Review of the existing maximum residue levels for pyriofenone 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 pyriofenone. To assess the occurrence of pyriofenone residues in plants, processed commodities, rotational crops and livestock, EFSA considered the conclusions derived in the framework of Regulation (EC) No 1107/2009, as well as the European authorisations reported by Member States (including the supporting residues data). Based on the assessment of the available data, MRL proposals were derived and a consumer risk assessment was carried out. No risk to consumers was identified but some information required by the regulatory framework was missing. Hence, the consumer risk assessment is considered indicative only and some MRL proposals derived by EFSA still require further consideration by risk managers.

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Summary

Pyriofenone was approved on 1 February 2014 by means of Commission Implementing Regulation (EU) No 833/2013 under Regulation (EC) No 1107/2009 as amended by Commission Implementing Regulations (EU) No 540/2011 and 541/2011.

As the active substance was approved after the entry into force of Regulation (EC) No 396/2005 on 2 September 2008, the European Food Safety Authority (EFSA) is required to provide a reasoned opinion on the review of the existing maximum residue levels (MRLs) for that active substance in compliance with Article 12(1) of the aforementioned regulation.

As the basis for the MRL review, on 12 January 2018 EFSA initiated the collection of data for this active substance. In a first step, Member States were invited to submit by 12 February 2018 their national Good Agricultural Practices (GAPs) in a standardised way, in the format of specific GAP forms, allowing the designated rapporteur Member State Latvia 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 7 June 2018. On the basis of all the data submitted by Member States and by the EU Reference Laboratories for Pesticides Residues (EURL), EFSA asked the rapporteur Member State (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 were provided by the RMS to EFSA on 17 August 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 EURL, and taking into account the conclusions derived by EFSA in the framework of Regulation (EC) No 1107/2009, EFSA prepared in February 2019 a draft reasoned opinion, which was circulated to Member States for consultation via a written procedure. Comments received by 22 March 2019 were considered during the finalisation of this reasoned opinion. The following conclusions are derived.

The metabolism of pyriofenone in plant was investigated in primary and rotational crops. According to the results of the metabolism studies performed on fruit crops and cereals and on rotational crops, the residue definition for enforcement and risk assessment can be proposed as ‘pyriofenone’. This residue definition is also applicable to processed commodities. Fully validated analytical methods are available for the enforcement of the proposed residue definition in the main four plant matrices at the limit of quantification (LOQ) of 0.01 mg/kg. According to the EURLs, the LOQ of 0.01 mg/kg is achievable by using the QuEChERS method in routine analyses.

Available residue trials data were considered sufficient to derive MRL proposals as well as risk assessment values for all commodities under evaluation.

Pyriofenone is authorised for use on cereals that might be fed to livestock. Livestock dietary burden calculations were therefore performed for different groups of livestock according to OECD guidance. The dietary burdens calculated for cattle and sheep were found to exceed the trigger value of 0.1 mg/kg dry matter (DM). Behaviour of residues was therefore assessed in these groups of livestock.

The metabolism of pyriofenone residues in livestock was investigated in lactating goats at dose rate covering the maximum dietary burdens calculated in this review. According to the results of these studies, no residues are expected to be transferred in the different tissues of ruminants and in milk. The residue definition for enforcement and risk assessment in commodities of ruminants was proposed as ‘pyriofenone’ only; this might be extended if future uses would significantly increase the livestock exposure. It was pointed out that no analytical methods for the enforcement of the proposed residue definition were available.

The above mentioned metabolism study was sufficient to conclude the MRLs and risk assessment values in milk and all tissues of ruminants could be established at the LOQ level. However, in the absence of analytical methods for enforcement of pyriofenone in animal matrices, tentative MRLs were proposed at an indicative default LOQ of 0.01 mg/kg.

Chronic 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 represented 0.7% of the acceptable daily intake (ADI; FR toddlers). Acute exposure calculations were not carried out because an acute reference dose (ARfD) was not deemed necessary for this active substance.
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Review of the existing MRLs for pyriofenone

Background

Regulation (EC) No 396/20051 (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/EEC2 a reasoned opinion on the review of the existing MRLs for that active substance.

As pyriofenone was approved on 1 February 2014 by means of Commission Implementing Regulation (EU) No 833/20133 under Regulation (EC) No 1107/20094 as amended by Commission Implementing Regulations (EU) No 540/20115 and 541/20116, EFSA initiated the review of all existing MRLs for that active substance.

By way of background information, in the framework of Regulation (EC) No 1107/2009 pyriofenone was evaluated by Latvia, 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 as set out in the EFSA conclusion (EFSA, 2013a). Pyriofenone was approved for the use as a fungicide.

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 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 12 January 2018 EFSA initiated the collection of data for this active substance. In a first step, Member States were invited to submit by 12 February 2018 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, 18 Member States provided feedback on their national authorisations of active substance. Based on the GAP data submitted, the designated RMS Latvia 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 7 June 2018.

On the basis of all the data submitted by Member States and the EU Reference Laboratories for Pesticides Residues (EURL), EFSA asked Latvia 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, were submitted to EFSA on 14 August 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.

Considering all the available information, EFSA prepared in February 2019 a draft reasoned opinion, which was circulated to Member States for commenting via a written procedure. All comments received by 22 March 2019 were considered by EFSA during the finalisation of the reasoned opinion.

The evaluation report submitted by the RMS (Latvia, 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 EFSA 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

Pyriofenone is the ISO common name for (5-chloro-2-methoxy-4-methyl-3-pyridyl)(4,5,6-trimethoxy-o-toly)methanone (IUPAC).

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

The EU MRLs for pyriofenone are established in Annex IIIA of Regulation (EC) No 396/2005. An overview of the MRL changes that occurred since the entry into force of the Regulation mentioned above is provided below (Table 1).

Table 1: Overview of the MRL changes since the entry into force of Regulation (EC) No 396/2005

| Procedure                  | Legal implementation | Remarks                                         |
|----------------------------|----------------------|--------------------------------------------------|
| MRL application            | Regulation (EC) No 2016/1(ª) | Table grapes (EFSA, 2015)                      |
| MRL application            | Regulation (EC) No 36/2014(b)      | Cereals, grapes and animal products (EFSA, 2013b) |

MRL: maximum residue level.
(ª): Commission Regulation (EU) 2016/1 of 3 December 2015 amending Annexes II and III to Regulation (EC) No 396/2005 of the European Parliament and of the Council as regards maximum residue levels for bifenthrin, boscalid, cyazofamid, cyromazine, dazomet, dithiocarbamates, fluazifop-P, mepanipyrim, metrafenone, picloram, propamocarb, pyraben, pyriofenone, sulfoxaflor, tebuconazole, tebufenpyrad and thiram in or on certain products. OJ L 2, 5.1.2016, p. 1–62.
(b): Commission Regulation (EU) No 36/2014 of 16 January 2014 amending Annexes II and III to Regulation (EC) No 396/2005 of the European Parliament and of the Council as regards maximum residue levels for aminopyralid, chlorantraniliprole, cyflufenamid, meipquat, metalaxyl-M, propamocarb, pyriofenone and quinoxyfen in or on certain products. OJ L 17, 21.1.2014, p. 1–41.

For the purpose of this MRL review, all the uses of pyriofenone 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 pyriofenone 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 (Latvia, 2018);
- the draft assessment report (DAR) and its addenda prepared under Council Directive 91/414/EEC (United Kingdom, 2012, 2013);
- the conclusion on the peer review of the pesticide risk assessment of the active substance pyriofenone (EFSA, 2013a);
- the previous reasoned opinions on pyriofenone (EFSA, 2013b, 2015).

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 pyriofenone was investigated after foliar treatment in fruits and cereals (United Kingdom, 2012) and assessed in the framework of the peer-review (EFSA, 2013a). In all studies, pyriofenone was radiolabelled in the phenyl and pyridyl rings of the molecule. The parameters of the available metabolism studies are representative of the GAPs under assessment.

The major component of the residues in the fruit crops (grapes and tomatoes) was pyriofenone, representing more than 50% of the total radioactive residues (TRR), up to 0.08 mg/kg in grapes and up to 0.18 mg/kg in tomatoes. The same was observed in cereals where the parent compound accounted for 13–29% of the TRR in wheat grain (up to 0.013 mg/kg) and 35–49 of the TRR in wheat straw (up to 0.61 mg/kg).

