Review of the existing maximum residue levels for 8-hydroxyquinoline according to Article 12 of Regulation (EC) No 396/2005

European Food Safety Authority (EFSA), Maria Anastassiadou, Giulia Bellisai, Giovanni Bernasconi, Alba Brancato, Luis Carrasco Cabrera, Lucien Ferreira, Luna Greco, Samira Jarrah, Aija Kazocina, Renata Leuschner, Jose Oriol Magrans, Ileana Miron, Stefanie Nave, Ragnor Pedersen, Hermine Reich, Miguel Santos, Alessia Pia Scarlato, Anne Theobald, Benedicte Vagenende and Alessia Verani

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 8-hydroxyquinoline. To assess the occurrence of 8-hydroxyquinoline residues in plants, processed commodities, rotational crops and livestock, EFSA considered the conclusions derived in the framework of Commission Regulation (EC) No 33/2008, as well as the European authorisations reported by Member States (including the supporting residues data). Based on the assessment of the available data, MRL proposals were derived and a consumer risk assessment was carried out. Although no apparent risk to consumers was identified, some information required by the regulatory framework was missing. Hence, the consumer risk assessment is considered indicative only and all MRL proposals derived by EFSA still require further consideration by risk managers.

© 2021 European Food Safety Authority. EFSA Journal published by John Wiley and Sons Ltd on behalf of European Food Safety Authority.

Keywords: 8-hydroxyquinoline, MRL review, Regulation (EC) No 396/2005, consumer risk assessment, fungicide, bactericide

Requestor: European Commission

Question number: EFSA-Q-2011-01093

Correspondence: pesticides.mrl@efsa.europa.eu
Declarations of interest: The declarations of interest of all scientific experts active in EFSA’s work are available at https://ess.efsa.europa.eu/doi/doiweb/doisearch.

Acknowledgement: EFSA wishes to thank the rapporteur Member State Spain for the preparatory work and Stathis Anagnos, Laszlo Bura and Silvia Ruocco for the support provided to this scientific output.

Suggested citation: EFSA (European Food Safety Authority), Anastassiadou M, Bellisai G, Bernasconi G, Brancato A, Carrasco Cabrera L, Ferreira L, Greco L, Jarrah S, Kazocina A, Leuschner R, Magrans JO, Miron I, Nave S, Pedersen R, Reich H, Santos M, Scarlato AP, Theobald A, Vagenende B and Verani A, 2021. Reasoned opinion on the review of the existing maximum residue levels for 8-hydroxyquinoline according to Article 12 of Regulation (EC) No 396/2005. EFSA Journal 2021;19(4):6566, 30 pp. https://doi.org/10.2903/j.efsa.2021.6566

ISSN: 1831-4732

© 2021 European Food Safety Authority. EFSA Journal published by John Wiley and Sons Ltd on behalf of European Food Safety Authority.

This is an open access article under the terms of the Creative Commons Attribution-NoDerivs License, which permits use and distribution in any medium, provided the original work is properly cited and no modifications or adaptations are made.

The EFSA Journal is a publication of the European Food Safety Authority, a European agency funded by the European Union.
Summary

8-Hydroxyquinoline was approved on 1 January 2012 by means of Commission Implementing Regulation (EU) No 993/2011 in the framework of Regulation (EC) No 1107/2009 as amended by Commission Implementing Regulations (EU) No 540/2011 and 541/2011.

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

As the basis for the MRL review, on 15 April 2020 EFSA initiated the collection of data for this active substance. In a first step, Member States and the United Kingdom were invited to submit by 15 May 2020 their national Good Agricultural Practices (GAPs) in a standardised way, in the format of specific GAP forms, allowing the designated rapporteur Member State, Spain, to identify the critical GAPs in the format of a specific GAP overview file. Subsequently, Member States and the United Kingdom were requested to provide residue data supporting the critical GAPs, within a period of 1 month, by 1 August 2020. On the basis of all the data submitted by Member States, the United Kingdom 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 16 October 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, the United Kingdom and the EURLs, and taking into account the conclusions derived by EFSA in the framework of Commission Regulation (EC) No 33/2008, EFSA prepared in February 2021 a draft reasoned opinion, which was circulated to Member States and EURLs for consultation via a written procedure. Comments received by 03 March 2021 were considered during the finalisation of this reasoned opinion. The following conclusions are derived.

The metabolism of 8-hydroxyquinoline in plant was investigated in primary crops. According to the results of the metabolism study, the residue definition for enforcement can be proposed as ‘8-hydroxyquinoline and its salts expressed as 8-hydroxyquinoline’. The risk assessment residue definition can be proposed as ‘8-hydroxyquinoline (free and conjugated) and its salts expressed as 8-hydroxyquinoline’. These residue definitions are restricted to fruit crops only and for treatments by soil drip irrigation.

Specific residue definitions for rotational and processed commodities were not deemed necessary considering the very limited persistence of 8-hydroxyquinoline in the soil and the results from the residue trials (residues in the raw commodities were below 0.01 mg/kg) and the risk assessment (total theoretical maximum daily intake is below 10% of the acceptable daily intake (ADI)).

Fully validated analytical methods are available for the enforcement of the proposed residue definition in high water and acidic commodities at the limit of quantification (LOQ) of 0.01 mg/kg. According to the EURLs, using QuEChERS combined with APCI-LC-MS/MS, this LOQ is achievable in high water and acidic commodities while a higher LOQ of 0.02 mg/kg is achievable in dry and high fat content matrices.

Available residue trials data were considered sufficient to derive MRL proposals as well as risk assessment values for all commodities under evaluation. Considering the missing residue trials on strawberries, the MRL proposal for this commodity should be considered tentative only.

8-Hydroxyquinoline 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.

Chronic and acute consumer exposure resulting from the authorised uses reported in the framework of this review was calculated using revision 3.1 of the EFSA PRIMo. The highest chronic exposure was calculated for GEMS/Food G06, representing 0.3% of the ADI, and the highest acute exposure was calculated for melons, representing 6% of the acute reference dose (ARfD).
# Table of contents

Abstract ................................................................................................................................................... 1  
Summary ................................................................................................................................................. 3  
Background ............................................................................................................................................. 5  
Terms of Reference .................................................................................................................................. 6  
The active substance and its use pattern ................................................................................................. 7  
Assessment .............................................................................................................................................. 7  
1. Residues in plants .................................................................................................................................. 8  
1.1. Nature of residues and methods of analysis in plants ........................................................................ 8  
1.1.1. Nature of residues in primary crops ................................................................................................. 8  
1.1.2. Nature of residues in rotational crops .............................................................................................. 8  
1.1.3. Nature of residues in processed commodities ................................................................................... 8  
1.1.4. Methods of analysis in plants ........................................................................................................... 8  
1.1.5. Stability of residues in plants ........................................................................................................... 8  
1.1.6. Proposed residue definitions ........................................................................................................... 9  
1.2. Magnitude of residues in plants ....................................................................................................... 9  
1.2.1. Magnitude of residues in primary crops ............................................................................................ 9  
1.2.2. Magnitude of residues in rotational crops ......................................................................................... 10  
1.2.3. Magnitude of residues in processed commodities ............................................................................ 10  
1.2.4. Proposed MRLs .............................................................................................................................. 10  
2. Residues in livestock ........................................................................................................................... 10  
3. Consumer risk assessment ................................................................................................................. 10  
Conclusions .............................................................................................................................................. 10  
Recommendations .................................................................................................................................... 11  
References ............................................................................................................................................... 12  
Abbreviations ........................................................................................................................................... 13  
Appendix A – Summary of authorised uses considered for the review of MRLs ............................................ 15  
Appendix B – List of end points ............................................................................................................... 19  
Appendix C – Pesticide Residue Intake Model (PRIMo) ........................................................................ 25  
Appendix D – Input values for the exposure calculations ........................................................................ 27  
Appendix E – Decision tree for deriving MRL recommendations ............................................................. 28  
Appendix F – Used compound codes .................................................................................................... 30
Background

Regulation (EC) No 396/2005\(^1\) (hereinafter referred to as ‘the Regulation’) establishes the rules governing the setting and the review of pesticide maximum residue levels (MRLs) at European level. Article 12(1) of that Regulation stipulates that the European Food Safety Authority (EFSA) shall provide, within 12 months from the date of the inclusion or non-inclusion of an active substance in Annex I to Directive 91/414/EEC\(^2\) a reasoned opinion on the review of the existing MRLs for that active substance.

