Review of the existing maximum residue levels for quinoxyfen 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 quinoxyfen. Although this active substance is no longer authorised within the European Union, MRLs were established by the Codex Alimentarius Commission (Codex maximum residue limits; CXLs) and an import tolerance was reported by Member States (including the supporting residues data). Based on the assessment of the available data, EFSA assessed the CXLs and import tolerance requested, and a consumer risk assessment was carried out considering the toxicological reference value established for the first inclusion under Directive 91/414/EEC. All CXLs and import tolerance were found to be adequately supported by data and no risk to consumers was identified.

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Keywords: quinoxyfen, MRL review, Regulation (EC) No 396/2005, consumer risk assessment, fungicide

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Summary

Quinoxyfen was included in Annex I to Directive 91/414/EEC on 1 September 2004 by Commission Directive 2004/60/EC, and has been deemed to be approved under Regulation (EC) No 1107/2009, in accordance with Commission Implementing Regulation (EU) No 540/2011, as amended by Commission Implementing Regulation (EU) No 541/2011.

As the active substance was approved before 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(2) of the aforementioned regulation.

Meanwhile, the decision on non-renewal of approval of quinoxyfen was taken by Commission Implementing Regulation (EU) 2018/1914 of October 2018. As the basis for the MRL review, on 18 December 2019, EFSA initiated the collection of data for this active substance. In a first step, in order to verify whether import tolerances may still be in place, the Member States were invited to submit by 30 January 2020 their Good Agricultural Practices (GAPs) for the import tolerances in a standardised way, in the format of specific GAP forms, allowing the designated rapporteur Member State (RMS), Austria, 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 6 May 2020. On the basis of all the data submitted by Member States and by the EU Reference Laboratories for Pesticides Residues (EURLs), EFSA asked the RMS to complete the Pesticide Residues Overview File (PROFile) and to prepare a supporting evaluation report. The PROFile and evaluation report, together with Pesticide Residues Intake Model (PRIMo) calculations and an updated GAP overview file were provided by the RMS to EFSA on 30 June 2020. 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 EURLs, and taking into account the conclusions of the targeted hazard assessment derived by EFSA in the framework of Regulation (EC) No 1107/2009 and the MRLs established by the Codex Alimentarius Commission, EFSA prepared in September 2020 a draft reasoned opinion, which was circulated to Member States and EURLs for consultation via a written procedure. No comments were received by 27 October 2020. The reasoned opinion was finalised, and the following conclusions are derived.

The metabolism of quinoxyfen in plant was investigated in primary and rotational crops. According to the results of the metabolism studies, the residue definition for enforcement and risk assessment can be proposed as quinoxyfen. This residue definition is also applicable to processed commodities. A specific residue definition for rotational crops is not deemed necessary under this review considering that quinoxyfen is only authorised for imported crops (hop). Fully validated analytical methods are available for the enforcement of the proposed residue definition at the limit of quantification (LOQ) of 0.01 mg/kg in the four main matrix groups, and of 0.05 mg/kg in hops. According to the EURLs, the LOQ of 0.01 mg/kg is achievable in all four main matrices as well as in specific/difficult matrices, by using the QuEChERS method in routine analyses. Available residue trials data were considered sufficient to derive MRL proposal as well as risk assessment values for the commodity under evaluation.

Quinoxyfen is not authorised for use on crops that might be fed to livestock. Further investigation of the occurrence of residues in commodities of animal origin is not required and the setting of MRLs in these commodities is not considered necessary. Nevertheless, based on the available metabolism studies, an animal residue definition for enforcement and risk assessment could be proposed for the current assessment as quinoxyfen by default. However, if required in the future, the inclusion of additional metabolites to the residue definition for risk assessment may need to be reconsidered. Analytical methods were validated for the determination of quinoxyfen at an LOQ of 0.01 mg/kg in all livestock commodities. According to the EURLs, the LOQ of 0.01 mg/kg is expected to be achievable to monitor quinoxyfen in all animal matrices.

Chronic consumer exposure resulting from the authorised use reported in the framework of this review was calculated using revision 3.1 of the EFSA PRIMo. The toxicological reference values established for the first inclusion under Directive 91/414/EEC were considered, as the renewal peer review was limited to a targeted environmental hazard assessment. The highest chronic exposure represented 0% of the acceptable daily intake (ADI) (UK adult, DE general). Acute exposure calculations were not carried out because an acute reference dose (ARfD) was not deemed necessary for this active substance. Apart from the MRL evaluated in the framework of this review, internationally...
recommended CXLs have also been established for quinoxyfen. Additional calculations of the consumer exposure considering these CXLs were therefore carried out. The highest chronic exposure represented 1% of the ADI (ES adult). Therefore, it can be concluded that the use under assessment and the CXLs are not expected to pose a risk to European consumers.
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Review of the existing MRLs for quinoxyfen

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(2) of that Regulation stipulates that the European Food Safety Authority (EFSA) shall provide by 1 September 2009 a reasoned opinion on the review of the existing MRLs for all active substances included in Annex I to Directive 91/414/EEC² before 2 September 2008.

Quinoxyfen was included in Annex I to Council Directive 91/414/EEC on 1 September 2004 by means of Commission Directive 2004/60/EC³ which has been deemed to be approved under Regulation (EC) No 1107/2009⁴, in accordance with Commission Implementing Regulation (EU) No 540/2011⁵, as amended by Commission Implementing Regulation (EU) No 541/2011⁶. Therefore, EFSA initiated the review of all existing MRLs for that active substance.

In the framework of Regulation (EC) No 1107/2009, the potential renewal of approval of quinoxyfen was evaluated by the United Kingdom, designated as rapporteur Member State (RMS). The United Kingdom conducted a targeted hazard assessment of the pesticide active substance quinoxyfen. 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 scientific output (EFSA, 2018a). In 2018, a decision of non-renewal of quinoxyfen was taken by Commission Implementing Regulation (EU) 2018/1914⁶.

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 18 December 2019, EFSA initiated the collection of data for this active substance. In a first step, Member States were invited to submit by 30 January 2020 their Good Agricultural Practices (GAPs) for the import tolerances, in a standardised way, in the format of specific GAP forms. In the framework of this consultation, two Member States provided feedback on their import tolerance for quinoxyfen. Based on the GAP data submitted, the designated RMS, Austria, 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 6 May 2020.

On the basis of all the data submitted by Member States and the EU Reference Laboratories for Pesticides Residues (EURLs), EFSA asked Austria to complete the PROFile and to prepare a supporting evaluation report. The PROFile and the supporting evaluation report, together with the Pesticide Residues Intake Model (PRIMo) calculations and an updated GAP overview file were submitted to EFSA on 30 June 2020. 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.

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¹ Regulation (EC) No 396/2005 of the European Parliament and of the Council of 23 February 2005 on maximum residue levels of pesticides in or on food and feed of plant and animal origin and amending Council Directive 91/414/EEC. OJ L 70, 16.3.2005, p. 1–16.
² Commission Directive 2004/60/EC of 23 April 2004 amending Council Directive 91/414/EEC to include quinoxyfen as active substance. OJ L 120, 24.4.2004, p. 39–42.
³ Regulation (EC) No 1107/2009 of the European Parliament and of the Council of 21 October 2009 concerning the placing of plant protection products on the market and repealing Council Directives 79/117/EEC and 91/414/EEC. OJ L 309, 24.11.2009, p. 1–50.
⁴ Commission Implementing Regulation (EU) No 540/2011 of 25 May 2011 implementing Regulation (EC) No 1107/2009 of the European Parliament and of the Council as regards the list of approved active substances. OJ L 153, 11.6.2011, p. 1–50.
⁵ Commission Implementing Regulation (EU) No 541/2011 of 1 June 2011 amending Implementing Regulation (EU) No 540/2011 implementing Regulation (EC) No 1107/2009 of the European Parliament and of the Council as regards the list of approved active substances. OJ L 153, 11.6.2011, p. 187–188.
⁶ Commission Implementing Regulation (EU) 2018/1914 of 6 December 2018 concerning the non-renewal of approval of the active substance quinoxyfen, in accordance with Regulation (EC) No 1107/2009 of the European Parliament and of the Council concerning the placing of plant protection products on the market, and amending Commission Implementing Regulation (EU) No 540/2011. OJ L 311, 7.12.2018, p. 17–19.
Considering all the available information, and taking into account the MRLs established by the Codex Alimentarius Commission (CAC) (i.e. codex maximum residue limit; CXLs), EFSA prepared in September 2020 a draft reasoned opinion, which was circulated to Member States and EURLs for commenting via a written procedure. No comments were received by 27 October 2020. The reasoned opinion was finalised, and the following conclusions are derived.

The evaluation report submitted by the RMS (Austria, 2020), taking into account also the information provided by Member States during the collection of data, and the EURLs report on analytical methods (EURLs, 2020) 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, 2020a) and the Member States consultation report (EFSA, 2020b). 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 Pesticide Residues Intake Model (PRIMO) and the PROFile as well as the GAP overview file listing all authorised uses and import tolerances 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

Quinoxyfen is the ISO common name for 5,7-dichloro-4-quinolyl 4-fluorophenyl ether (IUPAC).

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

The EU MRLs for quinoxyfen are established in Annexes II and IIIB of Regulation (EC) No 396/2005. Codex maximum residue limits (CXLs) for quinoxyfen were also established by the Codex Alimentarius Commission (CAC). 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 36/2014 | Hops (dried) (EFSA, 2013)                     |
| MRL application | No implementation    | Hops (EFSA, 2010)                            |
|                 |                      | Data were not sufficient to propose any MRL  |

For the purpose of this MRL review, all the uses of quinoxyfen currently authorised in third countries 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 quinoxyfen are given in Appendix A.