The rest of the radioactive residues was composed of a vast number of individual fractions, including several hydroxy metabolites related to pyriofenone, each observed at low level and proportion (mostly < 2% TRR). The metabolism was seen to be similar in all plants investigated and proceeds first by demethylation at the positions 3 or/and 4 of the phenyl moiety to give the hydroxy metabolites 3HDPM, 4HDPM and 2MDPM, followed by further glucose conjugations. Additional demethylation of the 3HDPM metabolite at the carbon 2 gives the 4MDPM metabolite.

1.1.2. Nature of residues in rotational crops

Pyriofenone is authorised on cereals, which may be grown in rotation. The field DT₉₀ reported in the soil degradation studies evaluated in the framework of the peer review is the range of 413–2,415 days (EFSA, 2013a), indicating that pyriofenone is a persistent compound. Considering the critical GAP authorised on cereals (2 applications of 90 g a.s./ha at BBCH 21–65), a plateau soil concentration of 0.025 mg/kg is expected after 5 years of consecutive applications.

A confined rotational crop study with pyriofenone radiolabelled on the phenyl ring was reported and assessed during the peer review (United Kingdom, 2012; EFSA, 2013a). Pyriofenone was applied at a rate of 284 g a.s./ha onto bare soil. Crops were planted at nominal plant-back intervals (PBI) of 30, 122 and 364 days after treatment (DAT). Crops planted at each interval consisted of leafy vegetable (lettuce), roots (carrots) and cereals (wheat).

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7 Commission Regulation (EU) No 546/2011 of 10 June 2011 implementing Regulation (EC) No 1107/2009 of the European Parliament and of the Council as regards uniform principles for evaluation and authorisation of plant protection products. OJ L 155, 11.6.2011, p. 127-175.

8 Assuming a soil tillage depth of 5 cm and soil bulk density 1.5 g/cm³, the total PEC soil (including background plateau plus maximum seasonal application rate) was calculated at 0.0969 mg/kg soil (EFSA, 2013a). Considering a mixing depth of 20 cm (commonly used in crop growing), the total PEC soil is estimated at 0.025 mg/kg soil.
In soil, levels of unchanged pyriofenone accounted for 0.11–0.19 mg/kg in the 31-day aged samples, 0.05–0.14 mg/kg in the 122-day aged samples and to 0.05–0.08 mg/kg in the 364-day aged samples. Therefore, the study covers the plateau soil concentration of 0.018 mg/kg expected from the critical authorised GAP by an overdosing factor of 2–8N.

Total radioactive residues remained below 0.01 mg eq./kg in wheat grain and lettuce, at all plant back intervals. Therefore, no further characterisation/identification was conducted in these commodities. Total residues were very low in carrot roots (< 0.02 mg eq./kg), with 40–81% of the TRR being composed of parent compound (up to 0.014 mg/kg). Residues were higher in wheat straw (0.06–0.23 mg eq./kg), where parent compound consisted of only 14–18% of the TRR. The other constituents of the radioactivity in carrots and wheat straw were mainly conjugates of the hydroxy metabolite 4HDPM.

Consequently, the metabolic pathway was concluded to be similar to the metabolism in primary crops with the radioactive residues mainly constituted of the parent pyriofenone and hydroxymetabolite 4HDPM under its conjugated forms.

### 1.1.3. Nature of residues in processed commodities

Studies investigating the nature of residues in processed commodities were assessed (United Kingdom, 2012; EFSA, 2013a). Studies were conducted with radiolabelled pyriofenone on the phenyl and pyridyl rings simulating representative hydrolytic conditions for pasteurisation (20 min at 90°C, pH 4), boiling/brewing/baking (60 min at 100°C, pH 5) and sterilisation (20 min at 120°C, pH 6). Pyriofenone was stable to hydrolysis under standard conditions of pasteurisation, baking/brewing/boiling and sterilisation (EFSA, 2013a).

### 1.1.4. Methods of analysis in plants

In the framework of the peer review, a hyphenated analytical method based on high performance liquid chromatography HPLC coupled to tandem mass spectrometric detection (MS/MS) was reported and assessed. This method was validated for the analysis of pyriofenone in commodities with high acid content, dry content, high water content and high oil content, with a limit of quantification (LOQ) of 0.01 mg/kg (EFSA, 2013a). A confirmatory method was also provided and the primary method is supported by an independent laboratory validation (ILV).

During the completeness check, the EURLs provided a QuEChERS multiresidue analytical method using liquid chromatography with tandem mass spectrometry (LC–MS/MS), with a LOQ of 0.01 mg/kg for the routine analysis of pyriofenone in the four main plant matrices (EURL, 2018).

### 1.1.5. Stability of residues in plants

In the framework of the peer review, the storage stability of pyriofenone was investigated in commodities with high starch content (wheat grain), in wheat straw and in commodities with high acid content (grapes) (EFSA, 2013a).

The available study demonstrated storage stability for pyriofenone for a period of 12 months when stored at −20°C.

### 1.1.6. Proposed residue definitions

The metabolism of pyriofenone is similar in all crops assessed (fruits and cereals). The metabolism in rotational crops is similar to the metabolism observed in primary crops and the processing of pyriofenone is not expected to modify the nature of residues.

Pyriofenone was shown to be the major component of the radioactive residues in both primary and rotational crops. Therefore, the residue definition for enforcement and risk assessment, limited to pyriofenone only, as proposed in the peer review is still applicable (EFSA, 2013a). This residue definition is restricted to fruits and cereals.

An analytical method for the enforcement of the proposed residue definition at the LOQ of 0.01 mg/kg in all four main plant matrices is available (EFSA, 2013a). According to the EURLs, a QuEChERS method is applicable in routine analysis, which confirms the capabilities of the official laboratories (EURL, 2018).
1.2. Magnitude of residues in plants

1.2.1. Magnitude of residues in primary crops

To assess the magnitude of pyriofenone residues resulting from the reported GAPs, EFSA considered all residue trials reported by the RMS in its evaluation report (Latvia, 2018) as well as the residue trials evaluated in the framework of the peer review (EFSA, 2013a) or in the framework of a previous MRL application (EFSA, 2013b, 2015). 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 under assessment, the available residue trials are sufficient to derive MRL and risk assessment values. A minor consideration is noted for wheat:

- Wheat: the southern GAP on wheat is not supported by GAP-compliant trials but only by 4 overdosed residue trials performed on wheat. Nevertheless, this deficiency is deemed acceptable in this case considering that MRL and risk assessment values for wheat (grain and straw) are derived from the northern GAP (more critical), for which 11 GAP-compliant residue trials are available. It is noted that in wheat grain a no residue situation is anyway expected (based on metabolism study and confirmed by the available trials). For wheat straw, the northern GAP is more critical and the northern trials show higher residue levels than the southern ones. Further residue trials are therefore not required.

1.2.2. Magnitude of residues in rotational crops

There were no studies investigating the magnitude of residues in rotational crops available for this review.

Nevertheless, based on the rotational confined crop study and considering that this was overdosed by a factor of minimum 2.5N (see Section 1.1.2), it can be concluded that pyriofenone residue levels in rotational commodities are not expected to exceed 0.01 mg/kg, provided that pyriofenone is applied in compliance with the GAPs reported in Appendix A.

1.2.3. Magnitude of residues in processed commodities

The effect of industrial processing and/or household preparation was assessed on studies conducted on table and wine grapes (United Kingdom, 2012, EFSA, 2013a,b). An overview of all available processing studies is available in Appendix B.1.2.3. Robust processing factors (fully supported by data) could be derived for raisins, wine and grape juice.

Further processing studies are not required as they are not expected to affect the outcome of the risk assessment.

1.2.4. Proposed MRLs

The available data are considered sufficient to derive MRL proposals as well as risk assessment values for all commodities under evaluation. Tentative MRLs were derived for cereal straw in view of the future need to set MRLs in feed items.

