057 RA: 8 × 0.04*,(f), 2 × 0.053, 0.057 | Combined data set. Residue trials on barley and wheat compliant with GAP. Populations NEU+SEU similar according to Mann-Whitney U-test. Residue trials are sufficient for extrapolation to barley, oat, rye and wheat | –                      | Mo: 0.057       | RA: 0.057        | 1      |

**MRL**: maximum residue level; **GAP**: Good Agricultural Practice;  
* indicates that the MRL is proposed at the limit of quantification.  
(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): Mo: According to the residue definition for monitoring; RA: According to the residue definition for risk assessment.  
(c): HR: Highest residue. The highest residue for risk assessment refers to the whole commodity and not to the edible portion.  
(d): STMR: Supervised trials median residue. The median residue for risk assessment refers to the whole commodity and not to the edible portion.  
(e): CF: Conversion factor to recalculate residues according to the residue definition for monitoring to the residue definition for risk assessment.  
(f): Overdosed trial (> 25% GAP application rate) leading to residue levels less than the LOQ.  
(g): Samples of wheat grain reported to be stored frozen for period up to 13 months until analysis, slightly exceeding the demonstrated acceptable storage stability time period of 12 months for pyraflufen-ethyl in dry/high starch category commodities.
B.1.2.2. Residues in rotational crops

| Residues in rotational and succeeding crops expected based on confined rotational crop study? | No |
| Residues in rotational and succeeding crops expected based on field rotational crop study? | No |

Field rotational crop trials in lettuce, spring barley, sugar beet, cabbage and maize after a bare soil treatment at 42.4 g a.s./ha with plant-back intervals of 6 and 30 days. Residues of pyraflufen-ethyl and pyraflufen < LOQ in all edible parts of the following crops at all sampling intervals. Significant residue levels of the high persistent E-3 metabolite are not expected in rotational crops since the field trials were conducted at a rate covering the calculated plateau concentration of E-3 in soil (EFSA, 2015)

a.s.: active substance; LOQ: limit of quantification.

B.1.2.3. Processing factors

No processing studies were submitted in the framework of the present confirmatory data assessment.

B.2. Residues in livestock

| Relevant groups (subgroups) | Dietary burden expressed in mg/kg bw per day Median | Maximum | mg/kg DM Median | Maximum | Most critical subgroup(a) | Most critical commodity(b) | Trigger exceeded (Y/N) |
|----------------------------|---------------------------------|--------|-----------------|--------|--------------------------|---------------------------|------------------------|
| Cattle (all)               | 0.0027                          | 0.0033 | 0.08            | 0.09   | Cattle (dairy)            | Potato, culls             | No                     |
| Cattle (dairy only)        | 0.0027                          | 0.0033 | 0.07            | 0.09   | Cattle (dairy)            | Potato, culls             | No                     |
| Sheep (all)                | 0.0030                          | 0.0041 | 0.08            | 0.10   | Sheep (lamb)              | Potato, culls             | No                     |
| Sheep (ewe only)           | 0.0026                          | 0.0033 | 0.08            | 0.10   | Sheep (ram/ewe)           | Potato, culls             | No                     |
| Swine (all)                | 0.0018                          | 0.0018 | 0.07            | 0.07   | Swine (finishing)         | Potato, culls             | No                     |
| Poultry (all)              | 0.0030                          | 0.0031 | 0.04            | 0.04   | Poultry (layer)           | Wheat, straw              | No                     |
| Poultry (layer only)       | 0.0027                          | 0.0031 | 0.04            | 0.04   | Poultry (layer)           | Wheat, straw              | No                     |

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.2.2. Nature of residues and methods of analysis in livestock

Not relevant.
### B.3. Consumer risk assessment

| ARfD | 0.2 mg/kg bw (EFSA, 2015) |
|------|--------------------------|
| Highest IESTI, according to EFSA PRIMo | Wheat: 0.1% of ARfD  
Rye: 0.1% of ARfD  
Oats: 0.04% of ARfD  
Barley: 0.02% of ARfD |
| Assumptions made for the calculations | The calculation was performed only for those crops for which new residue data were provided (i.e. wheat, rye, oats, barley, and cotton) using STMR levels expected in raw agricultural commodities. For cotton seeds, no consumption data are available. For the remaining commodities, the risk assessment presented in the MRL review is still valid (EFSA, 2013) |