As 8-Hydroxyquinoline was approved on 1 January 2012 by means of Commission Implementing Regulation (EU) No 993/2011\(^3\) in the framework of Regulation (EC) No 1107/2009\(^4\) as amended by Commission Implementing Regulations (EU) No 540/2011\(^5\) and 541/2011\(^6\), EFSA initiated the review of all existing MRLs for that active substance.

By way of background information, 8-hydroxyquinoline was evaluated by Spain, designated as rapporteur Member State (RMS), upon resubmission in the framework of Commission Regulation (EC) No 33/2008\(^7\). Subsequently, a peer review on the initial evaluation of the RMS was conducted by EFSA, leading to the conclusions as set out in the EFSA conclusion (EFSA, 2011). The approval of 8-hydroxyquinoline is restricted to uses as fungicide and bactericide in greenhouses. Furthermore, according to the provisions of the approval regulation, confirmatory information was requested, among others, as regards a new storage stability covering the storage time periods of samples from both the metabolism study and from the supervised residue trials, to be submitted by 31 December 2013. Confirmatory data were evaluated and submitted by the RMS in September 2013 (Spain, 2013b) and considered as well in the framework of an MRL application on tomatoes (EFSA, 2013).

In December 2013, the rapporteur Member State (RMS) Spain received an application from Probelte S.A. for amendment to the conditions of approval of 8-hydroxyquinoline to lift the restriction and to allow other uses as a fungicide/bactericide on field tomatoes. The RMS provided its initial evaluation of the dossier on 8-hydroxyquinoline in addenda to all parts of the draft assessment report (DAR), which were received by EFSA on 27 March 2015. The studies submitted were peer reviewed, but data gaps were identified in several areas (EFSA, 2016).

On 24 January 2017 the Standing Committee on Plants, Animals, Food and Feed took note of the revision of the review report after the assessment of the confirmatory data, but the conditions of approval were not modified (European Commission, 2017a,b).

According to the legal provisions, EFSA shall base its reasoned opinion in particular on the relevant assessment report prepared under Directive 91/414/EEC repealed by Regulation (EC) No 1107/2009. It should be noted, however, that, in the framework of Regulation (EC) No 1107/2009, only a few representative uses are evaluated, whereas MRLs set out in Regulation (EC) No 396/2005 should accommodate all uses authorised within the European Union (EU), and uses authorised in third countries that have a significant impact on international trade. The information included in the assessment report prepared under Regulation (EC) No 1107/2009 is therefore insufficient for the assessment of all existing MRLs for a given active substance.

---

\( ^{1}\) Regulation (EC) No 396/2005 of the European Parliament and of the Council of 23 February 2005 on maximum residue levels of pesticides in or on food and feed of plant and animal origin and amending Council Directive 91/414/EEC. OJ L 70, 16.3.2005, p. 1–16.

\( ^{2}\) Council Directive 91/414/EEC of 15 July 1991 concerning the placing of plant protection products on the market. OJ L 230, 19.8.1991, p. 1–32. Repealed by Regulation (EC) No 1107/2009.

\( ^{3}\) Commission Implementing Regulation (EU) No 993/2011 of 6 October 2011 approving the active substance 8-hydroxyquinoline, 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 the Annex to Commission Implementing Regulation (EU) No 540/2011. OJ L 263, 7.10.2011, p. 1–4.

\( ^{4}\) Regulation (EC) No 1107/2009 of the European Parliament and of the Council of 21 October 2009 concerning the placing of plant protection products on the market and repealing Council Directives 79/117/EEC and 91/414/EEC. OJ L 309, 24.11.2009, p. 1–50.

\( ^{5}\) Commission Implementing Regulation (EU) No 540/2011 of 25 May 2011 implementing Regulation (EC) No 1107/2009 of the European Parliament and of the Council as regards the list of approved active substances. OJ L 153, 11.6.2011, p. 1–186.

\( ^{6}\) 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.

\( ^{7}\) Commission Regulation (EC) No 33/2008 of 17 January 2008 laying down detailed rules for the application of Council Directive 91/414/EEC as regards a regular and an accelerated procedure for the assessment of active substances which were part of the programme of work referred to in Article 9(2) of that Directive but have not been included into its Annex I. OJ L 15, 18.1.2008, p. 5–12.
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 15 April 2020, EFSA initiated the collection of data for this active substance. In a first step, Member States and the United Kingdom were invited to submit by 15 May 2020 their Good Agricultural Practices (GAPs) that are authorised nationally, in a standardised way, in the format of specific GAP forms. In the framework of this consultation, 15 Member States and the United Kingdom provided feedback on their national authorisations of 8-hydroxyquinoline. Based on the GAP data submitted, the designated RMS, Spain, 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 and the United Kingdom were requested to provide residue data supporting the critical GAPs by 1 August 2020.

On the basis of all the data submitted by Member States and the United Kingdom and the EU Reference Laboratories for Pesticides Residues (EURLs), EFSA asked Spain 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 16 October 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.

Considering all the available information, EFSA prepared in February 2021 a draft reasoned opinion, which was circulated to Member States and EURLs for commenting via a written procedure. All comments received by 03 March 2021 were considered by EFSA during the finalisation of the reasoned opinion.

The evaluation report submitted by the RMS (Spain, 2020), taking into account also the information provided by Member States and the United Kingdom 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, 2021a) and the Member States consultation report (EFSA, 2021b). 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 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.

8 The United Kingdom withdrew from EU on 1 February 2020. In accordance with the Agreement on the Withdrawal of the United Kingdom from the EU, and with the established transition period, the EU requirements on data reporting also apply to the United Kingdom data collected until 31 December 2020.
The active substance and its use pattern

8-Hydroxyquinoline is the given common name for 8-quinolinol (IUPAC). There is no ISO common name for this compound.

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

It is underlined that after the first approval, the classification has been reconsidered and 8-hydroxyquinoline has a harmonised classification and labelling as toxic for reproduction category 1B according to Commission Regulation (EU) 2017/776 amending, for the purposes of its adaptation to technical and scientific progress, Regulation (EC) No 1272/2008.

The EU MRLs for 8-hydroxyquinoline are established in Annexes IIIA of Regulation (EC) No 396/2005. Codex maximum residue limits (CXLs) for 8-hydroxyquinoline are not available. 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 | Commission Regulation (EU) No 1004/2013 (a) | Tomatoes (EFSA, 2013) |

(a): Commission Regulation (EU) No 1004/2013 of 15 October 2013 amending Annexes II and III to Regulation (EC) No 396/2005 of the European Parliament and of the Council as regards maximum residue levels for 8-hydroxyquinoline, cyproconazole, cyprodinil, fluopyram, nicotine, pendimethalin, penthiopyrad and trifloxystrobin in or on certain products. OJ L 279, 19.10.2013, p. 10–56.

For the purpose of this MRL review, all the uses of 8-hydroxyquinoline currently authorised within the EU as submitted by the Member States and the United Kingdom during the GAP collection have been reported by the RMS in the GAP overview file. The critical GAP identified in the GAP overview file were then summarised in the PROFile and considered in the assessment. The details of the authorised critical GAP for 8-hydroxyquinoline are given in Appendix A. The RMS did not report any use authorised in third countries that might have a significant impact on international trade.