2. Residues in livestock

Pyriofenone is authorised for use on cereals 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.1. The dietary burdens calculated for cattle and sheep were found to exceed the trigger value of 0.1 mg/kg dry matter (DM). Behaviour of residues was therefore assessed in these groups of livestock.
2.1. Nature of residues and methods of analysis in livestock

The metabolism of pyriofenone residues was investigated in a study performed with lactating goats (United Kingdom, 2012). This study was assessed in the framework of the peer review (EFSA, 2013a). Lactating goats were dosed for five consecutive days with pyriofenone at the rate of 0.3 mg/kg bw per day, which largely covers the maximum dietary burdens calculated in this review for ruminant (45N for cattle and 21–25N for sheep). Pyriofenone was radiolabelled in the phenyl and pyridyl rings of the molecule.

The study indicates that transfer of residues to milk and tissues is insignificant. Pyriofenone was intensively excreted and less than 1.5% of the administered radioactivity was recovered in goat matrices. The total radioactivity in muscle, fat and milk was less than 0.005 mg eq./kg. The characterisation of the residues was only investigated in kidney and liver where the total residues were up to 0.05 and 0.16 mg eq./kg, respectively. Most of the radioactivity was characterised as individual fractions reported as L12, L13/K13 or L14/K14 accounting individually for 8–60% TRR (0.01–0.04 mg eq./kg) and identified following various enzymatic or acid/basic hydrolysis, as mixtures of glucuronide conjugates of 2MDPM and 3- and/or 4HDPM.

Based on these data, EFSA concluded that the metabolism of pyriofenone in ruminants was adequately elucidated and proposed to define the residues for ruminant products as pyriofenone for monitoring. For risk assessment, a provisional residue definition was previously proposed as the ‘sum of pyriofenone and its metabolite 2MDPM (free and conjugated)’ (EFSA, 2013a). Considering the dietary burden for ruminants calculated in this review and the total radioactivity found in the study (at a dose rate more than 20N), it should be noted that the total residues levels in ruminant tissues and milk is not expected to exceed 0.008 mg eq./kg in any tissues. Therefore, it is proposed to also simplify the residue definition for risk assessment and to define it as ‘pyriofenone’ only. This residue definition is limited to ruminant products. Should the dietary burden increase in the future, further considerations for the metabolite 2MDPM and its conjugates may be done. Considering the extremely low levels of residues found in fat, the residue definition is not deemed fat soluble.

The storage stability of pyriofenone in animal commodities was not investigated. However, considering that feeding studies are not necessary to derive MRLs and risk assessment values (see Section 2.2), this is not deemed as a data gap in the framework of the present review.

Analytical methods for the enforcement of pyriofenone in all animal tissues are not available. Since MRLs are to be proposed for milk and ruminants tissues (see Section 2.2), this is deemed as a data gap.

2.2. Magnitude of residues in livestock

There are no feeding studies performed with pyriofenone. However, the metabolism study performed on ruminants (at 21N rate compared to the maximum dietary burden calculated for sheep) is sufficient to conclude that residue levels would remain below a default enforcement LOQ of 0.01 mg/kg in ruminants muscle, fat, liver, kidney and milk. Hence, no livestock feeding study is needed and MRLs and risk assessment values for the relevant commodities in different categories of ruminants can be established at the LOQ level. However, in the absence of analytical methods for enforcement of pyriofenone in animal matrices, tentative MRLs were proposed at a default LOQ of 0.01 mg/kg.

It is noted that MRLs for pigs and poultry products are not required because these categories of livestock are not expected to be exposed to significant levels of pyriofenone residues.

3. Consumer risk assessment

Chronic 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.1. Acute exposure calculations were not carried out because an acute reference dose (ARfD) was not deemed necessary for this active substance.

The exposure values calculated were compared with the toxicological reference value for pyriofenone, derived by EFSA (2013a). The highest chronic exposure was calculated for French...
toddler, representing 0.7% of the acceptable daily intake (ADI). These calculations indicate that the uses assessed under this review result in a consumer exposure lower than the toxicological reference values. Therefore, these uses are unlikely to pose a risk to consumer's health.

Conclusions

The metabolism of pyriofenone in plant was investigated in primary and rotational crops. According to the results of the metabolism studies performed on fruit crops and cereals and on rotational crops, the residue definition for enforcement and risk assessment can be proposed as ‘pyriofenone’. This residue definition is also applicable to processed commodities. Fully validated analytical methods are available for the enforcement of the proposed residue definition in the main four plant matrices at the LOQ of 0.01 mg/kg. According to the EURLs, the LOQ of 0.01 mg/kg is achievable by using the QuEChERS method in routine analyses.

Available residue trials data were considered sufficient to derive MRL proposals as well as risk assessment values for all commodities under evaluation.

Pyriofenone is authorised for use on cereals that might be fed to livestock. Livestock dietary burden calculations were therefore performed for different groups of livestock according to OECD guidance. The dietary burdens calculated for cattle and sheep were found to exceed the trigger value of 0.1 mg/kg DM. Behaviour of residues was therefore assessed in these groups of livestock.

The metabolism of pyriofenone residues in livestock was investigated in lactating goats at dose rate covering the maximum dietary burdens calculated in this review. According to the results of these studies, no residues are expected to be transferred in the different tissues and in milk. The residue definition for enforcement and risk assessment in commodities of ruminants was proposed as ‘pyriofenone’ only; this might be extended if future uses would significantly increase the livestock exposure. It was pointed out that no analytical methods for the enforcement of the proposed residue definition were available.

The above-mentioned metabolism study was sufficient to conclude the MRLs and risk assessment values in milk and all tissues of ruminants could be established at the LOQ level. However, in the absence of analytical methods for enforcement of pyriofenone in animal matrices, tentative MRLs were proposed at an indicative default LOQ of 0.01 mg/kg.

Chronic 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 represented 0.7% of the ADI (FR toddlers). Acute exposure calculations were not carried out because an ARfD was not deemed necessary for this active substance.

Recommendations

MRL recommendations were derived in compliance with the decision tree reported in Appendix E of the reasoned opinion (see Table 2). All MRL values listed as ‘Recommended’ in the table are sufficiently supported by data and are therefore proposed for inclusion in Annex II to the Regulation. The remaining MRL values listed in the table are not recommended for inclusion in Annex II because they require further consideration by risk managers (see Table 2 footnotes for details). In particular, tentative MRLs proposed for livestock commodities need to be supported by an analytical method for enforcement; the following data gap is identified:

- A fully validated analytical method for enforcement of pyriofenone in livestock commodities.

If this data gap is not addressed in the future, risk managers will not be able to enforce pyriofenone residues in animal commodities.

Table 2: Summary table

| Code number | Commodity     | Existing EU MRL (mg/kg) | Outcome of the review | Comment            |
|-------------|---------------|-------------------------|-----------------------|-------------------|
|             | Enforcement residue definition (existing): pyriofenone |                         |                       |                   |
| 151010      | Table grapes  | 0.9                     | Recommended(0)        |                   |
| 151020      | Wine grapes   | 0.2                     | Recommended(0)        |                   |
| 500010      | Barley grain  | 0.03                    | Recommended(0)        |                   |
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### Table