Assessment

EFSA has based its assessment on the following documents:

- the PROFile submitted by the RMS;
- the evaluation report accompanying the PROFile (Austria, 2020);
- the draft assessment report (DAR) prepared under Council Directive 91/414/EEC (United Kingdom, 2000);
- the revised renewal assessment report (RAR) (United Kingdom, 2017) prepared in the framework of Commission Implementing Regulation (EU) No 844/2012;
the conclusion on the peer review of the targeted hazard assessment of the pesticide active substance quinoxyfen (EFSA, 2018a);
the review report on quinoxyfen (European Commission, 2003);
the Joint Meeting on Pesticide residues (JMPR) Evaluation report (FAO, 2006, 2007);
the previous reasoned opinions on quinoxyfen (EFSA, 2010, 2013).

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\(^7\) and the currently applicable guidance documents relevant for the consumer risk assessment of pesticide residues (European Commission, 1996, 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 quinoxyfen was investigated after foliar treatment in wheat in the framework of the peer review under Directive 91/414/EEC (United Kingdom, 2000), and in sugar beet, grapes, tomato and cucumber by the JMPR (FAO, 2006). None of these studies were peer reviewed by EFSA; nevertheless, the available studies on grapes and sugar beets have been assessed in the framework of previous MRL applications (United Kingdom, 2009; EFSA, 2010, 2013). All studies were performed with \(^{14}\)C-labelled quinoxyfen in the quinoline or the fluoroxy ring of the molecule.

After one foliar application of 250 g a.s./ha (at BBCH 32 or 49) and 1,000 g a.s./ha (at BBCH 32 only) on wheat, the total radioactivity was low in wheat grain (0.03–0.05 mg eq/kg) and parent quinoxyfen was present at very low levels in harvested grain (0.03–0.11% of the total radioactive residues; TRR). In wheat straw, the major component identified at harvest was quinoxyfen, representing 8–27% TRR (0.08–1.28 mg eq/kg), while metabolite A, consisting of at least six components possibly organic acids, was found both in grain and straw at 9–27% TRR. This study showed that quinoxyfen is extensively metabolised in grain, where similar metabolites as in straw were found but at low levels (<0.01 mg eq/kg). About 13–50% TRR in grain was considered to be incorporated into starch, while 25% TRR in straw was associated with cellulose (United Kingdom, 2000; EFSA, 2010, 2013).

After one application of 375 or 750 mg a.s./L sprayed to grape berries, the major component identified in the mature grapes was quinoxyfen largely unmetabolised, representing 93–98% TRR (1.8–4.1 mg eq/kg) in both labels. The study showed no translocation of radioactivity from the treated foliage to the untreated vines or grapes (FAO, 2006; United Kingdom, 2009). On sugar beet, a treatment with a maximum of 300 g a.s./ha in two foliar applications was performed. Separated plots were treated with a higher rate of 600 g a.s./ha to facilitate the identification of radioactive residues. In this study, the major component identified with both labels was parent quinoxyfen, representing up to 26% TRR (0.02 mg eq/kg) in roots and up to 30% TRR (0.56 mg eq/kg) in tops. The remaining radioactivity was formed of polar residues consisting of multiple metabolites (FAO, 2006; United Kingdom, 2009; EFSA, 2013). In sugar beet tops, metabolite 4-fluorophenol was present at 17% TRR (0.32 mg eq/kg) in the phenyl label only, resulting from the cleavage of the ether bond. Additional studies on tomato and cucumber assessed by the JMPR (FAO, 2006) also showed parent quinoxyfen to be the major residue identified with both labels. Quinoxyfen accounted for 64–74% TRR (0.05–0.06 mg eq/kg) in cucumber fruits and 56–74% TRR (1.9–3.1 mg eq/kg) in foliage (here also no translocation from treated foliage to other parts of the plant occurred). In tomato, quinoxyfen accounted for 63–65% TRR (0.12–0.16 mg eq/kg) in fruits and 43% TRR (4.6–6.1 mg eq/kg) in foliage. About 10% TRR in tomato was associated with lignin, cellulose and hemicellulose.

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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.
As a summary, parent quinoxyfen was the main residue identified in all crops. The metabolic pathway was similar in cereals, fruits/fruiting vegetables and root crops, involving hydroxylation of the quinoline or phenoxy rings. Cleavage of the ether bond was a minor pathway (observed in sugar beet) (FAO, 2006; EFSA, 2013).

1.1.2. Nature of residues in rotational crops

Quinoxyfen may be considered persistent (P) and very persistent (vP) in both soil and natural water systems when a comparison is made to the relevant P and vP triggers specified in Annex II of Regulation (EC) No 1107/2009. The range DT$_{90}$ reported in the soil degradation field studies evaluated in the framework of the peer review was from 391 to > 10,000 days (EFSA, 2018a).

Since quinoxyfen is only authorised for imported hop, investigation of residues in rotational crops is not required. Nevertheless, one confined study was available for this review (United Kingdom, 2000) but not peer reviewed, and is summarised here for completeness.

In the available confined rotational crop study, quinoxyfen radiolabelled on the fluoro phenoxy or quinoline ring of the molecule was applied at a rate of 400 g a.s./ha onto bare soil. Turnip (root/tuber crops), cabbage (leafy crops) and sunflower (pulses and oilseeds) were planted at a nominal plant back interval (PBI) of 30 days after treatment (DAT). Crop samples were taken at maturity. In all crops and with both labels, total radioactive residues were very low (< 0.004 mg eq/kg); therefore, the identity of any metabolites that could be present was not further investigated (United Kingdom, 2000).

Thus, it cannot be concluded whether the metabolic pathway of quinoxyfen is the same in primary and in rotational crops. However, a study to further characterise the residues is not deemed necessary.

1.1.3. Nature of residues in processed commodities

Although not required, studies investigating the nature of residues in processed commodities were assessed under the current review, but not peer reviewed (Austria, 2020).

Studies were conducted with radiolabelled quinoxyfen on the fluoro phenoxy or quinoline ring 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). Only minor degradation products were observed, identified as 4-fluorophenol and dichloro-hydroxyquinoline (DCHQ), from 2% to 8.5% TRR.

Quinoxyfen was found to be stable to hydrolysis under standard conditions of pasteurisation, baking/brewing/boiling and sterilisation.

1.1.4. Methods of analysis in plants

During the peer review of the targeted hazard assessment, a hyphenated analytical method based on liquid chromatography coupled to tandem mass spectrometry (LC-MS/MS) was validated in dry commodities (barley grains), high water content (lettuce), high oil content (oilseed rape) and high acid content (lemon) commodities with a limit of quantification (LOQ) of 0.01 mg/kg; two ion transitions were monitored for confirmation purposes. This primary method is supported by an independent laboratory validation (ILV) and is considered suitable for enforcing quinoxyfen in high water content, high acid content, high oil content and dry commodities (United Kingdom, 2017; EFSA, 2018a).

In addition, a QuEChERS method using LC-MS/MS technique and supported by an ILV was validated in high water content, high acid content and dry commodities with an LOQ of 0.01 mg/kg (United Kingdom, 2017; EFSA, 2018a).

In the framework of previous MRL applications (EFSA, 2010, 2013), an analytical method based on gas chromatography coupled to mass spectrometry detection (GC-MSD) was reported but not peer reviewed by ESFA. This method previously assessed by the JMPR (FAO, 2006) and during the peer review under Directive 91/414/EEC (United Kingdom, 2000) was sufficiently validated for the determination of quinoxyfen in several plant matrices, including hops with an LOQ of 0.05 mg/kg.

Under the current review during the completeness check, the EURLs provided a QuEChERS multi-residue analytical method using LC or GC-MS/MS techniques, with an LOQ of 0.01 mg/kg for the routine analysis of quinoxyfen in all four plant matrices and in specific/difficult matrices (EURLs, 2020).

EFSA concludes that sufficiently validated analytical methods are available for the enforcement of the commodities under assessment in this MRL review.
1.1.5. Stability of residues in plants

The storage stability of quinoxyfen was investigated in cereals in the framework of the peer review under Directive 91/414/EEC (United Kingdom, 2000). Quinoxyfen residues were found to be stable at ≤ –18°C for up to 15 months in dry matrices (cereals).

It is noted that no specific study is available for the storage stability in hops (no group). However, the stability of the residues in hops (dried cones) was investigated as part of the supervised residue trials where integrity of the samples was demonstrated for about 200 days (ca. 7 months) (Austria, 2020). In addition, the JMPR reports a study where the storage stability of quinoxyfen residues was demonstrated in hops (dried cones) under deep frozen conditions for a maximum storage interval of 113 days (ca. 4 months) (FAO, 2006).

EFSA considers the storage stability as sufficiently addressed for the current authorised import tolerance.

1.1.6. Proposed residue definitions

The metabolism of quinoxyfen was similar in all primary crops assessed and the processing of quinoxyfen is not expected to modify the nature of residues. Considering that quinoxyfen is only authorised for imported hop, a specific residue definition for rotational crops is not deemed necessary.

Since parent quinoxyfen was found as a large portion of the TRR in grapes, tomato, cucumber, sugar beet and wheat straw, this compound is considered a sufficient marker in fruits, roots and cereals and the residue definition for enforcement and risk assessment is proposed as quinoxyfen only. This proposal is identical with the current residue definition set in Regulation (EC) No 396/2005 and with the JMPR conclusions based on the same metabolism studies.

An analytical method for the enforcement of the proposed residue definition at the LOQ of 0.05 mg/kg in hops and of 0.01 mg/kg in all other plant matrices is available (EFSA, 2010, 2018a). According to the EURLs, the LOQ of 0.01 mg/kg is achievable in the four main matrix groups, as well as in special matrices by using the QuEChERS method in routine analyses (EURLs, 2020).