Assessment

EFSA has based its assessment on the following documents:

- the PROFile submitted by the RMS;
- the evaluation report accompanying the PROFile (Spain, 2020);
- the revised evaluation report for the approval of 8-hydroxyquinoline as active substance in accordance with Regulation (EC) No 1107/2009 (European Commission, 2017a,b);
- the draft assessment report (DAR) and its final addendum prepared under Council Directive 91/414/EEC and Regulation (EC) No 33/2008 (Spain, 2009, 2010);
- the final addendum to the additional report prepared by the rapporteur Member State, Spain, in the framework of Commission Regulation (EC) No 33/2008 (Spain 2013b).
- the conclusion on the peer review of the pesticide risk assessment of the active substance 8-hydroxyquinoline (EFSA, 2011); the previous reasoned opinion on 8-hydroxyquinoline (EFSA, 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 and the currently applicable guidance documents relevant for the consumer risk assessment of pesticide residues (European Commission, 1997a-g, 2000, 2010a,b, 2017a,b; 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 8-hydroxyquinoline after soil treatment by drip irrigation was investigated in fruit crops (Spain, 2009) and assessed in the framework of the peer review (EFSA, 2011).

At harvest, low residue levels were observed both in the green and the ripe tomato fruit (0.02 and 0.015 mg eq./kg, respectively) and the radioactive residues were mainly recovered in tomato shoots (0.17 mg eq./kg) and roots (10.5 mg eq./kg). The main compound identified both in green and ripe tomatoes was the parent 8-hydroxyquinoline, free (36% and 35% total radioactive residue (TRR) in green and ripe tomatoes, respectively) while two additional fractions were characterised as conjugates of 8-hydroxyquinoline (M1 and M2) that accounted for 13.7% and 39% of the TRR in green and ripe tomatoes, respectively. From the available metabolism study, it was not clear whether these fractions M1 and M2 represent either conjugates of 8-hydroxyquinoline (glucosides, glucuronides) or a complex bound structure of 8-hydroxyquinoline. Since no information was provided on the efficiency of the extraction procedure of the analytical methods to release conjugates, a conversion factor of 2 for monitoring to risk assessment was derived from the metabolism study, in order to consider by default the residue levels of these possible conjugates M1 and M2 (EFSA, 2011).

A data gap regarding the storage stability was identified by the peer review which did not allow to conclude on the stability of 8-hydroxyquinoline residues in samples from metabolism study and residue trials (EFSA, 2011). The applicant was requested to submit a new storage stability study. The requested study has been submitted as confirmatory data and in the framework of an MRL application and is described under Section 1.1.5. Following assessment of this study, the results of the metabolism studies were considered valid with regard to storage stability (EFSA, 2013; Spain, 2013a,b).

1.1.2. Nature of residues in rotational crops

8-Hydroxyquinoline is authorised on crops that may be grown in rotation. The soil degradation studies demonstrated that the degradation rate of 8-hydroxyquinoline is rapid with the maximum DT90 value of 34 days. Moreover, no relevant soil metabolites were identified (EFSA, 2011). Thus, no further studies investigating the nature of residues in rotational crops are required (European Commission, 1997c).

1.1.3. Nature of residues in processed commodities

There were no studies investigating the nature of residues of 8-hydroxyquinoline in processed commodities available for this review. Nevertheless, in all commodities, residues were below 0.01 mg/kg and the total theoretical maximum daily intake is below 10% of the ADI (see Section 3). Therefore, the investigation of the nature of residues in processed commodities is not required (European Commission, 1997d).

1.1.4. Methods of analysis in plants

Analytical methods and their respective independent laboratory validation (ILV) for the determination of residues of 8-hydroxyquinoline in plant commodities were assessed in the framework of the peer review (Spain, 2010). The residues of 8-hydroxyquinoline and its salts can be analysed by LC-MS/MS method in high water (tomato) and acidic commodities (orange pulp) at a validated limit of quantification (LOQ) of 0.01 mg/kg (EFSA, 2011).

According to the EURLs, 8-hydroxyquinoline can be monitored in high water content and high acid content commodities with an LOQ of 0.01 mg/kg and in dry and high fat content commodities with an LOQ of 0.02 mg/kg. In high water content and high acid content commodities, even lower levels (down to 0.005 mg/kg) were successfully validated (EURLs, 2020).

1.1.5. Stability of residues in plants

A new study investigating the freezer storage stability of 8-hydroxyquinoline residues in tomato was submitted as confirmatory data and in the framework of an MRL application (Spain, 2013a,b) to address the data gap identified in the framework of the peer review (see also Section 1.1.1). The
stability of 8-hydroxyquinoline in tomato matrix was demonstrated under deep frozen conditions for the investigated storage period of 190 days (ca. 6 months). Although the active substance in its salts form has been used both in metabolism studies and residue trials, the stability of the salts of 8-hydroxyquinoline in tomato has not been investigated. However, due to the ionic nature of the molecule, in water solutions 8-hydroxyquinoline and the variant 8-hydroxyquinoline sulfate may dissociate (Spain, 2009). By modifying the pH, the molecule can be interconverted to other ionic forms (anionic, cationic, neutral). Since the neutral form of 8-hydroxyquinoline when applied on tomato as watery/acidic matrix would form a salt, the storage stability of 8-hydroxyquinoline salts can be considered as addressed by the submitted storage stability study (EFSA, 2013).

Moreover, a study investigating the storage stability of 8-hydroxyquinoline in strawberry fruits (acidic matrix) was submitted in the framework of this MRL review (Spain, 2020). According to the results of this study, 8-hydroxyquinoline is stable in strawberries stored under deep frozen conditions (≤ -18°C) for a storage period of 3 months. As in the study on tomatoes, also in this study, the stability of the salts of 8-hydroxyquinoline has not been investigated. However, for the same reasons reported above, the storage stability of 8-hydroxyquinoline salts can be considered as addressed by the submitted storage stability study.

1.1.6. Proposed residue definitions

Based on the available metabolism study, the peer review proposed to establish the enforcement residue definition as ‘8-hydroxyquinoline and its salts expressed as 8-hydroxyquinoline’. The risk assessment residue definition was proposed as ‘8-hydroxyquinoline (free and conjugated) and its salts expressed as 8-hydroxyquinoline’. These residue definitions are restricted to fruit crops only and for treatments by soil drip irrigation. A conversion factor of 2 for monitoring to risk assessment was derived from the metabolism study (EFSA, 2011). As only uses by drip irrigations on fruit crops are currently authorised, these residue definitions are considered applicable to the uses assessed in the present review.

Specific residue definitions for rotational and processed commodities were not deemed necessary considering the very limited persistence of 8-hydroxyquinoline in the soil and the results from the residue trials (residues in the raw commodities were below 0.01 mg/kg) and from the risk assessment (total theoretical maximum daily intake is below 10% of the ADI).

Fully validated analytical methods are available for the enforcement of the proposed residue definition in high water and acidic commodities at the LOQ of 0.01 mg/kg. According to the EURLs, using QuEChERS combined with APCI-LC-MS/MS, this LOQ is achievable in high water and acidic commodities while a higher LOQ of 0.02 mg/kg is achievable in dry and high fat content matrices (EURLs, 2020).

1.2. Magnitude of residues in plants

1.2.1. Magnitude of residues in primary crops

To assess the magnitude of 8-hydroxyquinoline residues resulting from the reported GAPs, EFSA considered all residue trials reported by the RMS in its evaluation report (Spain, 2020). All residue trial samples considered in this framework were stored in compliance with the conditions for which storage stability of residues was demonstrated. Decline of residues during storage of the trial samples is therefore not expected.

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

Available residue trials are sufficient to derive (tentative) MRL and risk assessment values for all crops, taking note of the following considerations:

- Strawberries: No GAP compliant trials are available. Considering the results of the metabolism study, the mode of application (soil treatment by drip application) and the low persistence of 8-hydroxyquinoline in the soil, a no residue situation is expected and the MRL can be tentatively derived at the LOQ of 0.01 mg/kg. Nevertheless, this MRL should be confirmed by at least two trials compliant with the indoor GAP and analysing simultaneously for enforcement and risk assessment residue definitions. Pending the submission of these trials, a conversion factor of 2 is tentatively proposed for risk assessment.
• Fruiting vegetables, except sweet corn: The number of residue trials supporting the indoor GAPs is not compliant with the data requirements for these crops. Moreover, trials were performed according to a more critical GAP (last application at BBCH of 79 instead of 60). However, the available residue trials are considered acceptable in this case because all results were below the LOQ and a no residues situation is expected.