| Code number | Commodity        | Existing EU MRL (mg/kg) | Outcome of the review | Comment                                      |
|-------------|------------------|-------------------------|-----------------------|----------------------------------------------|
| 500050      | Oat grain        | 0.03                    | 0.03                  | Recommended<sup>(a)</sup>                    |
| 500070      | Rye grain        | 0.01*                   | 0.01*                 | Recommended<sup>(a)</sup>                    |
| 500090      | Wheat grain      | 0.01*                   | 0.01*                 | Recommended<sup>(a)</sup>                    |
| 1012010     | Bovine muscle    | –                       | 0.01*                 | Further consideration needed<sup>(b)</sup>   |
| 1012020     | Bovine fat tissue| –                       | 0.01*                 | Further consideration needed<sup>(b)</sup>   |
| 1012030     | Bovine liver     | –                       | 0.01*                 | Further consideration needed<sup>(b)</sup>   |
| 1012040     | Bovine kidney    | –                       | 0.01*                 | Further consideration needed<sup>(b)</sup>   |
| 1013010     | Sheep muscle     | –                       | 0.01*                 | Further consideration needed<sup>(b)</sup>   |
| 1013020     | Sheep fat tissue | –                       | 0.01*                 | Further consideration needed<sup>(b)</sup>   |
| 1013030     | Sheep liver      | –                       | 0.01*                 | Further consideration needed<sup>(b)</sup>   |
| 1013040     | Sheep kidney     | –                       | 0.01*                 | Further consideration needed<sup>(b)</sup>   |
| 1014010     | Goat muscle      | –                       | 0.01*                 | Further consideration needed<sup>(b)</sup>   |
| 1014020     | Goat fat tissue  | –                       | 0.01*                 | Further consideration needed<sup>(b)</sup>   |
| 1014030     | Goat liver       | –                       | 0.01*                 | Further consideration needed<sup>(b)</sup>   |
| 1014040     | Goat kidney      | –                       | 0.01*                 | Further consideration needed<sup>(b)</sup>   |
| 1015010     | Equine muscle    | –                       | 0.01*                 | Further consideration needed<sup>(b)</sup>   |
| 1015020     | Equine fat tissue| –                       | 0.01*                 | Further consideration needed<sup>(b)</sup>   |
| 1015030     | Equine liver     | –                       | 0.01*                 | Further consideration needed<sup>(b)</sup>   |
| 1015040     | Equine kidney    | –                       | 0.01*                 | Further consideration needed<sup>(b)</sup>   |
| 1020010     | Cattle milk      | –                       | 0.01*                 | Further consideration needed<sup>(b)</sup>   |
| 1020020     | Sheep milk       | –                       | 0.01*                 | Further consideration needed<sup>(b)</sup>   |
| 1020030     | Goat milk        | –                       | 0.01*                 | Further consideration needed<sup>(b)</sup>   |
| 1020040     | Horse milk       | –                       | 0.01*                 | Further consideration needed<sup>(b)</sup>   |
| –           | Other commodities of plant and/or animal origin | See Reg. 2016/1 | – | Further consideration needed<sup>(c)</sup> |

MRL: maximum residue level.

*: 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 is identified; no CXL is available (combination H-I in Appendix E).

(b): Tentative MRL is derived from a GAP evaluated at EU level, which is not fully supported by data but for which no risk to consumers was identified; no CXL is available (combination F-I in Appendix E).

(c): 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**

- **a.i.** active ingredient
- **a.s.** active substance
- **ADI** acceptable daily intake
- **ARFD** acute reference dose
- **BBCH** growth stages of mono- and dicotyledonous plants
- **bw** body weight
- **CXL** codex maximum residue limit
- **DALA** days after last application
- **DAR** draft assessment report
- **DAT** days after treatment
- **DB** dietary burden
- **DM** dry matter
- **DT<sub>90</sub>** period required for 90% dissipation (define method of estimation)
- **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
| Acronym | Definition |
|---------|------------|
| GAP     | Good Agricultural Practice |
| HPLC    | high performance liquid chromatography |
| HR      | highest residue |
| IEDI    | international estimated daily intake |
| ILV     | independent laboratory validation |
| InChIKey| International Chemical Identifier Key |
| ISO     | International Organisation for Standardization |
| IUPAC   | International Union of Pure and Applied Chemistry |
| LC–MS/MS| liquid chromatography with tandem mass spectrometry |
| LOQ     | limit of quantification |
| Mo      | monitoring |
| MRL     | maximum residue level |
| MS      | Member States |
| MS/MS   | tandem mass spectrometry detector |
| MW      | molecular weight |
| NEU     | northern European Union |
| OECD    | Organisation for Economic Co-operation and Development |
| PBI     | plant-back interval |
| PECsoil | Predicted Environmental Concentration in soil |
| PF      | processing factor |
| PHI     | pre-harvest interval |
| PRIMo   | (EFSA) Pesticide Residues Intake Model |
| PROFile| (EFSA) Pesticide Residues Overview File |
| QuEChERS| Quick, Easy, Cheap, Effective, Rugged, and Safe (analytical method) |
| RA      | risk assessment |
| RD      | residue definition |
| RAC     | raw agricultural commodity |
| 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 |
| TMDI    | theoretical maximum daily intake |
| TRR     | total radioactive residue |
| WHO     | World Health Organization |
### Appendix A – Summary of authorised uses considered for the review of MRLs

#### A.1. Authorised outdoor uses in northern 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) | Remarks |
|-----------------------|---------------|-------------|-----------------------------------|-------------|------------|--------------------------------|------------|---------|
| Table grapes           | HU, AT        | F           | Grape powdery mildew *(Erysiphe necator)* | SC 300 g/L | Foliar treatment – spraying | 14–85 | 1–3 | 10 | – | – | 90 g a.i./ha | 28 | In case of danger of infection and/or after warning service appeal |
| Wine grapes            | AT, HU        | F           | – | SC 300 g/L | Foliar treatment – spraying | 1–3 | 10 | – | – | 90 g a.i./ha | 28 | In case of danger of infection and/or after warning service appeal |
| Barley                 | LT, FI, HU, EE, DE, SE, PL | F | Powdery mildew | SC 180 g/L | Foliar treatment – spraying | 21–50 | 1–2 | 14 | – | – | 90 g a.i./ha | n.a. | – |
| Oat                    | LT, FI, HU, EE, SE | F | Powdery mildew | SC 180 g/L | Foliar treatment – spraying | 21–50 | 1–2 | 14 | – | – | 90 g a.i./ha | n.a. | – |
| Rye                    | LT, FI, EE, HU, SE | F | Powdery mildew | SC 180 g/L | Foliar treatment – spraying | 21–65 | 1–2 | 14 | – | – | 90 g a.i./ha | n.a. | – |
| Wheat                  | LT, BE, NL, FI, UK, EE, PL, HU, DE, SE | F | Powdery mildew | SC 180 g/L | Foliar treatment – spraying | 21–65 | 1–2 | 14 | – | – | 90 g a.i./ha | n.a. | – |

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

(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.
## A.2. 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 |
|-----------------------|---------------|----------------------|-----------------------------------|-------------|-----------------|--------------------------------|----------------|---------|
| Table grapes          | PT            | F                    | *Erysiphe necator*                | SC 300 g/L | Foliar treatment – general (see also comment field) | 53–79 1–3 12 | – – | 90 g a.i./ha | 14 | Spraying |
| Wine grapes           | IT            | F                    | Powdery mildew (*Erysiphe necator*) | SC 300 g/L | Foliar treatment – general (see also comment field) | 11–85 1–3 10 | – – | 90 g a.i./ha | 28 | Tractor mounted/trailed vineyard air blast sprayer is used. |
| Wheat                 | FR            | F                    | Powdery mildew (*Blumeria graminis*) | SC 180 g/L | Foliar treatment – spraying | 65 1 – – | – – | 90 g a.i./ha | n.a. | BBCH 30–31 or BBCH 49–65 |

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

\(^{(a)}\): 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(s)       | Application(s)                                           | Sampling (DAT) | Comment/Source                                                                 |
|----------------------------------|----------------------|---------------|----------------------------------------------------------|----------------|-------------------------------------------------------------------------------|
| Fruit crops                      |                      | Grape         | Foliar: 3 × 100 g a.s./ha (at BBCH 77, 79 and 85)       | 29             | Phenyl-UL-^{14}C and pyridyl-UL-^{14}C (United Kingdom, 2012 assessed in EFSA, 2013a) |
|                                  |                      | Tomato        | Foliar: 3 × 100 g a.s./ha (interval 12 days)            | 7              | Phenyl-UL-^{14}C and pyridyl-UL-^{14}C (United Kingdom, 2012 assessed in EFSA, 2013a) |
|                                  | Cereals/grass        | Wheat         | Foliar: 2 × 100 g a.s./ha (at BBCH 31 and 71)           | 7 DAT<sub>1</sub> (forage) 6 DAT<sub>2</sub> (hay) 40 DALA (grain and straw) | Phenyl-UL-^{14}C and pyridyl-UL-^{14}C (United Kingdom, 2012 assessed in EFSA, 2013a) |

| Rotational crops (available studies) | Crop groups          | Crop(s)       | Application(s)                                           | PBI (DAT)      | Comment/Source                                                                 |
|-------------------------------------|----------------------|---------------|----------------------------------------------------------|----------------|-------------------------------------------------------------------------------|
| Root/tuber crops                    | Carrot               | Bare soil, 284 g a.s./ha | 31, 122, 364                                           | Phenyl-UL-^{14}C (United Kingdom, 2012 assessed in EFSA, 2013a) |
| Leafy crops                        | Lettuce              | Bare soil, 284 g a.s./ha | 31, 122, 364                                           | Phenyl-UL-^{14}C (United Kingdom, 2012 assessed in EFSA, 2013a) |
| Cereal (small grain)                | Wheat                | Bare soil, 284 g a.s./ha | 31, 122, 364                                           | Phenyl-UL-^{14}C (United Kingdom, 2012 assessed in EFSA, 2013a) |