1.2. Magnitude of residues in plants

1.2.1. Magnitude of residues in primary crops

To assess the magnitude of quinoxyfen residues resulting from the reported GAP, EFSA considered all residue trials already evaluated in the framework of previous MRL applications (EFSA, 2010, 2013) that were reported by the RMS in its evaluation report (Austria, 2020). All residue trial samples considered in this framework were stored in compliance with, or slightly above (up to 224 days) the conditions for which storage stability of residues was demonstrated. However, all residue trials were deemed acceptable to support the import tolerance on hops. Decline of residues during storage of the trial samples is not expected, considering also that storage stability in dry matrices was demonstrated for 15 months.

The number of residue trials and extrapolations was evaluated in accordance with the European guidelines on comparability, extrapolation, group tolerances and data requirements for setting MRLs (European Commission, 2017). Available residue trials were sufficient to derive MRL and risk assessment values for the crop under evaluation.

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.

In the available confined rotational crop study, it was concluded that quinoxyfen residues are not expected to exceed 0.01 mg/kg in rotational commodities (see Section 1.1.2). Though, due to the high persistence of quinoxyfen in soil, the effect of multiple years of consecutive applications (estimating the plateau concentration levels in soil) should in principle be evaluated to allow to conclude properly on the possible accumulation in plants.

However, since quinoxyfen is only authorised for imported crops (hop), further investigations of residues in rotational crops are not required.
1.2.3. Magnitude of residues in processed commodities

No studies to assess the effect of industrial processing and/or household preparation was available for this review. Considering the outcome of the risk assessment (see Section 3) and that processing is not expected to change the nature of quinoxyfen residues (see Section 1.1.3), further studies are not necessary.

If more robust processing factors were to be required by risk managers, in particular for enforcement purposes, processing studies would be required.

1.2.4. Proposed MRLs

The available data are considered sufficient to derive MRL proposal as well as risk assessment values for the commodity under evaluation.

2. Residues in livestock

Quinoxyfen is not authorised for use on crops that might be fed to livestock. Further investigation of the occurrence of residues in commodities of animal origin is not required and the setting of MRLs in these commodities is not considered necessary (European Commission, 1996).

Nevertheless, metabolism studies were available and described here for completeness. The metabolism of quinoxyfen residues in livestock was investigated in lactating goats (United Kingdom, 2000) and laying hens (Austria, 2020), but these studies were not peer reviewed. In all studies, quinoxyfen was radiolabelled in the fluoroxy or quinoline ring of the molecule.

The study performed on lactating goats indicates that quinoxyfen residues are largely excreted (80% of total radioactivity was found in urine and faeces). Parent quinoxyfen was the main compound identified in milk (35–50% TRR; 0.02–0.04 mg eq/kg), liver (74–90% TRR, present as parent and 3-hydroxyquinoxyfen) and in fat (50–98% TRR; 0.06–0.2 mg eq/kg). Other metabolites were identified but were not measured at significant levels (United Kingdom, 2000).

The study performed on laying hens confirmed that quinoxyfen is rapidly excreted. In eggs and with both labels, unchanged quinoxyfen accounted for 23–34% TRR (up to 0.09 mg eq/kg). Parent quinoxyfen was also the most predominant compound present in significant proportions in muscles (19–79% TRR; < 0.01–0.10 mg eq/kg) and in fat (93–96% TRR; 1.68–1.85 mg eq/kg). In liver, the major compounds identified were the sulfate conjugates of bis-hydroxy/hydroxy quinoxyfen (13% TRR; 0.24 mg eq/kg) with the phenyl label, and DCHQ (55% TRR; 0.88 mg eq/kg) with the quinoline label. The metabolism in hen, goat and rat is qualitatively similar (Austria, 2020).

EFSA concludes that the metabolism of quinoxyfen in livestock is adequately elucidated. In case a residue definition for livestock would need to be established in the future, quinoxyfen is considered a sufficient marker for enforcement, while the inclusion of additional metabolites to the residue definition for risk assessment may need to be reconsidered.

An analytical method using high-performance liquid chromatography with tandem mass spectroscopy (HPLC-MS/MS) supported by an ILV was sufficiently validated for the determination of quinoxyfen in animal muscle, fat, liver, milk and egg, with an LOQ of 0.01 mg/kg. A QuEChERS multiresidue method (ILV available) using the same technique was also validated with an LOQ of 0.01 mg/kg in muscle, kidney, milk and egg (United Kingdom, 2017; EFSA, 2018a). According to the EURLs, the LOQ of 0.01 mg/kg is achievable to monitor quinoxyfen residues in milk and muscle (even lower levels were successfully validated in these commodities). Based on this and on screening validation data, the EURLs concluded that quinoxyfen can be monitored in milk, muscle, egg and honey with an LOQ of 0.01 mg/kg. An LOQ of 0.01 mg/kg is expected to be achievable also for the remaining main groups of animal products (liver, kidney, fat) (EURLs, 2020).

The storage stability of quinoxyfen was demonstrated when stored deep frozen (−20°C) for a period of 6 months in muscle and kidney, 7 months in fat, 8 months in milk and 10 months in liver (United Kingdom, 2000).

Even though not required under the current assessment, a residue definition for enforcement and risk assessment is proposed as quinoxyfen by default.

3. Consumer risk assessment

In the framework of this review, only the uses of quinoxyfen reported by the RMS in Appendix A were considered; however, the use of quinoxyfen was previously also assessed by the JMPR (FAO, 2006, 2007). The CXLs, resulting from these assessments by JMPR and adopted by the CAC, are now
international recommendations that need to be considered by European risk managers when establishing MRLs. To facilitate consideration of these CXLs by risk managers, the consumer exposure was calculated both with and without consideration of the existing CXLs.

During the peer review under Directive 91/414/EEC, an acute acceptable daily intake (ADI) of 0.2 mg/kg body weight (bw) per day was derived for quinoxyfen and, due to the low acute toxicity, it was concluded that no acute reference dose (ARfD) has to be established (European Commission, 2003). The JMPR came to the same conclusions regarding the toxicological reference values (FAO, 2006). It should be highlighted that these toxicological reference values were never peer reviewed by EFSA. As the renewal peer review was limited to a targeted environmental hazard assessment, no assessment of the toxicological profile of quinoxyfen was conducted and no toxicological reference values were set.

3.1. Consumer risk assessment without consideration of the existing CXLs

Chronic exposure calculations for the crop reported in the framework of this review were performed using revision 3.1 of the EFSA PRIMo (EFSA, 2018b, 2019). Input values for the exposure calculations were derived in compliance with the decision tree reported in Appendix E. Hence, for the commodity where an 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.

Acute exposure calculations were not carried out because an ARfD was not deemed necessary for this active substance.

The exposure values calculated were compared with the toxicological reference value for quinoxyfen, derived by the European Commission under Directive 91/414/EEC. The highest chronic exposure represented 0% of the ADI, calculated for the diets UK adult and DE General. These calculations indicate that the use assessed under this review is unlikely to pose a risk to consumer’s health.

3.2. Consumer risk assessment with consideration of the existing CXLs

To include the CXLs in the calculations of the consumer exposure, CXLs were compared with the EU MRL proposals in compliance with Appendix E and all data relevant to the consumer exposure assessment have been collected from JMPR evaluations. The EU MRLs and the CXLs established by JMPR were derived following the same residue definition, namely quinoxyfen both for plant and animal commodities, and are therefore comparable. An overview of the input values used for this exposure calculation is also provided in Appendix D.

Chronic exposure calculations were also performed using revision 3.1 of the EFSA PRIMo and the exposure values calculated were compared with the toxicological reference value derived for quinoxyfen. The highest chronic exposure was calculated for ES adult, representing 1% of the ADI. Based on these calculations, EFSA concludes that the CXLs are not expected to be of concern for European consumers.

Conclusions

The metabolism of quinoxyfen in plant was investigated in primary and rotational crops. According to the results of the metabolism studies, the residue definition for enforcement and risk assessment can be proposed as quinoxyfen. This residue definition is also applicable to processed commodities. A specific residue definition for rotational crops is not deemed necessary under this review considering that quinoxyfen is only authorised for imported crops (hop). Fully validated analytical methods are available for the enforcement of the proposed residue definition at the LOQ of 0.01 mg/kg in the four main matrix groups, and of 0.05 mg/kg in hops. According to the EURs, the LOQ of 0.01 mg/kg is achievable in all four main matrices as well as in specific/difficult matrices, by using the QuEChERS method in routine analyses. Available residue trials data were considered sufficient to derive MRL proposal as well as risk assessment values for the commodity under evaluation.

Quinoxyfen is not authorised for use on crops that might be fed to livestock. Further investigation of the occurrence of residues in commodities of animal origin is not required and the setting of MRLs in these commodities is not considered necessary. Nevertheless, based on the available metabolism studies, an animal residue definition for enforcement and risk assessment could be proposed for the current assessment as quinoxyfen by default. However, if required in the future, the inclusion of
additional metabolites to the residue definition for risk assessment may need to be reconsidered. Analytical methods were validated for the determination of quinoxyfen at an LOQ of 0.01 mg/kg in all livestock commodities. According to the EURs, the LOQ of 0.01 mg/kg is expected to be achievable to monitor quinoxyfen in all animal matrices.

Chronic consumer exposure resulting from the use reported in the framework of this review was calculated using revision 3.1 of the EFSA PRIMo. The toxicological reference values established for the first inclusion under Directive 91/414/EEC were considered, as the renewal peer review was limited to a targeted environmental hazard assessment. The highest chronic exposure represented 0% of the ADI (UK adult, DE general). Acute exposure calculations were not carried out because an ARfD was not deemed necessary for this active substance. Apart from the MRL evaluated in the framework of this review, internationally recommended CXLs have also been established for quinoxyfen. Additional calculations of the consumer exposure considering these CXLs were therefore carried out. The highest chronic exposure represented 1% of the ADI (ES adult). Therefore, it can be concluded that the use under assessment and the CXLs are not expected to pose a risk to European consumers.