The method used to analyse residue trial samples did not include a hydrolysis step to release the conjugates; to express residues for the risk assessment residue definition, the conversion factor of 2 as derived by the peer review from the metabolism studies, is proposed. In principle additional trials with samples analysed with a method including a hydrolysis step are still required. Nevertheless, additional trials are only desirable since according to the metabolism study conjugates are expected at the same level as parent and parent was always below the LOQ, and considering the large margin of safety observed in the risk assessment (see Section 3).

1.2.2. Magnitude of residues in rotational crops

Since 8-hydroxyquinoline is not persistent in the soil and no relevant soil metabolites were identified, studies investigating the magnitude of the compound uptake in rotational crops are not required (European Commission, 1997c).

1.2.3. Magnitude of residues in processed commodities

Processing studies were not submitted in the framework of this review. Nevertheless, they are not required since residues in the raw commodities were below 0.01 mg/kg and the total theoretical maximum daily intake is below 10% of the ADI (see Section 3).

1.2.4. Proposed MRLs

Available residue trials data were considered sufficient to derive MRL proposals as well as risk assessment values for all commodities under evaluation. Considering the missing residue trials on strawberries, the MRL proposal for this commodity should be considered tentative only.

2. Residues in livestock

8-Hydroxyquinoline 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).

3. Consumer risk assessment

Chronic and acute exposure calculations for all crops reported in the framework of this review were performed using revision 3.1 of the EFSA PRIMO (EFSA, 2019). Input values for the exposure calculations were derived in compliance with the decision tree reported in Appendix E. Hence, for those commodities where a (tentative) MRL could be derived by EFSA in the framework of this review, input values were derived according to the internationally agreed methodologies (FAO, 2009). All input values included in the exposure calculations are summarised in Appendix D.

The exposure values calculated were compared with the toxicological reference values for 8-hydroxyquinoline, derived by EFSA (2011) and endorsed by the European Commission (European Commission, 2017a,b). The highest chronic exposure was calculated for GEMS/Food G06, representing 0.3% of the acceptable daily intake (ADI), and the highest acute exposure was calculated for melons, representing 6% of the ARfD. Although uncertainties remain due to the data gap identified in the previous sections, this indicative exposure calculation did not indicate a risk to consumer’s health.

Conclusions

The metabolism of 8-hydroxyquinoline in plant was investigated in primary crops. According to the results of the metabolism study, the residue definition for enforcement can be proposed as ‘8-hydroxyquinoline and its salts expressed as 8-hydroxyquinoline’. The risk assessment residue definition can be proposed as ‘8-hydroxyquinoline (free and conjugated) and its salts expressed as 8-hydroxyquinoline’. These residue definitions are restricted to fruit crops only and for treatments by soil drip irrigation.
Specific residue definitions for rotational and processed commodities were not deemed necessary considering the very limited persistence of 8-hydroxyquinoline in the soil and the results from the residue trials (residues in the raw commodities were below 0.01 mg/kg) and from the risk assessment (total theoretical maximum daily intake is below 10% of the ADI).

Fully validated analytical methods are available for the enforcement of the proposed residue definition in high water and acidic commodities at the LOQ of 0.01 mg/kg. According to the EURs, using QuECHERS combined with APCI-LC-MS/MS, this LOQ is achievable in high water and acidic commodities while a higher LOQ of 0.02 mg/kg is achievable in dry and high fat content matrices.

Available residue trials data were considered sufficient to derive MRL proposals as well as risk assessment values for all commodities under evaluation. Considering the missing residue trials on strawberries, the MRL proposal for this commodity should be considered tentative only.

8-Hydroxyquinoline 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.

Chronic and acute consumer exposure resulting from the authorised uses reported in the framework of this review was calculated using revision 3.1 of the EFSA PRIMo. The highest chronic exposure was calculated for GEMS/Food G06, representing 0.3% of the acceptable daily intake (ADI), and the highest acute exposure was calculated for melons, representing 6% of the ARfD.

**Recommendations**

MRL recommendations were derived in compliance with the decision tree reported in Appendix E of the reasoned opinion (see Table 2). None of the MRL values listed in the table are recommended for inclusion in Annex II to the Regulation as they need further considerations by risk managers. In particular one tentative MRL needs to be confirmed by the following data:

1) At least two residue trials on strawberries compliant with the indoor GAP and performed according to the residue definitions for enforcement and risk assessment.

If the above reported data gap is not addressed in the future, Member States are recommended to withdraw or modify the relevant authorisations at national level.

In order to allow risk managers to take an informed decision, it is underlined that 8-hydroxyquinoline has a harmonised classification and labelling as toxic for reproduction category 1B.

According to the information provided by the EURs, the analytical standard for 8-hydroxyquinoline is commercially available (EURs, 2020).

Minor deficiencies were also identified in the assessment, but these deficiencies are not expected to impact either on the validity of the MRLs derived or on the national authorisations. The following data are therefore considered desirable but not essential:

Additional residue trials on tomatoes and cucumbers compliant with the indoor GAP, with samples analysed by using a method including a hydrolysis step.

**Table 2:** Summary table

| Code number | Commodity | Existing EU MRL (mg/kg) | Existing CXL (mg/kg) | MRL(a) (mg/kg) | Comment |
|-------------|-----------|-------------------------|---------------------|----------------|---------|
| 152000 | Strawberries | 0.01* | – | 0.01* | Further consideration needed(b) |
| 231010 | Tomatoes | 0.1 | – | 0.01* | Further consideration needed(c) |
| 231020 | Sweet peppers/bell peppers | 0.01* | – | 0.01* | Further consideration needed(c) |
| 231030 | Aubergines/eggplants | 0.01* | – | 0.01* | Further consideration needed(c) |
| 231040 | Okra/lady’s fingers | 0.01* | – | 0.01* | Further consideration needed(c) |
| 232010 | Cucumbers | 0.01* | – | 0.01* | Further consideration needed(c) |
| 232020 | Gherkins | 0.01* | – | 0.01* | Further consideration needed(c) |
| 232030 | Courgettes | 0.01* | – | 0.01* | Further consideration needed(c) |
| 233010 | Melons | 0.01* | – | 0.01* | Further consideration needed(c) |
| Code number | Commodity                        | Existing EU MRL (mg/kg) | Existing CXL (mg/kg) | Outcome of the review          |
|------------|---------------------------------|-------------------------|----------------------|--------------------------------|
| 233020     | Pumpkins                        | 0.01*                   | –                    | 0.01* Further consideration needed (c) |
| 233030     | Watermelons                     | 0.01*                   | –                    | 0.01* Further consideration needed (c) |
| –          | Other commodities of plant and/or animal origin | See Reg. 1004/2013 | –                    | – Further consideration needed (d) |

MRL: maximum residue level; CXL: codex maximum residue limit.
*: Indicates that the MRL is set at the limit of quantification.
(a): The impact of the classification of 8-hydroxyquinoline as toxic for reproduction category 1B on the validity of the MRL proposal was not considered in the assessment.
(b): Tentative MRL is derived from a GAP evaluated at EU level, which is not fully supported by data but for which no risk to consumers was identified; no CXL is available (combination F-I in Appendix E). It is noted that 8-hydroxyquinoline is classified as toxic for reproduction category 1B.
(c): MRL is derived from a GAP evaluated at EU level, which is fully supported by data and for which no risk to consumers is identified; no CXL is available (combination H-I in Appendix E). It is noted that 8-hydroxyquinoline is classified as toxic for reproduction category 1B.
(d): 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).