| Processed commodities (hydrolysis study) | Conditions                       | Stable? | Comment/Source                                                                 |
|------------------------------------------|----------------------------------|---------|-------------------------------------------------------------------------------|
| Pasteurisation (20 min, 90°C, pH 4)      | Yes                              |         | Phenyl-UL-^{14}C and pyridyl-UL-^{14}C (United Kingdom, 2012 assessed in EFSA, 2013a) |
| Baking, brewing and boiling (60 min, 100°C, pH 5) | Yes                              |         | Phenyl-UL-^{14}C and pyridyl-UL-^{14}C (United Kingdom, 2012 assessed in EFSA, 2013a) |
| Sterilisation (20 min, 120°C, pH 6)      | Yes                              |         | Phenyl-UL-^{14}C and pyridyl-UL-^{14}C (United Kingdom, 2012 assessed in EFSA, 2013a) |
Can a general residue definition be proposed for primary crops?

|   | No | Limited to fruits and cereals |
|---|----|-------------------------------|

Rotational crop and primary crop metabolism similar?

|   | Yes | A general decrease in pyriofenone and metabolite levels was noted |
|---|-----|---------------------------------------------------------------|

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

|   | Yes | – |
|---|-----|---|

Plant residue definition for monitoring (RD-Mo)

|   | Fruits and cereals and processed commodities: pyriofenone |
|---|----------------------------------------------------------|

Plant residue definition for risk assessment (RD-RA)

|   | Fruits and cereals and processed commodities: pyriofenone |
|---|----------------------------------------------------------|

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

Matrices with high acid content, dry content, high water content, and high oil content matrices:
- HPLC–MS/MS, LOQ 0.01 mg/kg
- Validated on grape, wheat grain, wheat straw, cabbage and oilseed rape
- Confirmatory method available
- ILV available

(United Kingdom, 2012 assessed in EFSA, 2013a)

A QuEChERS method using LC–MS/MS applicable on the four main plant matrices was also provided by EURyL (2018), confirming the capability of official laboratories

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### B.1.1.2. Stability of residues in plants

| Plant products (available studies) | Category | Commodity | T (°C) | Stability period | Compounds covered | Comment/Source |
|-----------------------------------|----------|-----------|--------|-----------------|-------------------|----------------|
|                                    | High starch content | Wheat grain | −20    | 12 Months       | Pyriofenone       | United Kingdom 2012 assessed in EFSA, 2013a |
|                                    | High acid content | Grapes     | −20    | 12 Months       | Pyriofenone       | United Kingdom, 2012 assessed in EFSA, 2013a |
|                                    | Others     | Wheat straw| −20    | 12 Months       | Pyriofenone       | United Kingdom, 2012 assessed in EFSA, 2013a |

a.s.: active substance; DAT: days after treatment; DALA: days after last treatment; PBI: plant-back interval; HPLC–MS/MS: high-performance liquid chromatography with tandem mass spectrometry; LC–MS/MS: liquid chromatography with tandem mass spectrometry; LOQ: limit of quantification; ILV: independent laboratory validation; QuEChERS: Quick, Easy, Cheap, Effective, Rugged, and Safe; LC–MS/MS: high-performance liquid chromatography with tandem mass spectrometry.
### 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) |
|-------------------|------------------|------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------|---------------|-----------------|
| Table grapes      | NEU               | 0.05; 0.05; 0.06; 0.07; 0.08; 0.10; 0.10; 0.14                                                                 | Trials on wine grapes compliant with GAP (United Kingdom, 2012 assessed in EFSA, 2013b). Extrapolation to table grapes is applicable MRL\_OECD = 0.24                                                                                                                                                                                                 | 0.3                    | 0.14          | 0.08            |
|                   | SEU               | 0.03; 0.06; 0.06; 0.09; 0.1; 0.15; 0.31; 0.54                                                                 | Trials compliant with GAP (EFSA, 2015) MRL\_OECD = 0.86                                                                                                                                                                                                                                                                                       |                        |               |                 |
| Wine grapes       | NEU               | 0.05; 0.05; 0.06; 0.07; 0.08; 0.10; 0.10; 0.14                                                                 | Trials on wine grapes compliant with GAP (United Kingdom, 2012 assessed in EFSA, 2013b) MRL\_OECD = 0.24                                                                                                                                                                                                                                     | 0.3                    | 0.14          | 0.08            |
|                   | SEU               | 0.02; 0.03; 0.03; 0.04; 0.06; 0.08; 0.10; 0.11; 0.11                                                       | Trials compliant with GAP (United Kingdom, 2012 assessed in EFSA, 2013b) MRL\_OECD = 0.21                                                                                                                                                                                                                                                    | 0.3                    | 0.11          | 0.06            |
| Barley and oat    | NEU               | < 0.01; < 0.01; < 0.01; < 0.01; < 0.01; < 0.01; < 0.01; < 0.01; < 0.01; < 0.01; 0.01; 0.01; 0.02               | Trials performed on barley compliant with GAP (EFSA, 2013b). Extrapolation to oats is applicable MRL\_OECD = 0.023                                                                                                                                                                                                                              | 0.03                   | 0.02          | < 0.01          |
| grain             |                  |                                                                                                               |                                                                                                                                                                                                                                                                                                                                                   |                        |               |                 |
| Barley and oat    | NEU               | 0.01; 0.02; 0.02; 0.05; 0.05; 0.07; 0.12; 0.12; 0.18; 0.25; 0.48                                               | Trials on barley compliant with GAP (EFSA, 2013b). Extrapolation to oats is applicable MRL\_OECD = 0.68                                                                                                                                                                                                                                        | 0.7 (tentative)(d)     | 0.48          | 0.07            |
| straw             |                  |                                                                                                               |                                                                                                                                                                                                                                                                                                                                                   |                        |               |                 |
| Wheat and rye     | NEU               | 11 × < 0.01                                                                                                    | Trials performed on wheat compliant with GAP (EFSA, 2013b). Extrapolation to rye is applicable                                                                                                                                                                                                                                                | 0.01*                  | < 0.01        | < 0.01          |
| grain             | SEU               | 4 × < 0.01                                                                                                     | Overdosed trials performed on wheat with 2 applications instead of 1 (EFSA, 2013b). Not authorised on rye in southern zone                                                                                                                                                                                                                     | 0.01*                  | < 0.01        | < 0.01          |
| Wheat and rye     | NEU               | < 0.01; 0.02; 0.04; 0.05; 0.07; 0.07; 0.08; 0.12; 0.29; 0.33; 0.66                                             | Trials performed on wheat compliant with GAP (EFSA, 2013b). Extrapolation to rye is applicable MRL\_OECD = 0.95                                                                                                                                                                                                                              | 1                      | 0.66          | 0.07            |
| straw             | SEU               | 0.04; 0.08; 0.10; 0.15                                                                                          | Overdosed trials performed on wheat with 2 applications instead of 1 (EFSA, 2013b). Not authorised on rye in southern zone MRL\_OECD = 0.28                                                                                                                                                                                                      | 0.3 (tentative)(d)     | 0.15          | 0.09            |

GAP: Good Agricultural Practice; OECD: Organisation for Economic Co-operation and Development; MRL: maximum residue level; Mo: residue levels expressed according to the monitoring residue definition; RA: residue levels expressed according to risk assessment residue definition.

*: Indicates that the MRL is proposed at the limit of quantification.
Review of the existing MRLs for pyriofenone

(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.
(d): Tentative MRL is derived for feed items.

B.1.2.2. Residues in rotational crops

Residues in rotational and succeeding crops expected based on confined rotational crop study?

No

Confined rotational crops study is overdosed by a factor of 2.5–10N (based on soil concentration compared to Predicted Environmental Concentration in soil (PECsoil)). TRR was below 0.01 mg eq/kg in wheat grain and lettuce and below 0.02 mg/kg in carrots. TRR ranges between 0.06 and 0.23 mg eq/kg in wheat straw (parent compound up to 0.05 mg/kg).