**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 (see Table 2 footnotes for details).

**Table 2:** Summary table

| Code number | Commodity | Existing EU MRL (mg/kg) | Existing CXL (mg/kg) | Outcome of the review | Comment |
|-------------|-----------|------------------------|----------------------|-----------------------|---------|
| **Enforcement residue definition:** quinoxyfen(F) |           |                        |                      |          |         |
| 140020      | Cherries  | 0.3                    | 0.4                  | 0.4                   | Recommended(a) |
| 151010      | Table grapes | 1                      | 2                    | 2                     | Recommended(a) |
| 151020      | Wine grapes | 1                      | 2                    | 2                     | Recommended(a) |
| 152000      | Strawberries | 0.3                    | 1                    | 1                     | Recommended(a) |
| 154030      | Currants (red, black and white) | 2                      | 1                    | 1                     | Recommended(a) |
| 231020      | Peppers   | 0.02                   | 1                    | 1                     | Recommended(a) |
| 233010      | Melons    | 0.05                   | 0.1                  | 0.1                   | Recommended(a) |
| 251020      | Lettuce   | 0.02                   | 20                   | 20                    | Recommended(a) |
| 500010      | Barley grain | 0.2                    | 0.01*                | 0.01*                 | Recommended(a) |
| 500090      | Wheat grain | 0.02                   | 0.01*                | 0.01*                 | Recommended(a) |
| 700000      | Hops (dried), including hop pellets and unconcentrated powder | 2                      | 1                    | 3                     | Recommended(b) |
| 900010      | Sugar beet (root) | 0.02                   | 0.03                 | 0.03                  | Recommended(a) |
| 1011010     | Swine meat | 0.2                    | 0.2                  | 0.2                   | Recommended(a) |
| 1011020     | Swine fat (free of lean meat) | 0.2                    | 0.2                  | 0.2                   | Recommended(a) |
| 1011030     | Swine liver | 0.2                    | 0.01*                | 0.01*                 | Recommended(a) |
| 1011040     | Swine kidney | 0.2                    | 0.01*                | 0.01*                 | Recommended(a) |
| 1012010     | Bovine meat | 0.2                    | 0.2                  | 0.2                   | Recommended(a) |
| 1012020     | Bovine fat | 0.2                    | 0.2                  | 0.2                   | Recommended(a) |
| 1012030     | Bovine liver | 0.2                    | 0.01*                | 0.01*                 | Recommended(a) |
| 1012040     | Bovine kidney | 0.2                    | 0.01*                | 0.01*                 | Recommended(a) |
| 1013010     | Sheep meat | 0.2                    | 0.2                  | 0.2                   | Recommended(a) |
| 1013020     | Sheep fat | 0.2                    | 0.2                  | 0.2                   | Recommended(a) |
| 1013030     | Sheep liver | 0.2                    | 0.01*                | 0.01*                 | Recommended(a) |
| 1013040     | Sheep kidney | 0.2                    | 0.01*                | 0.01*                 | Recommended(a) |
| 1014010     | Goat meat | 0.2                    | 0.2                  | 0.2                   | Recommended(a) |
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### Table: Review of the existing MRLs for quinoxyfen

| Code number | Commodity       | Existing EU MRL (mg/kg) | Existing CXL (mg/kg) | Outcome of the review MRL (mg/kg) | Comment |
|-------------|-----------------|-------------------------|----------------------|----------------------------------|---------|
| 1014020     | Goat fat        | 0.2                     | 0.2                  | 0.2                             | Recommended<sup>(a)</sup> |
| 1014030     | Goat liver      | 0.2                     | 0.01*                | 0.01*                           | Recommended<sup>(a)</sup> |
| 1014040     | Goat kidney     | 0.2                     | 0.01*                | 0.01*                           | Recommended<sup>(a)</sup> |
| 1015010     | Horse meat      | 0.2                     | 0.2                  | 0.2                             | Recommended<sup>(a)</sup> |
| 1015020     | Horse fat       | 0.2                     | 0.2                  | 0.2                             | Recommended<sup>(a)</sup> |
| 1015030     | Horse liver     | 0.2                     | 0.01*                | 0.01*                           | Recommended<sup>(a)</sup> |
| 1015040     | Horse kidney    | 0.2                     | 0.01*                | 0.01*                           | Recommended<sup>(a)</sup> |
| 1016010     | Poultry meat    | 0.2                     | 0.02                 | 0.02                            | Recommended<sup>(a)</sup> |
| 1016020     | Poultry fat     | 0.2                     | 0.02                 | 0.02                            | Recommended<sup>(a)</sup> |
| 1016030     | Poultry liver   | 0.2                     | 0.01*                | 0.01*                           | Recommended<sup>(a)</sup> |
| 1020010     | Cattle milk     | 0.05                    | 0.01*                | 0.01*                           | Recommended<sup>(a)</sup> |
| 1020020     | Sheep milk      | 0.05                    | 0.01*                | 0.01*                           | Recommended<sup>(a)</sup> |
| 1020030     | Goat milk       | 0.05                    | 0.01*                | 0.01*                           | Recommended<sup>(a)</sup> |
| 1020040     | Horse milk      | 0.05                    | 0.01*                | 0.01*                           | Recommended<sup>(a)</sup> |
| 1030000     | Birds’ eggs     | 0.02                    | 0.01*                | 0.01*                           | Recommended<sup>(a)</sup> |
| –           | Other commodities of plant and/or animal origin | See Reg. (EU) No 36/2014 | –                  | –                               | Further consideration needed<sup>(c)</sup> |

MRL: maximum residue level; CXL: codex maximum residue limit.
(F): The residue definition is fat soluble.
*: Indicates that the MRL is set at the limit of quantification.
(a): MRL is derived from the existing CXL, which is supported by data and for which no risk to consumers is identified; there are no relevant authorisations or import tolerances reported at EU level (combination A-VII in Appendix E).
(b): 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; existing CXL is covered by the recommended MRL (combination H-III 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).
Review of the existing MRLs for quinoxyfen

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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
CAC Codex Alimentarius Commission
CAS Chemical Abstract Service
CF conversion factor for enforcement residue definition to risk assessment residue definition
CIRCA (EU) Communication & Information Resource Centre Administrator
CS capsule suspension
CV coefficient of variation (relative standard deviation)
CXL codex maximum residue limit
DAR draft assessment report
DAT days after treatment
DB dietary burden
DM dry matter
DP dustyable powder
DS powder for dry seed treatment
DT$_{90}$ period required for 90% dissipation (define method of estimation)
EDI estimated daily intake
EMS evaluating Member State
eq residue expressed as a.s. equivalent
EURLs European Union Reference Laboratories for Pesticide Residues (former CRLs)
FAO Food and Agriculture Organization of the United Nations
GAP Good Agricultural Practice
GC gas chromatography
GC-MS gas chromatography with mass spectrometry
gC-MSD gas chromatography with mass spectrometry detection
GC-MS/MS gas chromatography with tandem mass spectrometry
GS growth stage
HPLC high-performance liquid chromatography
HPLC-MS high-performance liquid chromatography with mass spectrometry
HPLC-MS/MS high-performance liquid chromatography with tandem mass spectrometry
HR highest residue
IEDI international estimated daily intake
ILV independent laboratory validation
ISO International Organisation for Standardization
IUPAC International Union of Pure and Applied Chemistry
JMPR Joint Meeting of the FAO Panel of Experts on Pesticide Residues in Food and the Environment and the WHO Expert Group on Pesticide Residues (Joint Meeting on Pesticide Residues)
LC liquid chromatography
LC-MS/MS liquid chromatography with tandem mass spectrometry
LOQ limit of quantification
MRL maximum residue level
MS Member States
MS mass spectrometry detector
MS/MS tandem mass spectrometry detector
MW molecular weight
NEDI national estimated daily intake
NTMDI national theoretical maximum daily intake
OECD Organisation for Economic Co-operation and Development
P persistent
PBI plant back interval
PF processing factor
PHI preharvest interval
PRIMo (EFSA) Pesticide Residues Intake Model
PROFile (EFSA) Pesticide Residues Overview File
QuEChERS Quick, Easy, Cheap, Effective, Rugged, and Safe (analytical method)
RA risk assessment
RD residue definition
RMS rapporteur Member State
SANCO Directorate-General for Health and Consumers
SC suspension concentrate
SEU southern European Union
SMILES simplified molecular-input line-entry system
SL soluble concentrate
| Acronym | Description |
|---------|-------------|
| SP      | water soluble powder |
| STMR    | supervised trials median residue |
| TAR     | total applied radioactivity |
| TMDI    | theoretical maximum daily intake |
| TRR     | total radioactive residue |
| vP      | very persistent |
| WHO     | World Health Organization |
## Appendix A – Summary of authorised uses considered for the review of MRLs

### A.1. Import tolerance

| Crop and/or situation | MS or country | F G or I<sup>(a)</sup> | Pests or group of pests controlled | Preparation | Application | Application rate per treatment | PHI (days)<sup>(d)</sup> | Remarks |
|-----------------------|---------------|-------------------------|-----------------------------------|-------------|-------------|-----------------------------|---------------------|---------|
| Hops                  | US            | F                       | Fungus                            | SC          | Foliar treatment - general   | 150 g a.s./ha             | 21      |         |

MS: Member State; a.s.: active substance, SC: suspension concentrate.

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

<sup>(b)</sup>: CropLife International Technical Monograph no 2, 7th Edition. Revised March 2017. Catalogue of pesticide formulation types and international coding system.

<sup>(c)</sup>: 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.