References

EFSA (European Food Safety Authority), 2011. Conclusion on the peer review of the pesticide risk assessment of the active substance 8-hydroxyquinoline. EFSA Journal 2011;9(1):1964, 49 pp. https://doi.org/10.2903/j.efsa.2011.1964

EFSA (European Food Safety Authority), 2013. Reasoned opinion on the modification of the existing MRL(s) for 8-hydroxyquinoline in tomatoes. EFSA Journal 2013;11(5):3224, 20 pp. https://doi.org/10.2903/j.efsa.2013.3224

EFSA (European Food Safety Authority), 2016. Conclusion on the peer review of the pesticide risk assessment of the active substance 8-hydroxyquinoline. EFSA Journal 2016;14(6):4493, 16 pp. https://doi.org/10.2903/j.efsa.2016.4493

EFSA (European Food Safety Authority), 2021a. Completeness check report on the review of the existing MRLs of 8-hydroxyquinoline prepared by EFSA in the framework of Article 12 of Regulation (EC) No 396/2005, 19 January 2021. Available online: www.efsa.europa.eu

EFSA (European Food Safety Authority), 2021b. Member States consultation report on the review of the existing MRLs of 8-hydroxyquinoline prepared by EFSA in the framework of Article 12 of Regulation (EC) No 396/2005, 15 March 2021. Available online: www.efsa.europa.eu

EFSA (European Food Safety Authority), Anastassiadou M, Brancato A, Carrasco Cabrera L, Ferreira L, Greco L, Jarrah S, Leuschner R, Kazocina A, Magrans JO, Miron I, Pedersen R, Raczky M, Reich H, Ruocco S, Sacchi A, Santos M, Stanek A, Tarazona J, Theobald A and Verani A, 2019. Pesticide Residue Intake Model - EFSA PRIMo revision 3.1. EFSA supporting publication 2019;16(3):EN-1605, 15 pp. https://doi.org/10.2903/sp.efsa.2019.EN-1605

EURLs (European Union Reference Laboratories for Pesticide Residues), 2020. Evaluation report prepared under Article 12 of Regulation (EC) No 396/2005. Analytical methods validated by the EURLs and overall capability of official laboratories to be considered for the review of the existing MRLs for 8-hydroxyquinoline. August 2020. Available online: www.efsa.europa.eu

European Commission, 1996. Appendix G. Livestock feeding studies. 7031/V1/95-rev 4, 22 July 1996.

European Commission, 1997a. Appendix A. Metabolism and distribution in plants. 7028/V1/95-rev.3, 22 July 1997.

European Commission, 1997b. Appendix B. General recommendations for the design, preparation and realization of residue trials. Annex 2. Classification of (minor) crops not listed in the Appendix of Council Directive 90/642/EEC. 7029/V1/95-rev. 6, 22 July 1997.

European Commission, 1997c. Appendix C. Testing of plant protection products in rotational crops. 7524/V1/95-rev. 2, 22 July 1997.

European Commission, 1997d. Appendix E. Processing studies. 7035/V1/95-rev. 5, 22 July 1997.

European Commission, 1997e. Appendix F. Metabolism and distribution in domestic animals. 7030/V1/95-rev. 3, 22 July 1997.

European Commission, 1997f. Appendix H. Storage stability of residue samples. 7032/V1/95-rev. 5, 22 July 1997.

European Commission, 1997g. Appendix I. Calculation of maximum residue level and safety intervals.7039/V1/95 22 July 1997. As amended by the document: classes to be used for the setting of EU pesticide maximum residue levels (MRLs). SANCO 10634/2010, finalised in the Standing Committee on the Food Chain and Animal Health at its meeting of 23–24 March 2010.
European Commission, 2000. Residue analytical methods. For pre-registration data requirement for Annex II (part A, section 4) and Annex III (part A, section 5 of Directive 91/414. SANCO/3029/99-rev. 4.
European Commission, 2010a. Classes to be used for the setting of EU pesticide Maximum Residue Levels (MRLs). SANCO 10634/2010-rev. 0, Finalised in the Standing Committee on the Food Chain and Animal Health at its meeting of 23–24 March 2010.
European Commission, 2010b. Residue analytical methods. For post-registration control. SANCO/825/00-rev. 8.1, 16 November 2010.
European Commission, 2017a. Review report for the active substance 8-hydroxyquinoline finalised in the Standing Committee on the Food Chain and Animal Health at its meeting on 15 July 2011 in view of the approval of 8-hydroxyquinoline as active substance in accordance with Regulation (EC) No 1107/2009. SANCO/11636/2011 rev 3, 24 January 2017.
European Commission, 2017b. Appendix D. Guidelines on comparability, extrapolation, group tolerances and data requirements for setting MRLs. 7525/VI/95-rev.10.3, June 2017.
FAO (Food and Agriculture Organization of the United Nations), 2009. Submission and evaluation of pesticide residues data for the estimation of Maximum Residue Levels in food and feed. Pesticide Residues. 2nd Edition. FAO Plant Production and Protection Paper 197, 264 pp.
OECD (Organisation for Economic Co-operation and Development), 2011. OECD MRL calculator: spreadsheet for single data set and spreadsheet for multiple data set, 2 March 2011. In: Pesticide Publications/Publications on Pesticide Residues. Available online: http://www.oecd.org
OECD (Organisation for Economic Co-operation and Development), 2013. Guidance document on residues in livestock. In: Series on Pesticides No 73. ENV/JM/MONO(2013)8, 4 September 2013.
Spain, 2009. Draft assessment report on the active substance 8-hydroxyquinoline prepared by the rapporteur Member State Spain in the framework of Council Directive 91/414/EEC, July 2009. Available online: www.efsa.europa.eu
Spain, 2010. Final Addendum to the draft assessment report on the active substance 8-hydroxyquinoline prepared by the Rapporteur Member State Spain in the framework of Council Directive 91/414/EEC and Regulation (EC) No 33/2008, October 2010. Available online: www.efsa.europa.eu
Spain, 2013a. Updated Evaluation report on the setting of MRLs for 8-hydroxyquinoline in tomatoes prepared by the evaluating Member State Spain under Article 8 of Regulation (EC) No 396/2005. February 2013, 34 pp.
Spain, 2013b. Final addendum to the additional report on the active substance 8-hydroxyquinoline prepared by the rapporteur Member State Spain in the framework of Commission Regulation (EC) No 33/2008, September 2013. Available online: www.efsa.europa.eu
Spain, 2020. Evaluation report prepared under Article 12.1 of Regulation (EC) No 396/2005. Review of the existing MRLs for 8-hydroxyquinoline, 15 October 2020. Available online: www.efsa.europa.eu

Abbreviations

| Abbreviation | Description |
|--------------|-------------|
| a.i. | active ingredient |
| a.s. | active substance |
| ADI | acceptable daily intake |
| ARID | acute reference dose |
| BBCH | growth stages of mono- and dicotyledonous plants |
| bw | body weight |
| 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 |
| 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 |
| EURls | European Union Reference Laboratories for Pesticide Residues (former CRLs) |
| FAO | Food and Agriculture Organization of the United Nations |
| FID | flame ionisation detector |
| GAP | Good Agricultural Practice |
| GC | gas chromatography |
Review of the existing MRLs for 8-hydroxyquinoline

GC-FID  gas chromatography with flame ionisation detector
GC-MS  gas chromatography with mass spectrometry
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
IESTI  international estimated short-term intake
ILV  independent laboratory validation
ISO  International Organisation for Standardization
IUPAC  International Union of Pure and Applied Chemistry
LC  liquid chromatography
LC-MS/MS  liquid chromatography with tandem mass spectrometry
LOQ  limit of quantification
Mo  monitoring
MRL  maximum residue level
MS  Member States
MS/MS  tandem mass spectrometry detector
MW  molecular weight
NEDI  national estimated daily intake
NESTI  national estimated short-term intake
NTMDI  national theoretical maximum daily intake
OECD  Organisation for Economic Co-operation and Development
PBI  plant back interval
PF  processing factor
PHI  preharvest interval
PRIMo  (EFSA) Pesticide Residues Intake Model
PROFile  (EFSA) Pesticide Residues Overview File
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
SP  water soluble powder
STMR  supervised trials median residue
TAR  total applied radioactivity
TMDI  theoretical maximum daily intake
TRR  total radioactive residue
UV  ultraviolet (detector)
WHO  World Health Organization
### Appendix A – Summary of authorised uses considered for the review of MRLs