| ADI | 0.2 mg/kg bw per day (EFSA, 2015) |
|------|---------------------------------|
| Highest IEDI, according to EFSA PRIMo | 0.3 % of ADI (DE child)  
Contribution of crops assessed:  
Wheat: 0.09% of ADI (WHO cluster diet B)  
Rye: 0.04% of ADI (DK child)  
Barley: 0.01% of ADI (IE adult)  
Hops: < 0.001% of ADI |
| Assumptions made for the calculations | The risk assessment performed in the framework of the MRL review (EFSA, 2013) has been updated, including the median residue levels derived for those commodities, for which new residue data were provided (i.e. wheat, rye, oats, barley, and cotton)  
Although the use in hops is not sufficiently supported by data, the HR value derived for hops was included in the calculation, to provide the necessary information to risk managers take an appropriate decision. The contributions of commodities where no GAP was reported in the framework of the MRL review were not included in the calculation |

ARfD: acute reference dose; bw: body weight; IESTI: international estimated short-term intake; PRIMo: (EFSA) Pesticide Residues Intake Model; STMR: supervised trials median residue; ADI: acceptable daily intake; IEDI: international estimated daily intake; MRL: maximum residue level; HR: highest residue; GAP: Good Agricultural Practice
### B.4. Recommended MRLs

| Code(a) | Commodity | Existing EU MRL(b) (mg/kg) | Proposed EU MRL (mg/kg) | Conclusion/recommendation |
|---------|-----------|---------------------------|-------------------------|--------------------------|
| 110000  | Citrus fruits | 0.02* (ft 1) | 0.02* | The confirmatory data requirement for information on analytical methods has been addressed. The available data are sufficient to confirm the existing MRLs. A consumer health risk was not identified |
| 120000  | Tree nuts | 0.02* (ft 1) | 0.02* |
| 130000  | Pome fruits | 0.02* (ft 1) | 0.02* |
| 140000  | Stone fruits | 0.02* (ft 1) | 0.02* |
| 151000  | Grapes (table and wine grapes) | 0.02* (ft 1) | 0.02* |
| 154030  | Currants (black, red and white) | 0.02* (ft 1) | 0.02* |
| 154040  | Gooseberries (green, red and yellow) | 0.02* (ft 1) | 0.02* |
| 154080  | Elderberries | 0.02* (ft 1) | 0.02* |
| 161030  | Table olives | 0.02* (ft 1) | 0.02* |
| 211000  | Potatoes | 0.02* (ft 1) | 0.02* |
| 401060  | Olives for oil production | 0.02* (ft 1) | 0.02* |
| 401080  | Rapeseeds/canola seeds | 0.02* (ft 1) | 0.02* |
| 401090  | Cotton seeds | 0.02* | 0.02* | The submitted data are sufficient to derive an MRL proposal. No MRL change is required. A consumer health risk was not identified |
| 402010  | Barley | 0.02* (ft 2) | 0.02* |
| 500010  | Oat | 0.02* (ft 2) | 0.02* |
| 500070  | Rye | 0.02* (ft 2) | 0.02* |
| 500090  | Wheat | 0.02* (ft 2) | 0.02* |
| 700000  | Hops | 0.1* (ft 3) | Further risk management considerations are required |

**MRL**: maximum residue level.

*: Indicates that the MRL is set at the limit of analytical quantification (LOQ).
(a): Commodity code number according to Annex I of Regulation (EC) No 396/2005.
(b): Existing EU MRL and corresponding footnote on confirmatory data in accordance with Commission Regulation (EU) No 703/2014.
(ft 1): The European Food Safety Authority identified some information on analytical methods as unavailable. When re-viewing the MRL, the Commission will take into account the information referred to in the first sentence, if it is submitted by 26 June 2016, or, if that information is not submitted by that date, the lack of it. (Footnote related to data gap No 3.)
(ft 2): Commission Regulation (EU) No 703/2014: The European Food Safety Authority identified some information on storage stability and analytical methods has been addressed. The available data are sufficient to confirm the existing MRL. A consumer health risk was not identified
(ft 3): The European Food Safety Authority identified some information on analytical methods as unavailable. When re-viewing the MRL, the Commission will take into account the information referred to in the first sentence, if it is submitted by 26 June 2016, or, if that information is not submitted by that date, the lack of it. (Footnote related to data gap No 1.)
# Appendix C – Pesticide Residue Intake Model (PRIMo)