<sup>(d)</sup>: 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                       | Grapes      |         | Early foliar/fruit spraying application, 1 × 375 mg a.s./L or 1 × 750 mg a.s./L | 0, 30, 45 DAT | [4-flurophenoxy-U-\(^{14}\)C]- or [2-quinoline-\(^{14}\)C]-quinoxyfen. Suspension concentrate applied directly to fruits (grape vines grown in glasshouse). Part of a whole vine was treated with 375 mg a.s./L to investigate translocation into untreated parts of the vine (FAO, 2006; United Kingdom, 2009; EFSA, 2010) |
|                                  |             |         | Late fruit spraying application, 1 × 375 mg a.s./L | 10 DAT | [4-flurophenoxy-U-\(^{14}\)C]- or [2-quinoline-\(^{14}\)C]-quinoxyfen. Suspension concentrate applied directly to fruits (grape vines grown in glasshouse) (FAO, 2006; United Kingdom, 2009; EFSA, 2010) |
|                                  | Tomato      |         | Foliar, 5 × 120 g a.s./ha (separated 7 days) | Immature fruit and foliage: 0, 7, 14, 28 days after 1st treatment (DAT), Mature fruit and foliage: 14 DAT | [4-flurophenoxy-U-\(^{14}\)C]- or [2-quinoline-\(^{14}\)C]-quinoxyfen (FAO, 2006) |
|                                  | Cucumber    |         | Foliar and fruit application, 3 × 75 mg a.s./L (separated by 10 and 26 days) | Mature fruit and foliage: 7 DAT (additional immature samples were taken just after 1st and just before 2nd and 3rd application) | [4-flurophenoxy-U-\(^{14}\)C]- or [2-quinoline-\(^{14}\)C]-quinoxyfen. Suspension concentrate. Translocation experiment done with one application only (FAO, 2006) |
|                                  | Sugar beet  |         | Foliar, 1 × 600 g a.s./ha | Immature leaves and roots: 7, 14 and 28 DAT | [4-flurophenoxy-U-\(^{14}\)C]- or [2-quinoline-\(^{14}\)C]-quinoxyfen (FAO, 2006; United Kingdom, 2009; EFSA, 2010) |
|                                  |             |         | Foliar, max. of 300 g a.s./ha in 2 applications separated by 60 days. | Immature roots and leaves: 0, 7, 14 and 28 DAT | [4-flurophenoxy-U-\(^{14}\)C]- or [2-quinoline-\(^{14}\)C]-quinoxyfen (FAO, 2006; United Kingdom, 2009, EFSA, 2010) |
|                                  | Wheat       |         | Foliar, 1 × 250 g a.s./ha at either BBCH 32 or 49 and 1 × 1,000 g a.s./ha at BBCH 32 | If application at BBCH 32: 0, 14, 29 and 105 DAT, If application at BBCH 49: 0 and 78 DAT | [4-flurophenoxy-U-\(^{14}\)C]- or [2-quinoline-\(^{14}\)C]-quinoxyfen (United Kingdom, 2000) |
| Rotational crops (available studies) | Crop groups | Crop(s) | Application(s) | PBI (DAT) | Comment/Source |
|------------------------------------|-------------|---------|----------------|-----------|----------------|
| Root/tuber crops                   | Turnip      | Bare soil, 400 g a.s./ha | 30 | [4-fluorophenoxy-U-14C]- or [2-quinoline-14C]-quinoxyfen (United Kingdom, 2000) |
| Leafy crops                        | Cabbage     | Bare soil, 400 g a.s./ha | 30 | [4-fluorophenoxy-U-14C]- or [2-quinoline-14C]-quinoxyfen (United Kingdom, 2000) |
| Pulses and oilseeds                | Sunflower   | Bare soil, 400 g a.s./ha | 30 | [4-fluorophenoxy-U-14C]- or [2-quinoline-14C]-quinoxyfen (United Kingdom, 2000) |

| Processed commodities (hydrolysis study) | Conditions | Stable? | Comment/Source |
|------------------------------------------|------------|---------|----------------|
| Pasteurisation (20 min, 90°C, pH 4)     | Yes        | Minor degradation products observed (< 9% TRR) (Austria, 2020) |
| Baking, brewing and boiling (60 min, 100°C, pH 5) | Yes        | Minor degradation products observed (< 6% TRR) (Austria, 2020) |
| Sterilisation (20 min, 120°C, pH 6)     | Yes        | Minor degradation products observed (< 2% TRR) (Austria, 2020) |
Can a general residue definition be proposed for primary crops? | Yes | Metabolism investigated in three different groups (fruits/fruiting vegetables, root crops and cereals)
---|---|---
Rotational crop and primary crop metabolism similar? | Not applicable | Residue levels were too low to allow characterisation of any possible metabolites (< 0.004 mg/kg). However, as quinoxyfen is authorised for imported crop only, a study is not required
Residue pattern in processed commodities similar to residue pattern in raw commodities? | Yes | –
Plant residue definition for monitoring (RD-Mo) | Quinoxyfen | Quinoxyfen
Plant residue definition for risk assessment (RD-RA) | Quinoxyfen | Quinoxyfen
Methods of analysis for monitoring of residues (analytical technique, matrix groups, LOQs)
- High water content, high oil content, high acid content and dry matrices:
  - LC–MS/MS, LOQ = 0.01 mg/kg in high water content (lettuce), high acid content (lemon), high oil content (oilseed rape) and dry commodities (barley)
    ILV available (validated in high oil and high water content matrices).
  - QuEChERS method, LC–MS/MS, LOQ = 0.01 mg/kg in high water content (lettuce), high acid content (orange) and dry commodities (dry beans)
    ILV available (on the same matrices).
(UK, 2017; EFSA, 2018a)
  - QuEChERS method using LC and/or GC-MS/MS, LOQ = 0.01 mg/kg in all four main matrices and in specific/difficult matrices (black tea)
(EURLs, 2020)
- Hops (no group):
  - GC-MSD, validated for hops, LOQ = 0.05 mg/kg
    ILV available on hops
(FAO, 2006; UK, 2009; EFSA, 2010)

a.s.: active substance; DAT: days after treatment; PBI: plant-back interval; BBCH: growth stages of mono- and dicotyledonous plants; TRR: total radioactive residue; LC–MS/MS: liquid chromatography with tandem mass spectrometry; QuEChERS: Quick, Easy, Cheap, Effective, Rugged, and Safe (analytical method); GC-MSD: gas chromatography with mass spectrometry detection; GC-MS/MS: gas chromatography with tandem mass spectrometry; LOQ: limit of quantification; ILV: independent laboratory validation.
### B.1.1.2. Stability of residues in plants

| Catégory | Commodity            | $T$ (°C) | Stability period | Compounds covered | Comment/Source                                                                 |
|----------|----------------------|----------|------------------|-------------------|-------------------------------------------------------------------------------|
| Dry commodities | Cereals grains and straw | −18      | 15 Months        | Quinoxyfen        | United Kingdom (2000)                                                         |
| Others   | Hops (dried cones)   | −15      | 4 Months         | Quinoxyfen        | The storage stability of quinoxyfen residues was investigated as part of the supervised residue trials (FAO, 2006) |
|          | Hops (dried cones)   | −17      | 7 Months         | Quinoxyfen        | The storage stability of quinoxyfen residues was investigated as part of the supervised residue trials (Austria, 2020) |

### 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) | $CF^{(d)}$ |
|-----------|--------------------------|---------------------------------------------------------------|-----------------|------------------------|-------------------|----------------------|------------|
| Hops      | Import (US)              | 0.39; 0.81; 0.86; 1.22                                        | Trials on hops compliant with GAP (Austria, 2020)         | 3.00                  | 1.22              | 0.84                 | 1.00       |

GAP: Good Agricultural Practice; OECD: Organisation for Economic Co-operation and Development; MRL: maximum residue level.

\(^{(a)}\): 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.

\(^{(d)}\): Conversion factor to recalculate residues according to the residue definition for monitoring to the residue definition for risk assessment.
B.1.2.2. Residues in rotational crops

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

| No | No study was required. However, the confined metabolism study available showed no significant uptake from the soil by the plants (in all crops, residue levels were below 0.004 mg eq/kg) |
|---|---|

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

| Not applicable | No study available and not required for the current assessment due to high persistence of quinoxyfen in soil, the effect of multiannual applications could be investigated further to confirm the limited uptake by the plants. However, as quinoxyfen is only authorised for imported crops (hop), a study is not deemed necessary |
|---|---|

B.1.2.3. Processing factors

No processing studies were submitted nor required in the framework of the present review.

B.2. Residues in livestock

Investigations on quinoxyfen residues in livestock are not required since quinoxyfen is not authorised on crops that are fed to livestock. However, studies are available and reported below for completeness.