Therefore, parent compound is expected to remain < LOQ in all crops when pyriofenone is applied in compliance with the authorized GAPs

Residues in rotational and succeeding crops expected based on field rotational crop study?

Not triggered

–

TRR: total radioactive residue; eq: residue expressed as a.s. equivalent; LOQ: limit of quantification; GAP: Good Agricultural Practice.

B.1.2.3. Processing factors

| Processed commodity | Number of valid studies | Processing Factor (PF) | Comment/Source |
|---------------------|-------------------------|------------------------|----------------|
|                     |                         | Individual values      | Median PF      |                  |
| Table grapes, raisin| 6                       | 1.50; 1.68; 2.43; 2.80; 3.00; 3.20; 3.78; 5.00 | 2.90 | United Kingdom, 2012, assessed in EFSA, 2013a,b |
| Wine grapes, wine   |                          | Red wine: 0.04; 0.08/White wine: 0.10; 0.15 | 0.09 | PF derived from 2 trials on red wine and 2 trials on white wine (United Kingdom, 2012, assessed in EFSA, 2013a,b). See also final addendum to DAR (United Kingdom, 2013). |
| (red and white)     | 4                       |                        |                |                  |
| Wine grapes, juice  | 4                       | 0.04; 0.07; 0.08; 0.10 | 0.08 | United Kingdom, 2012, assessed in EFSA, 2013a,b |

PF: Processing factor (\(\text{Processing factor} = \frac{\text{Residue level in processed commodity}}{\text{Residue level in raw commodity}}\)).

(a): Studies with residues in the RAC at or close to the LOQ were disregarded (unless concentration may occur).
### B.2. Residues in livestock

| Relevant groups (subgroups) | Dietary burden expressed in | Most critical subgroup | Most critical commodity (a) | Trigger exceeded (Y/N) | Comments |
|---------------------------|-----------------------------|------------------------|---------------------------|------------------------|----------|
|                           | mg/kg bw per day            | mg/kg DM               |                           |                        |          |
|                           | Median    | Maximum     | Median | Maximum |                      |          |
| Cattle (all)              | 0.0013    | 0.0066      | 0.03   | 0.17    | Cattle (dairy)        | Barley, straw | Y        |          |
| Cattle (dairy only)       | 0.0013    | 0.0066      | 0.03   | 0.17    | Cattle (dairy)        | Barley, straw | Y        |          |
| Sheep (all)               | 0.0024    | 0.0141      | 0.06   | 0.34    | Sheep (lamb)          | Barley, straw | Y        |          |
| Sheep (ewe only)          | 0.0026    | 0.0118      | 0.08   | 0.36    | Sheep (ram/ewe)       | Barley, straw | Y        |          |
| Swine (all)               | 0.0004    | 0.0004      | 0.01   | 0.01    | Swine (finishing)     | Barley, grain  | N        |          |
| Poultry (all)             | 0.0016    | 0.0060      | 0.02   | 0.09    | Poultry (layer)       | Wheat, straw  | N        |          |
| Poultry (layer only)      | 0.0016    | 0.0060      | 0.02   | 0.09    | Poultry (layer)       | Wheat, straw  | N        |          |
| Fish                      | --        | --          | --     | --      | --                    | --          | --       |          |

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              | –                       | –               | No study available and not required                                            |
|                               | Lactating ruminants     | 0.3                     | 5               | Study performed on lactating goat using phenyl-UL-14C and pyridyl-UL-14C (United Kingdom, 2012 assessed in EFSA, 2013a) |

Time needed to reach a plateau concentration in milk and eggs (days)

- Milk: 3 days
- Eggs: – Not investigated

Metabolism in rat and ruminant similar

Can a general residue definition be proposed for animals?

- No
- Only investigated in ruminants

Animal residue definition for monitoring (RD-Mo)

- Ruminants tissues and milk: Pyriofenone

Animal residue definition for risk assessment (RD-RA)

- Ruminants tissues and milk: Pyriofenone (a)

Fat soluble residues

- No
- Very low TRR in fat (< 0.01% TRR)

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

bw: body weight; TRR: total radioactive residue.

(a): It is noted that the RDRA was proposed as ‘sum of pyriofenone and its metabolite 2MDPM (free and conjugated)’ during the peer review (EFSA, 2013a); however, such a complex RD is not needed considering the total residue levels expected in livestock commodities are < 0.01 mg/kg.
B.2.1.2. Stability of residues in livestock

| Animal products (available studies) | Animal | Commodity | T (°C) | Stability period | Compounds covered | Comment/ Source |
|-------------------------------------|--------|-----------|--------|-----------------|-------------------|-----------------|
|                                     | --     | --        | --     | --              | --                | --              |
|                                     | 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

| Animal commodity | Residues at the closest feeding level (mg/kg) | Estimated value at 1N | MRL proposal (mg/kg) |
|------------------|---------------------------------------------|-----------------------|----------------------|
|                  | Mean | Highest | \( \text{STMR}_{\text{Mo}}^{(a)} \) (mg/kg) | \( \text{HR}_{\text{Mo}}^{(b)} \) (mg/kg) |
| **Cattle (all)** |      |         |                                     |                      |
| Muscle           | n.a. | < 0.005 | < 0.01 | < 0.01 | 0.01* (tentative)\(^{(c)}\) |
| Fat              | n.a. | < 0.005 | < 0.01 | < 0.01 | 0.01* (tentative)\(^{(c)}\) |
| Liver            | n.a. | 0.16    | < 0.01 | < 0.01 | 0.01* (tentative)\(^{(c)}\) |
| Kidney           | n.a. | 0.05    | < 0.01 | < 0.01 | 0.01* (tentative)\(^{(c)}\) |
| **Cattle (dairy only)** |      |         |                                     |                      |
| Milk             | n.a. | < 0.005 | < 0.01 | < 0.01 | 0.01* (tentative)\(^{(c)}\) |
| **Sheep (all)**  |      |         |                                     |                      |
| Muscle           | n.a. | < 0.005 | < 0.01 | < 0.01 | 0.01* (tentative)\(^{(c)}\) |
| Fat              | n.a. | < 0.005 | < 0.01 | < 0.01 | 0.01* (tentative)\(^{(c)}\) |
| Liver            | n.a. | 0.16    | < 0.01 | < 0.01 | 0.01* (tentative)\(^{(c)}\) |
| Kidney           | n.a. | 0.05    | < 0.01 | < 0.01 | 0.01* (tentative)\(^{(c)}\) |
| **Sheep (ewe only)** |      |         |                                     |                      |
| Milk             | n.a. | < 0.005 | < 0.01 | < 0.01 | 0.01* (tentative)\(^{(c)}\) |
| **Swine (all)**  |      |         |                                     |                      |
| Muscle           |      |         |                                     |                      |
| Fat              |      |         |                                     |                      |
| Liver            |      |         |                                     |                      |
| Kidney           |      |         |                                     |                      |
| **Poultry (all)** |      |         |                                     |                      |
| Muscle           |      |         |                                     |                      |
| Fat              |      |         |                                     |                      |
| Liver            |      |         |                                     |                      |
| **Poultry (layer only)** |      |         |                                     |                      |
| Eggs             |      |         |                                     |                      |

MRL: maximum residue level; STMR: supervised trials median residue; HR: highest residue; bw: body weight; Mo: monitoring; n.a.: not applicable.

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

(a): Median residues expressed according to the residue definition for monitoring, recalculated at the 1N rate for the median dietary burden.

(b): Highest residues expressed according to the residue definition for monitoring, recalculated at the 1N rate for the maximum dietary burden.

(c): Results of the metabolism study performed with lactating goat were sufficient to conclude on the residue levels (based on TRR levels) expected in ruminant tissues and milk.

(d): MRL is tentative because an analytical method for enforcement in livestock commodities is missing (data gap).
B.3. Consumer risk assessment

Acute exposure not relevant since no ARfD has been considered necessary.

| ADI (mg/kg bw per day) | 0.07 |
|------------------------|------|
| 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) | 0.7% ADI (FR toddler) |
| 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 contributions of commodities where no GAP was reported in the framework of the MRL review were not included in the calculation.