## Pyraflufen-ethyl

| Status of the active substance: | Approved | Code no. | LOQ (mg/kg bw): | 0.02 | Proposed LOQ: | 0.2 |
|--------------------------------|----------|----------|----------------|------|---------------|-----|
| Toxicological end points      |          |          | ADI (mg/kg bw per day): | 0.2 | ARfD (mg/kg bw): | 0.2 |
| Source of ADI:                | EFSA     |          | Year of evaluation:    | 2015| Source of ARfD: | EFSA|

### Year of evaluation:
- 2015

### Source:
- EFSA

### ADI (mg/kg bw per day):
- 0.2

### ADI Source:
- EFSA

### ARfD (mg/kg bw):
- 0.2

### ARfD Source:
- EFSA

### No of diets exceeding ADI:
- **---**

### Highest calculated TMDI values in % of ADI

| Commodity/group of commodities | TMDI (range) in % of ADI |
|--------------------------------|--------------------------|
|                                | Minimum – Maximum        |

### Evaluation of confirmatory data following the Article 12 MRL review for pyraflufen-ethyl

The risk assessment has been performed on the basis of the MRLs collected from Member States in April 2006. For each pesticide/commodity the highest national MRL was identified (proposed temporary MRL = pTMRL). The pTMRLs have been submitted to EFSA in September 2006.

### Chronic risk assessment – refined calculations

| Commodity/group of commodities | TMDI (range) in % of ADI |
|--------------------------------|--------------------------|
|                                | Minimum – Maximum        |

### Conclusion:

The estimated Theoretical Maximum Daily Intakes (TMDI), based on pTMRLs were below the ADI. A long-term intake of residues of Pyraflufen-ethyl 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 leads to an exposure equivalent to 100% of the ARfD.

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.

**Conclusion:**

For Pyraflufen-ethyl, IESTI 1 and IESTI 2 were calculated for food commodities for which pTMRLs were submitted and for which consumption data are available.

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

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

| Processed commodities | No of critical MRLs (IESTI 1) | 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 | Processed commodities          | pTMRL/ threshold MRL (mg/kg)                             | pTMRL/ threshold MRL (mg/kg)                             |
|                       | Commodity                       |                                                       |                                                         |
| 0.5                   | Apple juice                     | 0.02/-                                                  | 0.1 Orange juice                                        |
| 0.5                   | Orange juice                    | 0.02/-                                                  | 0.1 Apple juice                                         |
| 0.3                   | Grape juice                     | 0.02/-                                                  | 0.0 Bread/pizza                                          |
| 0.2                   | Peach juice                     | 0.02/-                                                  | 0.0 Wine                                                |
| 0.2                   | Pear juice                      | 0.02/-                                                  | 0.0 Peach preserved with syrup                           |