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/day) | Duration (days) | Comment/Source |
|---|---|---|---|---|
| Laying hen | 1.04–1.06 | 7 | [4-fluorophenoxy-U-14C]- or [2-quinoline-14C]-quinoxyfen (Austria, 2020) Dose rate recalculated assuming body weight of 1.9 kg and feed intake of 0.13 kg per day |
| Lactating ruminants | 0.29 | 5 | Study on goats, [4-fluorophenoxy-U-14C]- or [2-quinoline-14C]-quinoxyfen (United Kingdom, 2000) Dose rate recalculated assuming body weight of 70 kg and feed intake of 2 kg per day |
### Time needed to reach a plateau concentration in milk and eggs (days)

|                | Milk: -          | No detailed data available. |
|----------------|------------------|-----------------------------|
|                | Eggs: 4–7        | -                           |

### Metabolism in rat and ruminant similar

|                | Yes              | -                           |

### Can a general residue definition be proposed for animals?

|                | Not applicable   | -                           |

### Animal residue definition for monitoring (RD-Mo)

|                | Quinoxyfen, by default |

### Animal residue definition for risk assessment (RD-RA)

|                | Quinoxyfen, by default. However, in case a residue definition for livestock would need to be established in the future, the inclusion of additional metabolites to the residue definition for risk assessment may need to be reconsidered |

### Fat soluble residues

|                | Yes | Log POW = 5.1 (> 3) (EFSA, 2018a) |

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

|                | Milk, Eggs, Muscle, Fat, Kidney, Liver (United Kingdom, 2017; EFSA, 2018a): |
|----------------|--------------------------------------------------------------------------------|
|                | HPLC–MS/MS, LOQ = 0.01 mg/kg in milk, egg, fat and liver. ILV available (muscle, fat, egg) |
|                | QuEChERS multiresidue method with HPLC–MS/MS, LOQ = 0.01 mg/kg in milk, meat, kidney and egg. ILV available (meat, milk) |

|                | Milk, Eggs, Muscle, Fat, Kidney, Liver, Honey (EURLs, 2020): |
|----------------|----------------------------------------------------------------|
|                | GC–MS/MS, LOQ = 0.01 mg/kg in muscle and milk |
|                | Screening validation data show that quinoxyfen can be monitored with an SDL of 0.0025 mg/kg in muscle and honey, and with an SDL of 0.005 mg/kg in milk and egg |
|                | It is concluded in EURLs report that quinoxyfen can be monitored in milk, muscle, egg and honey with an LOQ of 0.01 mg/kg. An LOQ of 0.01 mg/kg is expected to be achievable also for the remaining main groups of animal products (liver, kidney, fat) |

bw: body weight; P: partition coefficient between n–octanol and water; QuEChERS: Quick, Easy, Cheap, Effective, Rugged, and Safe (analytical method); HPLC–MS/MS: high-performance liquid OW chromatography with tandem mass spectrometry; GC–MS/MS: gas chromatography with tandem mass spectrometry; LOQ: limit of quantification; ILV: independent laboratory validation; SDL: screening detection limit.
### B.2.1.2. Stability of residues in livestock

| Animal products (available studies) | Animal | Commodity | T (°C) | Stability period Value | Unit | Compounds covered | Comment/Source                  |
|------------------------------------|--------|-----------|--------|------------------------|------|-------------------|-------------------------------|
| Bovine                             | Muscle | –20       | 6      | Months                 |      | Quinoxyfen        | United Kingdom (2000)        |
| Bovine                             | Fat    | –20       | 7      | Months                 |      | Quinoxyfen        | United Kingdom (2000)        |
| Bovine                             | Liver  | –20       | 10     | Months                 |      | Quinoxyfen        | United Kingdom (2000)        |
| Bovine                             | Kidney | –20       | 6      | Months                 |      | Quinoxyfen        | United Kingdom (2000)        |
| Bovine                             | Milk   | –20       | 8      | Months                 |      | Quinoxyfen        | United Kingdom (2000)        |

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

Studies not available and not required.
### B.3. Consumer risk assessment

#### B.3.1. Consumer risk assessment without consideration of the existing CXLs

No acute consumer exposure assessment was performed since no acute reference dose (ARfD) has been considered necessary (European Commission, 2003).

| ADI | 0.2 mg/kg bw per day (European Commission, 2003) (toxicological reference value never peer-reviewed by EFSA) |
| 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.3.1) | Scenario EU: 0% ADI (UK adult, DE General) |
| NEDI (% ADI) | Not assessed in this review |
| Assumptions made for the calculations | Scenario EU: The calculation is based on the median residue levels (STMR) derived for hops according to the GAP reported in this review. 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.3.2. Consumer risk assessment with consideration of the existing CXLs

No acute consumer exposure assessment was performed since no acute reference dose (ARfD) has been considered necessary (European Commission, 2003).

| ADI | 0.2 mg/kg bw per day (European Commission, 2003) (toxicological reference value never peer-reviewed by EFSA) |
| --- | --- |

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.3.1)

Scenario CX:

1% ADI (ES adult)

NEDI (% ADI)

Assumptions made for the calculations

Scenario CX:
The calculation is based on the median residue level (SMTR) derived for hop according to the GAP reported in this review. For commodities where CXLs were established, the SMTR derived by JMPR was considered. The contributions of commodities where no uses were reported in the framework of the MRL review were not included in the calculation

ADH: acceptable daily intake; bw: body weight; TMDI: theoretical maximum daily intake; PRIMo: (EFSA) Pesticide Residues Intake Model; NTMDI: national theoretical maximum daily intake; IEDI: international estimated daily intake; NEDI: national estimated daily intake; JMPR: Joint Meeting on Pesticide Residues; STMR: supervised trials median residue; GAP: Good Agricultural Practice

B.4. Proposed MRLs

| Code number | Commodity | Existing EU MRL (mg/kg) | Existing CXL (mg/kg) | Outcome of the review MRL (mg/kg) | Comment |
| --- | --- | --- | --- | --- | --- |
| Enforcement residue definition: quinoxyfen(F) | | | | | |
| 140020 | Cherries | 0.3 | 0.4 | 0.4 | Recommended (a) |
| 151010 | Table grapes | 1 | 2 | 2 | Recommended (a) |
| 151020 | Wine grapes | 1 | 2 | 2 | Recommended (a) |
| 152000 | Strawberries | 0.3 | 1 | 1 | Recommended (a) |
| 154030 | Currants (red, black and white) | 2 | 1 | 1 | Recommended (a) |
| 231020 | Peppers | 0.02 | 1 | 1 | Recommended (a) |
| 233010 | Melons | 0.05 | 0.1 | 0.1 | Recommended (a) |
| 251020 | Lettuce | 0.02 | 20 | 20 | Recommended (a) |
| 500010 | Barley grain | 0.2 | 0.01* | 0.01* | Recommended (a) |
| 500090 | Wheat grain | 0.02 | 0.01* | 0.01* | Recommended (a) |
| 700000 | Hops (dried), including hop pellets and unconcentrated powder | 2 | 1 | 3 | Recommended (a) |
| 900010 | Sugar beet (root) | 0.02 | 0.03 | 0.03 | Recommended (a) |
| 1011010 | Swine meat | 0.2 | 0.2 | 0.2 | Recommended (a) |
| 1011020 | Swine fat (free of lean meat) | 0.2 | 0.2 | 0.2 | Recommended (a) |
| 1011030 | Swine liver | 0.2 | 0.01* | 0.01* | Recommended (a) |
| 1011040 | Swine kidney | 0.2 | 0.01* | 0.01* | Recommended (a) |
| 1012010 | Bovine meat | 0.2 | 0.2 | 0.2 | Recommended (a) |
| Code number | Commodity      | Existing EU MRL (mg/kg) | Existing CXL (mg/kg) | Outcome of the review |
|-------------|----------------|-------------------------|----------------------|-----------------------|
| 1012020     | Bovine fat     | 0.2                     | 0.2                  | Recommended (a)       |
| 1012030     | Bovine liver   | 0.2                     | 0.01*                | Recommended (a)       |
| 1012040     | Bovine kidney  | 0.2                     | 0.01*                | Recommended (a)       |
| 1013010     | Sheep meat     | 0.2                     | 0.2                  | Recommended (a)       |
| 1013020     | Sheep fat      | 0.2                     | 0.2                  | Recommended (a)       |
| 1013030     | Sheep liver    | 0.2                     | 0.01*                | Recommended (a)       |
| 1013040     | Sheep kidney   | 0.2                     | 0.01*                | Recommended (a)       |
| 1014010     | Goat meat      | 0.2                     | 0.2                  | Recommended (a)       |
| 1014020     | Goat fat       | 0.2                     | 0.2                  | Recommended (a)       |
| 1014030     | Goat liver     | 0.2                     | 0.01*                | Recommended (a)       |
| 1014040     | Goat kidney    | 0.2                     | 0.01*                | Recommended (a)       |
| 1015010     | Horse meat     | 0.2                     | 0.2                  | Recommended (a)       |
| 1015020     | Horse fat      | 0.2                     | 0.2                  | Recommended (a)       |
| 1015030     | Horse liver    | 0.2                     | 0.01*                | Recommended (a)       |
| 1015040     | Horse kidney   | 0.2                     | 0.01*                | Recommended (a)       |
| 1016010     | Poultry meat   | 0.2                     | 0.02                 | Recommended (a)       |
| 1016020     | Poultry fat    | 0.2                     | 0.02                 | Recommended (a)       |
| 1016030     | Poultry liver  | 0.2                     | 0.01*                | Recommended (a)       |
| 1020010     | Cattle milk    | 0.05                    | 0.01*                | Recommended (a)       |
| 1020020     | Sheep milk     | 0.05                    | 0.01*                | Recommended (a)       |
| 1020030     | Goat milk      | 0.05                    | 0.01*                | Recommended (a)       |
| 1020040     | Horse milk     | 0.05                    | 0.01*                | Recommended (a)       |
| 1030000     | Birds’ eggs    | 0.02                    | 0.01*                | Recommended (a)       |
| –           | Other commodities of plant and/or animal origin | See Reg. (EU) No 36/2014 | – | Further consideration needed (c) |

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

(F): The residue definition is fat soluble.

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

(a): MRL is derived from the existing CXL, which is supported by data and for which no risk to consumers is identified; there are no relevant authorisations or import tolerances reported at EU level (combination A-VII in Appendix E).