#### A.1. Authorised indoor uses in EU

| Crop and/or situation | MS or country | Pests or group of pests controlled | Preparation | Application | Application rate per treatment | PHI (days) | Remarks |
|-----------------------|---------------|-----------------------------------|-------------|-------------|--------------------------------|------------|---------|
| **Strawberries**      | FR, AT, DE    | I                                 | Soil treatment – general (see also comment field) | 10-59 | 2 | 14 | – | – | 1.496 kg a.i./ha | n.a. | Drip irrigation. Application rate reported as 8-hydroxyquinoline (corresponding to 2 kg/ha 8-hydroxyquinoline sulfate). |
| **Tomatoes**          | EL, ES        | I                                 | Soil treatment – general (see also comment field) | 60 | 2 | 14 | – | – | 1.496 kg a.i./ha | n.a. | Drip irrigation. Application rate reported as 8-hydroxyquinoline (corresponding to 2 kg/ha 8-hydroxyquinoline sulfate). |
| **Sweet peppers**     | EL, ES        | I                                 | Soil treatment – general (see also comment field) | 60 | 2 | 14 | – | – | 1.496 kg a.i./ha | n.a. | Drip irrigation. Application rate reported as 8-hydroxyquinoline (corresponding to 2 kg/ha 8-hydroxyquinoline sulfate). |
| Crop and/or situation | MS or country | Type | Conc. a.s. | Method kind | Range of growth stages and season | Number of application | Interval between application | Application rate per treatment | PHI (days)(d) | Remarks |
|-----------------------|---------------|------|------------|-------------|-------------------------------|----------------------|-----------------------------|-------------------------------|--------------|---------|
| Aubergines            | EL, ES        | I    |            | Soil treatment – general (see also comment field) | 60                | 2                             | 14                           | 1.496 kg a.i./ha          | n.a.         | Drip irrigation. Application rate reported as 8-hydroxyquinoline (corresponding to 2 kg/ha 8-hydroxyquinoline sulfate). |
| Okra                  | EL, ES        | I    |            | Soil treatment – general (see also comment field) | 60                | 2                             | 14                           | 1.496 kg a.i./ha          | n.a.         | Drip irrigation. Application rate reported as 8-hydroxyquinoline (corresponding to 2 kg/ha 8-hydroxyquinoline sulfate). |
| Cucumbers             | AT, EL, ES, DE, FR | I    |            | Soil treatment – general (see also comment field) | 60                | 2                             | 14                           | 1.496 kg a.i./ha          | n.a.         | Drip irrigation. Application rate reported as 8-hydroxyquinoline (corresponding to 2 kg/ha 8-hydroxyquinoline sulfate). |
| Gherkins              | EL, ES, DE, FR | I    |            | Soil treatment – general (see also comment field) | 60                | 2                             | 14                           | 1.496 kg a.i./ha          | n.a.         | Drip irrigation. Application rate reported as 8-hydroxyquinoline (corresponding to 2 kg/ha 8-hydroxyquinoline sulfate). |
| Crop and/or situation | MS or country | F G or r(a) | Pests or group of pests controlled | Preparation Type(b) | Conc. a.s. | Method kind | Application | Application rate per treatment | PHI (days)(d) | Remarks |
|-----------------------|---------------|-------------|-----------------------------------|---------------------|------------|-------------|-------------|--------------------------------|--------------|---------|
| Courgettes EL, ES, DE, FR | I | Soil treatment – general (see also comment field) | 60 | 2 | 14 | – | – | 1.496 kg a.i./ha | n.a. | Drip irrigation. Application rate reported as 8-hydroxyquinoline (corresponding to 2 kg/ha 8-hydroxyquinoline sulfate). |
| Melons EL, ES | I | Soil treatment – general (see also comment field) | 60 | 2 | 14 | – | – | 1.496 kg a.i./ha | n.a. | Drip irrigation. Application rate reported as 8-hydroxyquinoline (corresponding to 2 kg/ha 8-hydroxyquinoline sulfate). |
| Pumpkins DE, EL, ES | I | Soil treatment – general (see also comment field) | 60 | 2 | 14 | – | – | 1.496 kg a.i./ha | n.a. | Drip irrigation. Application rate reported as 8-hydroxyquinoline (corresponding to 2 kg/ha 8-hydroxyquinoline sulfate). |
| Watermelons EL, ES | I | Soil treatment – general (see also comment field) | 60 | 2 | 14 | – | – | 1.496 kg a.i./ha | n.a. | Drip irrigation. Application rate reported as 8-hydroxyquinoline (corresponding to 2 kg/ha 8-hydroxyquinoline sulfate). |
MS: Member State.
(a): Outdoor or field use (F), greenhouse application (G) or indoor application (I).
(b): CropLife International Technical Monograph no 2, 7th Edition. Revised March 2017. Catalogue of pesticide formulation types and international coding system.
(c): Growth stage range from first to last treatment (BBCH Monograph, Growth Stages of Plants, 1997, Blackwell, ISBN 3-8263-3152-4), including, where relevant, information on season at time of application.
(d): PHI – minimum preharvest interval.
Appendix B – List of end points

B.1. Residues in plants

B.1.1. Nature of residues and methods of analysis in plants

B.1.1.1. Metabolism studies, methods of analysis and residue definitions in plants

| Primary crops (available studies) | Crop groups | Crop(s) | Application(s) | Sampling (DAT) | Comment/Source |
|-----------------------------------|-------------|---------|----------------|----------------|----------------|
| Fruit crops                       | Tomatoes    | Soil drip irrigation, 2 × 1.47 kg 8-hydroxyquinoline/ha | 76; 118         | Study performed with 8-hydroxy (benzene ring-U-14C) quinoline sulfate (Spain, 2009; EFSA, 2011). Application rate reported as 8-hydroxyquinoline (corresponding to 2 kg/ha 8-hydroxyquinoline sulfate). |

| Rotational crops (available studies) | Crop groups | Crop(s) | Application(s) | PBI (DAT) | Comment/Source |
|--------------------------------------|-------------|---------|----------------|-----------|----------------|
| Not available and not required as 8-hydroxyquinoline is not persistent in the soil |

| Processed commodities (hydrolysis study) | Conditions | Stable? | Comment/Source |
|------------------------------------------|------------|---------|----------------|
| Pasteurisation (20 min, 90°C, pH 4)      | Not triggered |         | Residues in raw commodities were below 0.01 mg/kg and the total theoretical maximum daily intake is below 10% of the ADI. |
| Baking, brewing and boiling (60 min, 100°C, pH 5) | Not triggered |         |
| Sterilisation (20 min, 120°C, pH 6)      | Not triggered |         |
Can a general residue definition be proposed for primary crops?  
No

| Rotational crop and primary crop metabolism similar? | Not applicable | 8-Hydroxyquinoline is not persistent in the soil |
| Residue pattern in processed commodities similar to residue pattern in raw commodities? | Not applicable | Residues in raw commodities were below 0.01 mg/kg and the total theoretical maximum daily intake is below 10% of the ADI |

| Plant residue definition for monitoring (RD-Mo) | Fruit crops (soil treatment by drip application): 8-hydroxyquinoline and its salts expressed as 8-hydroxyquinoline |
| Plant residue definition for risk assessment (RD-RA) | Fruit crops (soil treatment by drip application): 8-hydroxyquinoline (free and conjugated) and its salts expressed as 8-hydroxyquinoline |

| Methods of analysis for monitoring of residues (analytical technique, matrix groups, LOQs) | Matrices with high water content and high acid content: LC–MS/MS, LOQ 0.01 mg/kg |
| | ILV available (Spain, 2010; EFSA, 2011) |
| | LOQ achievable by using QuEChERS combined with APCI-LC-MS/MS (EURIs, 2020) |