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

**pTMRL**: provisional temporary MRL.
### 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                |
| **Risk assessment residue definition:** Sum of pyraflufen-ethyl and pyraflufen, expressed as pyraflufen-ethyl |
| Grapefruits, dried pulp         | 0.02                  | STMR × PF (1) (EFSA, 2013) | 0.02 | STMR × PF (1) (EFSA, 2013) |
| Oranges, dried pulp             | 0.02                  | STMR × PF (1) (EFSA, 2013) | 0.02 | STMR × PF (1) (EFSA, 2013) |
| Lemons, dried pulp              | 0.02                  | STMR × PF (1) (EFSA, 2013) | 0.02 | STMR × PF (1) (EFSA, 2013) |
| Limes, dried pulp               | 0.02                  | STMR × PF (1) (EFSA, 2013) | 0.02 | STMR × PF (1) (EFSA, 2013) |
| Mandarins, dried pulp           | 0.02                  | STMR × PF (1) (EFSA, 2013) | 0.02 | STMR × PF (1) (EFSA, 2013) |
| Coconut, meal                   | 0.03                  | STMR × default PF (1.5) (EFSA, 2013) | 0.03 | STMR × default PF (1.5) (EFSA, 2013) |
| Apple, pomace, wet              | 0.02                  | STMR × PF (1) (EFSA, 2013) | 0.02 | STMR × PF (1) (EFSA, 2013) |
| Potato, culls                   | 0.02                  | STMR (EFSA, 2013)       | 0.02 | HR (EFSA, 2013) |
| Potato, process waste           | 0.01                  | STMR (a) (default PF not applied) (EFSA, 2013) | 0.01 | STMR (a) (default PF not applied) (EFSA, 2013) |
| Potato, dried pulp              | 0.01                  | STMR (a) (default PF not applied) (EFSA, 2013) | 0.01 | STMR (a) (default PF not applied) (EFSA, 2013) |
| Canola (Rape seed), meal        | 0.02                  | STMR × PF (1) (EFSA, 2013) | 0.02 | STMR × PF (1) (EFSA, 2013) |
| Rape, meal                      | 0.02                  | STMR × PF (1) (EFSA, 2013) | 0.02 | STMR × PF (1) (EFSA, 2013) |
| Cotton, undelinted seed         | 0.02                  | STMR                   |
| Cotton, meal                    | 0.02                  | STMR (b) (default PF not applied) | 0.02 | STMR (b) (default PF not applied) |
| Barley, grain                   | 0.02                  | STMR                   |
| Brewer’s grain, dried           | 0.07                  | STMR × default PF (3.3) | 0.07 | STMR × default PF (3.3) |
| Oat, grain                      | 0.02                  | STMR                   |
| Rye, grain                      | 0.02                  | STMR                   |
| Triticale, grain                | 0.02                  | STMR                   |
| Wheat, grain                    | 0.02                  | STMR                   |
| Wheat, distiller’s grain (dry)  | 0.07                  | STMR × default PF (3.3) | 0.07 | STMR × default PF (3.3) |
| Wheat gluten, meal              | 0.04                  | STMR × default PF (1.8) | 0.04 | STMR × default PF (1.8) |
| Wheat, milled by-pdts           | 0.02                  | STMR × PF (1)          | 0.02 | STMR × PF (1) |
| Barley, straw                   | 0.04                  | STMR                   | 0.06 | HR |
| Oat, straw                      | 0.04                  | STMR                   | 0.06 | HR |
| Rye, straw                      | 0.04                  | STMR                   | 0.06 | HR |
| Triticale, straw                | 0.04                  | STMR                   | 0.06 | HR |
| Wheat, straw                    | 0.04                  | STMR                   | 0.06 | HR |

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

(a): For potato process waste and dried pulp, considering that input values for potato used in the dietary burden calculations correspond to the LOQ value of the available trials supporting the southern use on potato (0.02 mg/kg), the exposure of meat ruminants is overestimated leading to a slight exceedance of the trigger value. On the basis of metabolism study in potatoes and the available trials supporting the northern use, residues levels in potatoes are likely to be below 0.01 mg/kg when the active substance is applied in compliance with the GAPs (EFSA, 2013). Thus, no default processing factor was applied because residues are expected to be below the LOQ; concentration of residues in these commodities is not expected.

(b): For cotton meal, no default processing factor was applied because 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               |
| **Risk assessment residue definition:** Sum of pyraflufen-ethyl and pyraflufen, expressed as pyraflufen-ethyl | | | |
| Grapefruits                | 0.020                   | STMR (EFSA, 2013)     | |                        |
| Oranges                    | 0.020                   | STMR (EFSA, 2013)     | |                        |
| Lemons                     | 0.020                   | STMR (EFSA, 2013)     | |                        |
| Limes                      | 0.020                   | STMR (EFSA, 2013)     | |                        |
| Mandarins                  | 0.020                   | STMR (EFSA, 2013)     | |                        |
| Almonds                    | 0.020                   | STMR (EFSA, 2013)     | |                        |
| Brazil nuts                | 0.020                   | STMR (EFSA, 2013)     | |                        |
| Cashew nuts                | 0.020                   | STMR (EFSA, 2013)     | |                        |
| Chestnuts                  | 0.020                   | STMR (EFSA, 2013)     | |                        |
| Coconuts                   | 0.020                   | STMR (EFSA, 2013)     | |                        |
| Hazelnuts/cobnuts          | 0.020                   | STMR (EFSA, 2013)     | |                        |
| Macadamias                 | 0.020                   | STMR (EFSA, 2013)     | |                        |
| Pecans                     | 0.020                   | STMR (EFSA, 2013)     | |                        |
| Pine nut kernels           | 0.020                   | STMR (EFSA, 2013)     | |                        |
| Pistachios                 | 0.020                   | STMR (EFSA, 2013)     | |                        |
| Walnuts                    | 0.020                   | STMR (EFSA, 2013)     | |                        |
| Apples                     | 0.020                   | STMR (EFSA, 2013)     | |                        |
| Pears                      | 0.020                   | STMR (EFSA, 2013)     | |                        |
| Quinces                    | 0.020                   | STMR (EFSA, 2013)     | |                        |
| Medlars                    | 0.020                   | STMR (EFSA, 2013)     | |                        |
| Loquats/Japanese medlars    | 0.020                   | STMR (EFSA, 2013)     | |                        |
| Apricots                   | 0.020                   | STMR (EFSA, 2013)     | |                        |
| Cherries (sweet)           | 0.020                   | STMR (EFSA, 2013)     | |                        |
| Peaches                    | 0.020                   | STMR (EFSA, 2013)     | |                        |
| Plums                      | 0.020                   | STMR (EFSA, 2013)     | |                        |
| Table grapes               | 0.020                   | STMR (EFSA, 2013)     | |                        |
| Wine grapes                | 0.020                   | STMR (EFSA, 2013)     | |                        |
| Currants (black, red and white) | 0.020               | STMR (EFSA, 2013)     | |                        |
| Gooseberries (green, red and yellow) | 0.020            | STMR (EFSA, 2013)     | |                        |
| Elderberries               | 0.020                   | STMR (EFSA, 2013)     | |                        |
| Table olives               | 0.020                   | STMR (EFSA, 2013)     | |                        |
| Potatoes                   | 0.020                   | STMR (EFSA, 2013)     | |                        |
| Rapeseeds/canola seeds     | 0.020                   | STMR (EFSA, 2013)     | |                        |
| Cotton seeds               | 0.020                   | STMR (EFSA, 2013)     | |                        |
| Olives for oil production  | 0.020                   | STMR (EFSA, 2013)     | |                        |
| Barley grains              | 0.020                   | STMR (EFSA, 2013)     | |                        |
| Oat grains                 | 0.020                   | STMR (EFSA, 2013)     | |                        |
| Rye grains                 | 0.020                   | STMR (EFSA, 2013)     | |                        |
| Wheat grains               | 0.020                   | STMR (EFSA, 2013)     | |                        |
| Hops                       | 0.010                   | STMR^{(a)} (EFSA, 2013)| 0.010              | HR^{(a)} (EFSA, 2013) |