(b): 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; existing CXL is covered by the recommended MRL (combination H-III 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)

**PRIMo(EU)**

**LOQs (mg/kg) range from:** 0.01 to 0.02

**ADI (mg/kg bw/day):** 0.2

**ARfD (mg/kg bw):** not necessary

**Source of ADI:** EC

**Source of ARfD:** EC

**EFSA PRIMo revision 3.1; 2019/03/19**

**Year of evaluation:** 2003

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

| Commodity/group of commodities | MRLs set at the LOQ (in % of ADI) | commodities not under assessment (in % of ADI) |
|-------------------------------|----------------------------------|-----------------------------------------------|
| Wheat                         | 1%                               | 0.0%                                          |
| Poultry: Muscle/meat          | 0.9%                             | 1.77%                                         |
| Wheat                         | 0.9%                             | 1.71%                                         |
| Wheat                         | 0.8%                             | 1.55%                                         |
| Strawberries                  | 0.8%                             | 1.52%                                         |
| Wheat                         | 0.8%                             | 1.31%                                         |
| Table grapes                  | 0.7%                             | 1.51%                                         |
| Strawberries                  | 0.7%                             | 1.26%                                         |
| Wheat                         | 0.6%                             | 1.12%                                         |
| Table grapes                  | 0.4%                             | 0.86%                                         |
| Strawberries                  | 0.4%                             | 0.78%                                         |
| Wheat                         | 0.4%                             | 0.74%                                         |
| Table grapes                  | 0.3%                             | 0.72%                                         |
| Strawberries                  | 0.3%                             | 0.69%                                         |
| Wheat                         | 0.2%                             | 0.66%                                         |
| Strawberries                  | 0.2%                             | 0.59%                                         |
| Wheat                         | 0.2%                             | 0.57%                                         |
| Strawberries                  | 0.2%                             | 0.47%                                         |
| Wheat                         | 0.2%                             | 0.45%                                         |
| Strawberries                  | 0.2%                             | 0.37%                                         |
| Wheat                         | 0.2%                             | 0.34%                                         |
| Strawberries                  | 0.2%                             | 0.3%                                          |
| Wheat                         | 0.2%                             | 0.23%                                         |
| Strawberries                  | 0.2%                             | 0.2%                                          |
| Wheat                         | 0.1%                             | 0.12%                                         |
| Strawberries                  | 0.1%                             | 0.1%                                          |
| Wheat                         | 0.0%                             | 0.0%                                          |
| Wheat                         | 0.0%                             | 0.0%                                          |
| Wheat                         | 0.0%                             | 0.0%                                          |
| Wheat                         | 0.0%                             | 0.0%                                          |
| Wheat                         | 0.0%                             | 0.0%                                          |

**Chronic risk assessment:** JMPR methodology (IEDI/TMDI)

**Conclusion:**

- FI 3 yr
- LT adult
- FR toddler 2 3 yr
- Strawberries
- Lettuce
- Wheat
- Milk: Cattle
- Table grapes
- Wine grapes
- Sweet peppers/bell peppers
- Sugar beet roots
- Table grapes
- Strawberries
- Wheat

**Toxicological reference values**

| Normal mode | Input values | Supplementary results – chronic risk assessment | Details – acute risk assessment/children | Details – acute risk assessment/adults | Details – chronic risk assessment |
|-------------|--------------|-----------------------------------------------|-----------------------------------------|----------------------------------------|---------------------------------|

**Supplementary results – chronic risk assessment**

- The estimated long-term dietary intake (TMDI/NEDI/IEDI) was below the ADI. The long-term intake of residues of quinoxyfen (F) is unlikely to present a public health concern.
As an ARfD is not necessary/not applicable, no acute risk assessment is performed.

### Show results for all crops

| Unprocessed commodities | Processed commodities |
|-------------------------|-----------------------|
| **Results for children** | **Results for adults** |
| No. of commodities for which ARfD/ADI is exceeded (IESTI): | No. of commodities for which ARfD/ADI is exceeded (IESTI): |
| | | |
| | | |

| | | | | | | | |
| | | | | | | | |

**Total number of commodities exceeding the ARfD/ADI in children and adult diets (IESTI calculation)**

| | | | | | | | |
| | | | | | | | |

**Conclusion:**
### quinoxyfen (F)

#### Toxicological reference values

- **ADI (mg/kg bw/day):** 0.2
- **ARfD (mg/kg bw):** not necessary
- **Source of ADI:** EC
- **Source of ARfD:** EC

#### EFSA PRIMo revision 3.1; 2019/03/19
- **Year of evaluation:** 2003

#### Calculated exposure (% of ADI)

| Source | Calculated exposure (% of ADI) | Exposure resulting from | MRLs set at the LOQ (% of ADI) | Commodities not under assessment (% of ADI) | % of total |
|--------|--------------------------------|-------------------------|--------------------------|--------------------------------------------|-----------|
| DE total | 0.0% | DE general | 0.01 | 0.0% | HOPS (dried) | FRUIT AND TREE NUTS | 0.0% | 0.0% | 0.0% | 0.0% | 0.0% |
| DE child | 0.0% | DE general | 0.00 | 0.0% | HOPS (dried) | FRUIT AND TREE NUTS | 0.0% | 0.0% | 0.0% | 0.0% | 0.0% |
| US general | 0.0% | DE women 16-50 yr | 0.00 | 0.0% | HOPS (dried) | FRUIT AND TREE NUTS | 0.0% | 0.0% | 0.0% | 0.0% | 0.0% |
| US general | 0.0% | US pregnant | 0.00 | 0.0% | HOPS (dried) | FRUIT AND TREE NUTS | 0.0% | 0.0% | 0.0% | 0.0% | 0.0% |
| US general | 0.0% | US lactating | 0.00 | 0.0% | HOPS (dried) | FRUIT AND TREE NUTS | 0.0% | 0.0% | 0.0% | 0.0% | 0.0% |
| US general | 0.0% | US vegetarians | 0.00 | 0.0% | HOPS (dried) | FRUIT AND TREE NUTS | 0.0% | 0.0% | 0.0% | 0.0% | 0.0% |
| DE general | 0.0% | DE child | 0.00 | 0.0% | HOPS (dried) | FRUIT AND TREE NUTS | 0.0% | 0.0% | 0.0% | 0.0% | 0.0% |
| DE child | 0.0% | DE child | 0.00 | 0.0% | HOPS (dried) | FRUIT AND TREE NUTS | 0.0% | 0.0% | 0.0% | 0.0% | 0.0% |
| DE child | 0.0% | DE child | 0.00 | 0.0% | HOPS (dried) | FRUIT AND TREE NUTS | 0.0% | 0.0% | 0.0% | 0.0% | 0.0% |
| DE child | 0.0% | DE child | 0.00 | 0.0% | HOPS (dried) | FRUIT AND TREE NUTS | 0.0% | 0.0% | 0.0% | 0.0% | 0.0% |
| DE child | 0.0% | DE child | 0.00 | 0.0% | HOPS (dried) | FRUIT AND TREE NUTS | 0.0% | 0.0% | 0.0% | 0.0% | 0.0% |
| DE child | 0.0% | DE child | 0.00 | 0.0% | HOPS (dried) | FRUIT AND TREE NUTS | 0.0% | 0.0% | 0.0% | 0.0% | 0.0% |
| DE child | 0.0% | DE child | 0.00 | 0.0% | HOPS (dried) | FRUIT AND TREE NUTS | 0.0% | 0.0% | 0.0% | 0.0% | 0.0% |

**Conclusion:**

The estimated long-term dietary intake (TMDI/NEDI/IEDI) was below the ADI.

The long-term intake of residues of quinoxyfen (F) is unlikely to present a public health concern.

**Details – acute risk assessment**: No international Codex standard was available for quinoxyfen.

**Details – chronic risk assessment**: JMPR methodology (IEDI/TMDI).

**Input values**

- **Source of TMDI**: JMPR (2019/03/19)
As an ARfD is not necessary/not applicable, no acute risk assessment is performed.

| Details – acute risk assessment/children | Details – acute risk assessment/adults/general population |
|-----------------------------------------|----------------------------------------------------------|

### Show results for all crops

| Unprocessed commodities | Results for children | Results for adults |
|-------------------------|----------------------|--------------------|
| No. of commodities for which ARfD/ADI is exceeded (ESTI): | — | — |

| MRL/input | Exposure | Highest % of ARfD/ADI Commodities | MRL/input | Exposure | Highest % of ARfD/ADI Commodities |
|-----------|----------|-----------------------------------|-----------|----------|-----------------------------------|
| for RA (mg/kg) | (µg/kg bw) | | for RA (mg/kg) | (µg/kg bw) |

| Processed commodities | Results for children | Results for adults |
|-----------------------|----------------------|--------------------|
| No of processed commodities for which ARfD/ADI is exceeded (ESTI): | — | — |

| MRL/input | Exposure | Highest % of ARfD/ADI Processed commodities | MRL/input | Exposure | Highest % of ARfD/ADI Processed commodities |
|-----------|----------|---------------------------------------------|-----------|----------|---------------------------------------------|
| for RA (mg/kg) | (µg/kg bw) | | for RA (mg/kg) | (µg/kg bw) |

### Conclusion:

Total number of commodities exceeding the ARfD/ADI in children and adult diets (ESTI calculation)

Results for adults

No. of commodities for which ARfD/ADI is exceeded (ESTI):

Results for children

No. of commodities for which ARfD/ADI is exceeded (ESTI):

Details – acute risk assessment/children

Details – acute risk assessment/adults
Appendix D – Input values for the exposure calculations

D.1. Livestock dietary burden calculations
Not relevant.

D.2. Consumer risk assessment without consideration of the existing CXLs

| Commodity               | Chronic risk assessment | Input value (mg/kg) | Comment   |
|-------------------------|-------------------------|---------------------|-----------|
| Risk assessment residue definition: quinoxyfen |
| Hops (dried)            |                         | 0.835               | STMR      |

STMR: median residue levels.