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 |

B.4. Proposed MRLs

| Code number | Commodity       | Existing EU MRL (mg/kg) | MRL (mg/kg) | Comment                  |
|-------------|-----------------|-------------------------|-------------|--------------------------|
| 151010      | Table grapes    | 0.9                     | 0.9         | Recommended(a)           |
| 151020      | Wine grapes     | 0.2                     | 0.3         | Recommended(a)           |
| 500010      | Barley grain    | 0.03                    | 0.03        | Recommended(a)           |
| 500050      | Oat grain       | 0.03                    | 0.03        | Recommended(a)           |
| 500070      | Rye grain       | 0.01*                   | 0.01*       | Recommended(a)           |
| 500090      | Wheat grain     | 0.01*                   | 0.01*       | Recommended(a)           |
| 1012010     | Bovine muscle   | –                       | 0.01*       | Further consideration needed(b) |
| 1012020     | Bovine fat tissue | –                      | 0.01*       | Further consideration needed(b) |
| 1012030     | Bovine liver    | –                       | 0.01*       | Further consideration needed(b) |
| 1012040     | Bovine kidney   | –                       | 0.01*       | Further consideration needed(b) |
| 1013010     | Sheep muscle    | –                       | 0.01*       | Further consideration needed(b) |
| 1013020     | Sheep fat tissue | –                     | 0.01*       | Further consideration needed(b) |
| 1013030     | Sheep liver     | –                       | 0.01*       | Further consideration needed(b) |
| 1013040     | Sheep kidney    | –                       | 0.01*       | Further consideration needed(b) |
| 1014010     | Goat muscle     | –                       | 0.01*       | Further consideration needed(b) |
| 1014020     | Goat fat tissue | –                       | 0.01*       | Further consideration needed(b) |
| 1014030     | Goat liver      | –                       | 0.01*       | Further consideration needed(b) |
| 1014040     | Goat kidney     | –                       | 0.01*       | Further consideration needed(b) |
| Code number | Commodity               | Existing EU MRL (mg/kg) | Outcome of the review      |
|------------|-------------------------|-------------------------|---------------------------|
| 1015010    | Equine muscle           | –                       | 0.01* Further consideration needed(b) |
| 1015020    | Equine fat tissue       | –                       | 0.01* Further consideration needed(b) |
| 1015030    | Equine liver            | –                       | 0.01* Further consideration needed(b) |
| 1015040    | Equine kidney           | –                       | 0.01* Further consideration needed(b) |
| 1020010    | Cattle milk             | –                       | 0.01* Further consideration needed(b) |
| 1020020    | Sheep milk              | –                       | 0.01* Further consideration needed(b) |
| 1020030    | Goat milk               | –                       | 0.01* Further consideration needed(b) |
| 1020040    | Horse milk              | –                       | 0.01* Further consideration needed(b) |
| –          | Other commodities of plant and/or animal origin | See Reg. 2016/1 | – Further consideration needed(c) |

MRL: maximum residue level.
*: 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 is identified; no CXL is available (combination H-I in Appendix E).
(b): Tentative MRL is derived from a GAP evaluated at EU level, which is not fully supported by data but for which no risk to consumers was identified; no CXL is available (combination F-I in Appendix E).
(c): 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)

**PRIMo(EU)**

| Pyriofenone |
|-------------|
| Toxicological end points |
| ADI (mg/kg bw per day): | 0.07 |
| ARD (mg/kg bw): | n.n. |
| Source of ADI: | EFSA |
| Source of ARD: | EFSA |
| Year of evaluation: | 2013 |

### Chronic risk assessment – refined calculations

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

| No of diets exceeding ADI: | 1 |

| Highest calculated TMDI values in % of ADI |
|-------------------------------------------|

| MS Diet | Commodity/group of commodities |
|---------|--------------------------------|
| FR toddler | 0.6 Milk and cream |
| NL child | 0.4 Milk and cream |
| UK infant | 0.6 Milk and cream |
| FR all population | 0.4 Wine grapes |
| DE child | 0.2 Milk and cream |
| WHO Cluster diet B | 0.2 Wine grapes |
| FR infant | 0.4 Milk and cream |
| UK Toddler | 0.3 Milk and cream |
| PT General population | 0.3 Wine grapes |
| DK child | 0.2 Milk and cream |
| WHO cluster diet E | 0.2 Wine grapes |
| DK adult | 0.1 Wine grapes |
| IE adult | 0.2 Milk and cream |
| ES child | 0.2 Milk and cream |
| WHO cluster diet D | 0.1 Milk and cream |
| NL general | 0.1 Milk and cream |
| SE general population 90th percentile | 0.2 Milk and cream |
| WHO Cluster diet F | 0.1 Wine grapes |
| UK Adult | 0.1 Wine grapes |
| WHO regional European diet | 0.1 Milk and cream |
| ES adult | 0.1 Milk and cream |
| UK vegetarian | 0.1 Wine grapes |
| FI adult | 0.1 Milk and cream |
| IT kids/toddler | 0.1 Milk and cream |
| LT adult | 0.1 Milk and cream |
| IT adult | 0.1 Milk and cream |
| PL general population | 0.0 Table grapes |

| 2nd contributor to MS diet (in % of ADI) |
|-----------------------------------------|
| Commodity/group of commodities |
| FR toddler | 0.1 Table grapes |
| NL child | 0.0 Wheat |
| UK infant | 0.0 Milk and cream |
| FR all population | 0.0 Wheat |
| DE child | 0.0 Milk and cream |
| WHO Cluster diet B | 0.1 Wheat |
| FR infant | 0.0 Wheat |
| UK Toddler | 0.1 Wheat |
| PT General population | 0.1 Wheat |
| DK child | 0.1 Wheat |
| WHO cluster diet E | 0.1 Wheat |
| DK adult | 0.1 Milk and cream |
| IE adult | 0.0 Milk and cream |
| ES child | 0.1 Wheat |
| WHO cluster diet D | 0.1 Milk and cream |
| NL general | 0.0 Wine grapes |
| SE general population 90th percentile | 0.0 Wheat |
| WHO Cluster diet F | 0.1 Milk and cream |
| UK Adult | 0.0 Milk and cream |
| WHO regional European diet | 0.0 Wheat |
| ES adult | 0.0 Wine grapes |
| UK vegetarian | 0.0 Wheat |
| FI adult | 0.0 Table grapes |
| IT kids/toddler | 0.0 Table grapes |
| LT adult | 0.0 Rye |
| IT adult | 0.0 Table grapes |
| PL general population | 0.0 Table grapes |

| 3rd contributor to MS diet (in % of ADI) |
|----------------------------------------|
| Commodity/group of commodities |
| FR toddler | 0.1 Wheat |
| NL child | 0.0 Milk and cream |
| UK infant | 0.0 Milk and cream |
| FR all population | 0.0 Wheat |
| DE child | 0.0 Milk and cream |
| WHO Cluster diet B | 0.1 Wheat |
| FR infant | 0.0 Wheat |
| UK Toddler | 0.1 Wheat |
| PT General population | 0.1 Wheat |
| DK child | 0.1 Wheat |
| WHO cluster diet E | 0.1 Wheat |
| DK adult | 0.1 Milk and cream |
| IE adult | 0.0 Milk and cream |
| ES child | 0.1 Wheat |
| WHO cluster diet D | 0.1 Milk and cream |
| NL general | 0.0 Wine grapes |
| SE general population 90th percentile | 0.0 Wheat |
| WHO Cluster diet F | 0.1 Milk and cream |
| UK Adult | 0.0 Milk and cream |
| WHO regional European diet | 0.0 Wheat |
| ES adult | 0.0 Wine grapes |
| UK vegetarian | 0.0 Wheat |
| FI adult | 0.0 Table grapes |
| IT kids/toddler | 0.0 Table grapes |
| LT adult | 0.0 Rye |
| IT adult | 0.0 Table grapes |
| PL general population | 0.0 Table grapes |

| pTMRLs at LOD (in % of ADI) |
|----------------------------|

### Conclusion:

The estimated Theoretical Maximum Daily Intakes (TMDI), based on pTMRLs were below the ADI. A long-term intake of residues of pyriofenone is unlikely to present a public health concern.
Acute risk assessment/children – refined calculations

| IESTI 1 | No of commodities for which ARfD/ADI is exceeded (ESTI 1): | --- | No of commodities for which ARfD/ADI is exceeded (ESTI 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) | --- |

Acute risk assessment/adults/general population – refined calculations

| IESTI 1 | No of commodities for which ARfD/ADI is exceeded (ESTI 1): | --- | No of commodities for which ARfD/ADI is exceeded (ESTI 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) | --- |

---

No of commodities for which ARfD/ADI is exceeded (IESTI 1):

No of commodities for which ARfD/ADI is exceeded (IESTI 2):

Threshold MRL is the calculated residue level which would lead to an exposure equivalent to 100% of 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.