STMR: supervised trials median residue; HR: highest residue.

^{(a)}: Use reported by the RMS is not fully supported by data but the risk assessment values derived in the MRL review are used for indicative exposure calculations (EFSA, 2013).

Acute risk assessment was undertaken only with regard to the crops under consideration.
### Appendix E – Used compound codes

| Code/trivial name (a) | IUPAC name/SMILES notation/InChiKey (b) | Structural formula (c) |
|-----------------------|----------------------------------------|------------------------|
| **Pyraflufen-ethyl**  | ethyl [2-chloro-5-(4-chloro-5-difluoromethoxy-1-methyl-1H-pyrazol-3-yl)-4-fluorophenoxy]acetate  
Cn1nc(c2cc(OCC(=O)OCC)c(Cl)cc2F)c(Cl)c1OC(F)F  
APTZNHMIGJTEW-UHFFFAOYSA-N | ![Structural formula for Pyraflufen-ethyl](image1) |
| **Pyraflufen**        | [2-chloro-5-(4-chloro-5-difluoromethoxy-1-methyl-1H-pyrazol-3-yl)-4-fluorophenoxy]acetic acid  
Cn1nc(c2cc(OCC(=O)O)c(Cl)cc2F)c(Cl)c1OC(F)F  
YXIIPOGVYWIW-UHFFFAOYSA-N | ![Structural formula for Pyraflufen](image2) |
| E-1  T-5067           | 4-chloro-3-(4-chloro-2-fluoro-5-methoxyphenyl)-5-(difluoromethoxy)-1-methyl-1H-pyrazole  
Cn1nc(c2cc(OC)c(Cl)cc2F)c(Cl)c1OC(F)F  
ZKSGROKQOMSPL-UHFFFAOYSA-N | ![Structural formula for E-1 T-5067](image3) |
| E-3 4-chloro-3-(4-chloro-2-fluoro-5-methoxyphenyl)-5-(difluoromethoxy)-1-methyl-1H-pyrazole  
Cn1nc(c2cc(OC)c(Cl)cc2F)c(Cl)c1OC(F)F  
ZKSGROKQOMSPL-UHFFFAOYSA-N | ![Structural formula for E-3](image4) |

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

(a): The metabolite name in bold is the name used in the conclusion.
(b): ACD/Name 2017.2.1 ACD/Labs 2017 Release (File version N40E41, Build 96719, 6 September 2017).
(c): ACD/ChemSketch 2017.2.1 ACD/Labs 2017 Release (File version C40H41, Build 99535, 14 February 2018).