D.3. Consumer risk assessment with consideration of the existing CXLs

| Commodity               | Chronic risk assessment | Input value (mg/kg) | Comment |
|-------------------------|-------------------------|---------------------|---------|
| Risk assessment residue definition: quinoxyfen |
| Cherries (sweet)        |                         | 0.12                | STMR (CXL) |
| Table grapes            |                         | 0.13                | STMR (CXL) |
| Wine grapes             |                         | 0.13                | STMR (CXL) |
| Strawberries            |                         | 0.33                | STMR (CXL) |
| Currants (red, black and white) |             | 0.2                 | STMR (CXL) |
| Sweet peppers/bell peppers |                     | 0.15                | STMR (CXL) |
| Melons                  |                         | 0.02                | STMR (CXL) |
| Lettuces                |                         | 3.85                | STMR (CXL) |
| Barley                  |                         | 0.01*               | STMR (CXL) |
| Wheat                   |                         | 0.01*               | STMR (CXL) |
| Hops (dried)            |                         | 0.835               | STMR      |
| Sugar beet roots        |                         | 0.01*               | STMR (CXL) |
| Swine: Meat             |                         | 0.002               | 0.8 STMR muscle + 0.2 STMR fat (CXL) |
| Swine: Fat tissue       |                         | 0.01*               | STMR (CXL) |
| Swine: Liver            |                         | 0.01*               | STMR (CXL) |
| Swine: Kidney           |                         | 0.01*               | STMR (CXL) |
| Bovine: Meat            |                         | 0.002               | 0.8 STMR muscle + 0.2 STMR fat (CXL) |
| Bovine: Fat tissue      |                         | 0.01*               | STMR (CXL) |
| Bovine: Liver           |                         | 0.01*               | STMR (CXL) |
| Bovine: Kidney          |                         | 0.01*               | STMR (CXL) |
| Sheep: Meat             |                         | 0.002               | 0.8 STMR muscle + 0.2 STMR fat (CXL) |
| Sheep: Fat tissue       |                         | 0.01*               | STMR (CXL) |
| Sheep: Liver            |                         | 0.01*               | STMR (CXL) |
| Sheep: Kidney           |                         | 0.01*               | STMR (CXL) |
| Goat: Meat              |                         | 0.002               | 0.8 STMR muscle + 0.2 STMR fat (CXL) |
| Goat: Fat tissue        |                         | 0.01*               | STMR (CXL) |
| Goat: Liver             |                         | 0.01*               | STMR (CXL) |
| Goat: Kidney            |                         | 0.01*               | STMR (CXL) |
| Equine: Meat            |                         | 0.002               | 0.8 STMR muscle + 0.2 STMR fat (CXL) |
| Commodity       | Input value (mg/kg) | Comment                                      |
|-----------------|---------------------|----------------------------------------------|
| Equine: Fat tissue | 0.01*               | STMR (CXL)                                  |
| Equine: Liver    | 0.01*               | STMR (CXL)                                  |
| Equine: Kidney   | 0.01*               | STMR (CXL)                                  |
| Poultry: Meat    | 0.02                | 0.9 STMR muscle + 0.1 STMR fat (CXL)         |
| Poultry: Fat tissue | 0.013              | STMR (CXL)                                  |
| Poultry: Liver   | 0.009               | STMR (CXL)                                  |
| Milk: Cattle     | 0.002               | STMR (CXL)                                  |
| Milk: Sheep      | 0.002               | STMR (CXL)                                  |
| Milk: Goat       | 0.002               | STMR (CXL)                                  |
| Milk: Horse      | 0.002               | STMR (CXL)                                  |
| Eggs: Chicken    | 0.003               | STMR (CXL)                                  |

STMR: median residue levels; CXL: Codex maximum residue limit.
*: Indicates that the input value is proposed at the limit of quantification.
Appendix E – Decision tree for deriving MRL recommendations

1. **Evaluation of the GAPs and available residues data at EU level**
   - GAP or QM ≥ 0.1 mg/kg QM in EU?
     - Yes → **MRL and RA derived in section 3**
     - No → GAP or QM < 0.1 mg/kg QM in EU?
       - Yes → MRL fully supported by data?
         - Yes → Risk identified?
           - Yes → Fall-back MRL available?
             - Yes → MRL is recommended. (H)
             - No → Recommendations resulting from EU authorisations and import tolerances
               - (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) Specific LOQ or default MRL?
               - (G) Specific LOQ or default MRL?
               - (H) MRL is recommended.
         - No → Not considered for the RA
       - No → RD-RA derived for this commodity?
         - Yes → MRL and RA derived in section 3?
           - Yes → Risk identified?
             - Yes → Fall-back MRL available?
               - Yes → MRL is recommended. (H)
               - No → Recommendations resulting from EU authorisations and import tolerances
                 - (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) Specific LOQ or default MRL?
                 - (G) Specific LOQ or default MRL?
                 - (H) MRL is recommended.
             - No → Not considered for the RA
           - No → MRL fully supported by data?
             - Yes → Risk identified?
               - Yes → Fall-back MRL available?
                 - Yes → MRL is recommended. (H)
                 - No → Recommendations resulting from EU authorisations and import tolerances
                   - (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) Specific LOQ or default MRL?
                   - (G) Specific LOQ or default MRL?
                   - (H) MRL is recommended.
             - No → Not considered for the RA
         - No → Not considered for the RA
   - No → Not considered for the RA

2. **Consumer risk assessment for GAPs evaluated at EU level - EU scenarios**
   - Not considered for the RA
   - Not considered for the RA
   - 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 → MRL is recommended. (H)
           - No → Recommendations resulting from EU authorisations and import tolerances
             - (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) Specific LOQ or default MRL?
             - (G) Specific LOQ or default MRL?
             - (H) MRL is recommended.
         - No → Tentative median/highest values are included in the RA?
           - Yes → Risk identified?
             - Yes → Fall-back MRL available?
               - Yes → MRL is recommended. (H)
               - No → Recommendations resulting from EU authorisations and import tolerances
                 - (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) Specific LOQ or default MRL?
                 - (G) Specific LOQ or default MRL?
                 - (H) MRL is recommended.
             - No → Not considered for the RA
           - No → Not considered for the RA
     - No → Not considered for the RA

3. **Recommendations resulting from EU authorisations and import tolerances**
   - Fall-back MRL available?
     - Yes → MRL is recommended. (H)
     - No → Not considered for the RA
   - Median/highest values are included in the RA?
     - Yes → Not considered for the RA
     - No → 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 → MRL is recommended. (H)
             - No → Recommendations resulting from EU authorisations and import tolerances
               - (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) Specific LOQ or default MRL?
               - (G) Specific LOQ or default MRL?
               - (H) MRL is recommended.
           - No → Tentative median/highest values are included in the RA?
             - Yes → Risk identified?
               - Yes → Fall-back MRL available?
                 - Yes → MRL is recommended. (H)
                 - No → Recommendations resulting from EU authorisations and import tolerances
                   - (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) Specific LOQ or default MRL?
                   - (G) Specific LOQ or default MRL?
                   - (H) MRL is recommended.
             - No → Not considered for the RA
           - No → Not considered for the RA
         - No → Not considered for the RA
       - No → Not considered for the RA
     - No → Not considered for the RA

4. **Comparison with CXLs**
   - Is RD-RA derived for this commodity?
     - Yes → Not considered for the RA
     - No → RD-RA derived for this commodity?
       - Yes → MRL And RA derived in section 3?
         - Yes → Risk identified?
           - Yes → Fall-back MRL available?
             - Yes → MRL is recommended. (H)
             - No → Recommendations resulting from EU authorisations and import tolerances
               - (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) Specific LOQ or default MRL?
               - (G) Specific LOQ or default MRL?
               - (H) MRL is recommended.
           - No → Not considered for the RA
         - No → MRL fully supported by data?
           - Yes → Risk identified?
             - Yes → Fall-back MRL available?
               - Yes → MRL is recommended. (H)
               - No → Recommendations resulting from EU authorisations and import tolerances
                 - (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) Specific LOQ or default MRL?
                 - (G) Specific LOQ or default MRL?
                 - (H) MRL is recommended.
             - No → Not considered for the RA
           - No → Not considered for the RA
         - No → Not considered for the RA
       - No → Not considered for the RA
   - No → Not considered for the RA
## Appendix F – Used compound codes

| Code/trivial name<sup>(a)</sup> | IUPAC name/SMILES notation/InChiKey<sup>(b)</sup> | Structural formula<sup>(c)</sup> |
|--------------------------------|-----------------------------------------------|---------------------------------|
| **Quinoxyfen**                 | 5,7-dichloro-4-quinolyl 4-fluorophenyl ether Fc1ccc(cc1)Oc1ccnc2cc(Cl)cc(Cl)c12 WRPIRSINYZBGPK-UHFFFAOYSA-N | ![Structural formula](image) |
| **4-fluorophenol**             | 4-fluorophenol Fc1ccc(O)cc1 RHIMPLDJXGPMEX-UHFFFAOYSA-N | ![Structural formula](image) |
| **3-hydroxyquinoxyfen**        | 5,7-dichloro-4-(4-fluorophenoxy)-3-hydroxy-quinoline Fc1ccc(cc1)Oc1c2c(Cl)cc(Cl)cc2ncc1O GNQKYTEVIIUPMTP-UHFFFAOYSA-N | ![Structural formula](image) |
| **Sulfate conjugates of hydroxy quinoxyfen** | Not defined | ![Structural formula](image) |
| **Sulfate conjugates of bis-hydroxy quinoxyfen** | Not defined | ![Structural formula](image) |
| **DCHQ** (dichloro-hydroxyquinoline) | 5,7-dichloro-4-hydroxyquinoline Clc1cc2nccc(O)c2c(Cl)c1 GESHYASHHORJB-UHFFFAOYSA-N | ![Structural formula](image) |

<sup>(a): The metabolite name in bold is the name used in the conclusion.</sup>  
<sup>(b): ACD/Name 2019.1.1 ACD/Labs 2019 Release (File version N05E41, Build 110555, 18 July 2019).</sup>  
<sup>(c): ACD/ChemSketch 2019.1.1 ACD/Labs 2019 Release (File version C05H41, Build 110712, 24 July 2019).</sup>