Conclusion:

As no ARfD was considered necessary, it is concluded that the short-term intake of pyriofenone residues is unlikely to present a public health concern.
### 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                |
| Risk assessment residue |                       |                        |                      |                        |
| definition: pyriofenone |                       |                        |                      |                        |
| Barley and oat, grain   | 0.01*                 | STMR                   | 0.01*               | STMR                   |
| Wheat and rye, grain    | 0.01*                 | STMR                   | 0.01*               | STMR                   |
| Brewer’s grain, dried   | 0.03                  | STMR × default PF (3.3)(a) | 0.03               | STMR × default PF (3.3)(a) |
| Wheat, distiller’s grain (dry) | 0.01* | STMR(b) | 0.01*               | STMR(b)                |
| Wheat gluten, meal      | 0.01*                 | STMR(b)                | 0.01*               | STMR(b)                |
| Wheat, milled by-pdts   | 0.01*                 | STMR(b)                | 0.01*               | STMR(b)                |
| Barley and oat, straw   | 0.07                  | STMR                   | 0.48                | HR                     |
| Wheat and rye, straw    | 0.07                  | STMR                   | 0.66                | HR                     |

STMR: supervised trials median residue; PF: processing factor.
*: Indicates that the input value is proposed at the limit of quantification.
(a): In the absence of processing factors supported by data, the default processing factor of 3.3 was included in the calculation to consider the potential concentration of residues in this commodity.
(b): For processed commodities of wheat no default processing factor was applied because residues are expected to be below the LOQ in wheat grain. Concentration of residues in these commodities is therefore not expected.

#### D.2. Consumer risk assessment

| Commodity               | Chronic risk assessment | Input value (mg/kg) | Comment                |
|-------------------------|-------------------------|---------------------|------------------------|
| Risk assessment residue | pyriofenone             |                      |                        |
| Table grapes            | 0.10                    | STMR                |                        |
| Wine grapes             | 0.08                    | STMR                |                        |
| Barley grain            | 0.01*                   | STMR                |                        |
| Oat grain               | 0.01*                   | STMR                |                        |
| Rye grain               | 0.01*                   | STMR                |                        |
| Wheat grain             | 0.01*                   | STMR                |                        |
| Bovine and equine meat  | 0.01*                   | STMR muscle (tentative) |                       |
| Bovine and equine fat   | 0.01*                   | STMR (tentative)    |                        |
| Bovine and equine liver | 0.01*                   | STMR (tentative)    |                        |
| Bovine and equine kidney| 0.01*                   | STMR (tentative)    |                        |
| Sheep and goat meat     | 0.01*                   | STMR muscle (tentative) |                       |
| Sheep and goat fat      | 0.01*                   | STMR (tentative)    |                        |
| Sheep and goat liver    | 0.01*                   | STMR (tentative)    |                        |
| Sheep and goat kidney   | 0.01*                   | STMR (tentative)    |                        |
| Cattle and horse milk   | 0.01*                   | STMR (tentative)    |                        |
| Sheep and goat milk     | 0.01*                   | STMR (tentative)    |                        |

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

1. GAP or DB > 0.1 mg/kg DM in EU?
   - Yes
     - Is RD-RA derived for this commodity?
       - Yes
         - MRL And RA derived in Section 3?
           - Yes
             - MRL fully supported by data?
               - Yes
                 - (A) Specific LOQ or default MRL?
                   - (B) Specific LOQ or default MRL?
                     - (C) Specific LOQ or default MRL?
                       - (D) Maintain current EU MRL?
                         - (E) Establish tentative EU MRL?
                           - (F) MRL is recommended.
        - No
          - (G) Specific LOQ or default MRL?
            - (H) MRL is recommended.
   - No
     - Not considered for the RA.

2. Current EU MRL is included in the RA.
   - Yes
     - Tentative median/highest values are included in the RA?
       - Yes
         - Risk identified?
           - Yes
             - Fall-back MRL available?
               - Yes
                 - (I) MRL is recommended.
               - No
                 - No
               - No
             - No
           - No
         - No
       - Yes
         - Risk identified?
           - Yes
             - Fall-back MRL available?
               - Yes
                 - (I) MRL is recommended.
               - No
                 - No
               - No
             - No
           - No
         - No
   - No
     - Not considered for the RA.

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

1. Not considered for the RA.
   - Yes
     - Not considered for the RA.
   - No
     - Current EU MRL is included in the RA.

2. Tentative median/highest values are included in the RA.
   - Yes
     - Risk identified?
       - Yes
         - Fall-back MRL available?
           - Yes
             - (I) MRL is recommended.
           - No
             - No
           - No
         - No
       - No
   - No
     - Not considered for the RA.

Recommendations resulting from EU authorisations and import tolerances

1. (A) Specific LOQ or default MRL?
2. (B) Specific LOQ or default MRL?
3. (C) Specific LOQ or default MRL?
4. (D) Maintain current EU MRL?
5. (E) Establish tentative EU MRL?
6. (F) MRL is recommended.

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

(CXL available?)

Yes

RD comparable?

Yes

CXL higher?

Yes

No

No

No

No

Consumer risk assessment with consideration of the existing CXL

(CXL supported by data?)

Yes

Risk identified?

Yes

No

No

Risk identified?

Yes

No

Input values for the RA remain unchanged.

CXL is included in the RA.

Input values for the RA remain unchanged.

Risk identified?

Yes

No

No

Input values for the RA remain unchanged.

Risk identified?

Yes

No

No

Input values for the RA remain unchanged.

Codex median/highest residues are included in the RA.

Yes

No

No

No

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> |
|--------------------------------|-----------------------------------------------|---------------------------------|
| **Pyriofenone**               | (5-chloro-2-methoxy-4-methyl-3-pyridyl)(4,5,6-trimethoxy-2-tolyl)methanone | ![Pyriofenone](image1.png) |
|                               | COc1ncc(C)c1c1C(-O)c1c(C)cOCc(OC)c(OC)c1OCNMVCBWZLCXANER-UHFFFAOYSA-N | |
| **3HDPM**                     | (5-chloro-2-methoxy-4-methyl-3-pyridinyl)(3-hydroxy-2,4-dimethoxy-6-methylphenyl)methanone | ![3HDPM](image2.png) |
|                               | COc1ncc(C)c1C(-O)c1c(C)cOCc(OC)c(OC)c1OCAFLIGDZOFOBEAI-UHFFFAOYSA-N | |
| **4HDPM**                     | (5-chloro-2-methoxy-4-methyl-3-pyridinyl)(4-hydroxy-2,3-dimethoxy-6-methylphenyl)methanone | ![4HDPM](image3.png) |
|                               | COc1ncc(C)c1C(-O)c1c(C)cOCc(OC)c(OC)c1OCSQPGTKSZOBCHJS-UHFFFAOYSA-N | |
| **2MDPM**                     | (5-chloro-2-methoxy-4-methyl-3-pyridinyl)(3,4-dihydroxy-2-methoxy-6-methylphenyl)methanone | ![2MDPM](image4.png) |
|                               | COc1ncc(C)c1C(-O)c1c(C)cOCc(OC)c(OC)c1OCYQCYVURJOBMYMI-UHFFFAOYSA-N | |
| **4MDPM**                     | (5-chloro-2-methoxy-4-methyl-3-pyridinyl)(2,3-dihydroxy-4-methoxy-6-methylphenyl)methanone | ![4MDPM](image5.png) |
|                               | COc1ncc(C)c1C(-O)c1c(C)cOCc(OC)c(OC)c1ODNIIZCDDKSLOID-UHFFFAOYSA-N | |

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 2015 ACD/Labs 2015 Release (File version N20E41, Build 75170, 19 December 2014).
(c): ACD/ChemSketch 2015 ACD/Labs 2015 Release (File version C10H41, Build 75059, 17 December 2014).