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

| Plant products (available studies) | Category | Commodity | T (°C) | Stability period Value | Units | Compounds covered | Comment/Source |
|---|---|---|---|---|---|---|---|
| High water content | Tomatoes | –18 | 6 | Months | 8-hydroxyquinoline and its salts expressed as 8-hydroxyquinoline | Storage stability study evaluated in the framework of a previous MRL assessment (Spain, 2013; EFSA, 2013). |
| High acid content | Strawberries | –18 | 3 | Months | 8-hydroxyquinoline and its salts expressed as 8-hydroxyquinoline | Storage stability study evaluated in the framework of this MRL review (Spain, 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\(^{(d)}\) |
|------------------------|--------------------------|---------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------------------------|----------------------|------------------------|-------------|
| Strawberries           | Indoor                   | Mo: – RA: –                                                   | No GAP compliant trials available. Considering the results of the metabolism study, the mode of application (soil treatment by drip application) and the low persistence of 8-hydroxyquinoline in the soil, a no residue situation is expected and the MRL can be proposed at the LOQ. Nevertheless, this MRL should be confirmed by 2 trials analysing for enforcement and risk assessment residue definition. |
|                        |                          |                                                               |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      | 0.01*                  | 0.01                 | 0.01                    | 2\(^{(f)}\)  |

*\(^{(e)}\): In absence of residue trials only a tentative MRL can be derived based on the properties of the active substances and the available metabolism study.

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

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

\(^{(e)}\): To express residues for the risk assessment residue definition, a conversion factor of 2 derived from the metabolism study was applied.

\(^{(f)}\): The analytical method used to analyse residue trial samples did not include a hydrolysis step to release the conjugates. Therefore, to express residues for the risk assessment residue definition, a conversion factor of 2 derived from the metabolism study was applied.
B.1.2.2. Residues in rotational crops

**Overall summary**

| Question                                                                 | Answer                                                                 |
|------------------------------------------------------------------------|------------------------------------------------------------------------|
| Residues in rotational and succeeding crops expected based on confined rotational crop study? | Not triggered. 8-Hydroxyquinoline is not persistent in the soil. No relevant soil metabolites were identified. |
| Residues in rotational and succeeding crops expected based on field rotational crop study? | Not triggered. 8-Hydroxyquinoline is not persistent in the soil. No relevant soil metabolites were identified. |

B.1.2.3. Processing factors

Not available and not required as residues in the raw commodities were below 0.01 mg/kg and the total theoretical maximum daily intake is below 10% of the ADI (see Section 3).

B.2. Residues in livestock

Not relevant as 8-hydroxyquinoline is not authorised for use on crops that might be fed to livestock.
### B.3. Consumer risk assessment

#### B.3.1. Consumer risk assessment

| ARfD | 0.05 mg/kg bw (European Commission, 2017) |
|------|------------------------------------------|
| Highest IESTI, according to EFSA PRIMo (rev.3.1) | Melons: 6% of ARfD |
| NESTI (% ARfD) | Not assessed in this review. |
| Assumptions made for the calculations | The calculation is based on the highest residue levels expected in raw agricultural commodities. The CF of 2 as derived from the metabolism studies was applied for risk assessment. |

| ADI | 0.05 mg/kg bw per day (European Commission, 2017) |
|-----|------------------------------------------|
| 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) | 0.3% ADI (GEMS/Food G06) |
| NEDI (% ADI) | Not assessed in this review. |
| Assumptions made for the calculations | The calculation is based on the median residue levels derived for raw agricultural commodities. The CF of 2 as derived from the metabolism studies was applied for risk assessment. |

Consumer exposure assessment through drinking water resulting from groundwater metabolite(s) according to SANCO/221/2000 rev.10 Final (25/2/2003).

| Metabolite(s) | Not assessed in this review. |
| ADI (mg/kg bw per day) | Not assessed in this review. |
| Intake of groundwater metabolites (% ADI) | Not assessed in this review. |
### B.4. Proposed MRLs

| Code number | Commodity | Existing EU MRL (mg/kg) | Existing CXL (mg/kg) | Outcome of the review | Comment |
|-------------|-----------|-------------------------|----------------------|-----------------------|---------|
| 152000      | Strawberries | 0.01*                   | –                    | 0.01*                 | Further consideration needed<sup>(b)</sup> |
| 231010      | Tomatoes   | 0.1                      | –                    | 0.01*                 | Further consideration needed<sup>(c)</sup> |
| 231020      | Sweet peppers/bell peppers | 0.01*                   | –                    | 0.01*                 | Further consideration needed<sup>(c)</sup> |
| 231030      | Aubergines/eggplants | 0.01*                   | –                    | 0.01*                 | Further consideration needed<sup>(c)</sup> |
| 231040      | Okra/lady’s fingers | 0.01*                   | –                    | 0.01*                 | Further consideration needed<sup>(c)</sup> |
| 232010      | Cucumbers  | 0.01*                   | –                    | 0.01*                 | Further consideration needed<sup>(c)</sup> |
| 232020      | Gherkins   | 0.01*                   | –                    | 0.01*                 | Further consideration needed<sup>(c)</sup> |
| 232030      | Courgettes | 0.01*                   | –                    | 0.01*                 | Further consideration needed<sup>(c)</sup> |
| 233010      | Melons     | 0.01*                   | –                    | 0.01*                 | Further consideration needed<sup>(c)</sup> |
| 233020      | Pumpkins   | 0.01*                   | –                    | 0.01*                 | Further consideration needed<sup>(c)</sup> |
| 233030      | Watermelons | 0.01*                   | –                    | 0.01*                 | Further consideration needed<sup>(c)</sup> |
| –           | Other commodities of plant and/or animal origin | See Reg. 1004/2013 | – | – | Further consideration needed<sup>(d)</sup> |

**Enforcement residue definition:** 8-hydroxyquinoline and its salts, expressed as 8-hydroxyquinoline

- **MRL:** maximum residue level; **CXL:** codex maximum residue limit.
- *: Indicates that the MRL is set at the limit of quantification.
- (a): The impact of the classification of 8-hydroxyquinoline as toxic for reproduction category 1B on the validity of the MRL proposal was not considered in the assessment.
- (b): Tentative MRL is derived from a GAP evaluated at EU level, which is not fully supported by data but for which no risk to consumers was identified; no CXL is available (combination F-I in Appendix E). It is noted that 8-hydroxyquinoline is classified as toxic for reproduction category 1B.
- (c): MRL is derived from a GAP evaluated at EU level, which is fully supported by data and for which no risk to consumers is identified; no CXL is available (combination H-I in Appendix E). It is noted that 8-hydroxyquinoline is classified as toxic for reproduction category 1B.
- (d): 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)

| Source of ADI | EC | Year of evaluation | Time of evaluation |
|---------------|----|--------------------|--------------------|
| Source of ADI  | EC | 2017               | 2017               |

#### Toxicological reference values

| ADI (mg/kg bw/day) | ARfD (mg/kg bw) |
|--------------------|-----------------|
| 0.05               | 0.05            |

#### Input values

| 8-Hydroxyquinoline | LOQs (mg/kg) range from: |
|--------------------|--------------------------|
| 0.01               | 0.01                     |

#### Details – chronic risk assessment

| ADI (mg/kg bw/day) | ARfD (mg/kg bw) |
|--------------------|-----------------|
| 0.05               | 0.05            |

#### Normal mode

#### Chronic risk assessment: JMPR methodology (EDI/TMDI)

| Commodity group of commodities | Commodity group of commodities |
|--------------------------------|--------------------------------|
| Watermelons                    | Strawberries                  |
| Tomatoes                       | Melons                        |
| Cucumbers                      | Sweet peppers/bell peppers    |
| Tomatoes                       | Melons                        |
| Cucumbers                      | Sweet peppers/bell peppers    |
| Tomatoes                       | Melons                        |
| Cucumbers                      | Sweet peppers/bell peppers    |
| Tomatoes                       | Melons                        |
| Cucumbers                      | Sweet peppers/bell peppers    |
| Tomatoes                       | Melons                        |
| Cucumbers                      | Sweet peppers/bell peppers    |
| Tomatoes                       | Melons                        |
| Cucumbers                      | Sweet peppers/bell peppers    |

#### Conclusion:

The estimated long-term dietary intake (TMDI/IEDI/NEDI) was below the ADI. The long-term intake of residues of 8-hydroxyquinoline is unlikely to present a public health concern.

**DISCLAIMER:** Dietary data from the UK were included in PRIMO when the UK was a member of the European Union.
### Acute risk assessment/children

#### Results for children

| Highest % of ARfD/ADI | Commodities                  | MRL/input for RA (mg/kg) | Exposure (µg/kg bw) | Highest % of ARfD/ADI | Commodities                  | MRL/input for RA (mg/kg) | Exposure (µg/kg bw) |
|-----------------------|------------------------------|--------------------------|---------------------|-----------------------|------------------------------|--------------------------|---------------------|
| 6%                    | Melons                       | 0.01/0.02                | 2.3                 | 5%                    | Watermelons                  | 0.01/0.02                | 2.4                 |
| 5%                    | Watermelons                  | 0.01/0.02                | 1.3                 | 3%                    | Cucumbers                    | 0.01/0.02                | 0.9                 |
| 3%                    | Cucumbers                    | 0.01/0.02                | 1.2                 | 2%                    | Tomatoes                     | 0.01/0.02                | 0.9                 |
| 2%                    | Tomatoes                     | 0.01/0.02                | 0.9                 | 2%                    | Courgettes                   | 0.01/0.02                | 0.6                 |
| 2%                    | Courgettes                   | 0.01/0.02                | 0.6                 | 1%                    | Aubergines/egg plants        | 0.01/0.02                | 0.3                 |
| 1%                    | Aubergines/egg plants        | 0.01/0.02                | 0.3                 | 0.7%                  | Strawberries                 | 0.01/0.02                | 0.2                 |
| 0.7%                  | Strawberries                 | 0.01/0.02                | 0.2                 | 0.1%                  | Gherkins                     | 0.01/0.02                | 0.1                 |

### Acute risk assessment/adults/general population

#### Results for adults

| Highest % of ARfD/ADI | Commodities                  | MRL/input for RA (mg/kg) | Exposure (µg/kg bw) | Highest % of ARfD/ADI | Commodities                  | MRL/input for RA (mg/kg) | Exposure (µg/kg bw) |
|-----------------------|------------------------------|--------------------------|---------------------|-----------------------|------------------------------|--------------------------|---------------------|
| 4%                    | Pumpkins/boiled              | 0.01/0.02                | 1.8                 | 2%                    | Pumpkins/boiled              | 0.01/0.02                | 1.1                 |
| 1%                    | Courgettes/boiled            | 0.01/0.02                | 0.7                 | 0.9%                  | Aubergines/egg plants        | 0.01/0.02                | 0.6                 |
| 0.9%                  | Gherkins/jickeled            | 0.01/0.02                | 0.4                 | 0.8%                  | Tomatoes/boiled              | 0.01/0.02                | 0.3                 |
| 0.8%                  | Tomatoes/boiled              | 0.01/0.02                | 0.3                 | 0.4%                  | Tomatoes/sauce/puree          | 0.01/0.02                | 0.2                 |

### Conclusion:

No exceedance of the toxicological reference value was identified for any unprocessed commodity. A short-term intake of residues of 8-hydroxyquinoline is unlikely to present a public health risk. For processed commodities, no exceedance of the ARfD/ADI was identified.
Appendix D – Input values for the exposure calculations

D.1. **Livestock dietary burden calculations**

Not applicable as 8-hydroxyquinoline is not authorised for use on crops that might be fed to livestock.

D.2. **Consumer risk assessment**

| Commodity             | Chronic risk assessment | Acute risk assessment |
|-----------------------|-------------------------|-----------------------|
|                       | Input value (mg/kg)     | Comment               | Input value (mg/kg) | Comment               |
| Risk assessment residue definition: 8-hydroxyquinoline (free and conjugated) and its salts expressed as 8-hydroxyquinoline |
| Strawberries          | 0.02                    | \(\text{STMR_{90}} \times \text{CF (2)}\)                                      | 0.02                    | \(\text{HR_{90}} \times \text{CF (2)}\)                                      |
| Tomatoes              | 0.02                    | \(\text{STMR_{90}} \times \text{CF (2)}\)                                      | 0.02                    | \(\text{HR_{90}} \times \text{CF (2)}\)                                      |
| Sweet peppers/bell peppers | 0.02                    | \(\text{STMR_{90}} \times \text{CF (2)}\)                                      | 0.02                    | \(\text{HR_{90}} \times \text{CF (2)}\)                                      |
| Aubergines/eggplants  | 0.02                    | \(\text{STMR_{90}} \times \text{CF (2)}\)                                      | 0.02                    | \(\text{HR_{90}} \times \text{CF (2)}\)                                      |
| Okra/lady’s fingers   | 0.02                    | \(\text{STMR_{90}} \times \text{CF (2)}\)                                      | 0.02                    | \(\text{HR_{90}} \times \text{CF (2)}\)                                      |
| Cucumbers             | 0.02                    | \(\text{STMR_{90}} \times \text{CF (2)}\)                                      | 0.02                    | \(\text{HR_{90}} \times \text{CF (2)}\)                                      |
| Gherkins              | 0.02                    | \(\text{STMR_{90}} \times \text{CF (2)}\)                                      | 0.02                    | \(\text{HR_{90}} \times \text{CF (2)}\)                                      |
| Courgettes            | 0.02                    | \(\text{STMR_{90}} \times \text{CF (2)}\)                                      | 0.02                    | \(\text{HR_{90}} \times \text{CF (2)}\)                                      |
| Melons                | 0.02                    | \(\text{STMR_{90}} \times \text{CF (2)}\)                                      | 0.02                    | \(\text{HR_{90}} \times \text{CF (2)}\)                                      |
| Pumpkins              | 0.02                    | \(\text{STMR_{90}} \times \text{CF (2)}\)                                      | 0.02                    | \(\text{HR_{90}} \times \text{CF (2)}\)                                      |
| Watermelons           | 0.02                    | \(\text{STMR_{90}} \times \text{CF (2)}\)                                      | 0.02                    | \(\text{HR_{90}} \times \text{CF (2)}\)                                      |
Appendix E – Decision tree for deriving MRL recommendations
## Appendix F – Used compound codes

| Code/trivial name(a)          | IUPAC name/SMILES notation/InChiKey(b)                                                                 | Structural formula(c) | M1                           | M2                           |
|------------------------------|---------------------------------------------------------------------------------------------------------|------------------------|-------------------------------|-------------------------------|
| 8-hydroxyquinoline sulfate   | bis(8-hydroxyquinolinium) sulfateYYVFXSYQSOZCOQ-UHFFFAOYSA-N                                                                                                   | ![Structural formula image](image) | Not identified               | Not identified               |
| (8-HQS)                      | InChI=1S/2C9H7NO.H2O4S/c2*11-8-5-1-3-7-4-2-6-10-9(7)B;1-5(2,3)4/h2*1-6,11H;(H2,1,2,3,4)                                                                 | ![Structural formula image](image) | Not identified               | Not identified               |

(a): The metabolite name in bold is the name used in the conclusion.
(b): ACD/Name 2019.1.3 ACD/Labs 2019 Release (File version N05E41, Build 111418, 3 September 2019).
(c): ACD/ChemSketch 2019.1.3 ACD/Labs 2019 Release (File version C05H41, Build 111302, 27 August 2019).