

## REASONED OPINION

### Reasoned opinion on the setting of a new maximum residues level (MRL) for metrafenone in hop cones<sup>1</sup>

European Food Safety Authority<sup>2</sup>

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#### ABSTRACT

In accordance with Article 6 of Regulation (EC) No 396/2005, Germany, hereafter referred to as the evaluating Member State (EMS), received an application from BASF SE to set a MRL for the active substance metrafenone in hops (dried). In order to accommodate for the intended use of metrafenone, Germany proposed to raise the existing MRL from the limit of quantification of 0.05mg/kg to 80 mg/kg. Germany drafted an evaluation report in accordance with Article 8 of Regulation (EC) No 396/2005, which was submitted to the European Commission and forwarded to EFSA. According to EFSA the data are sufficient to derive a MRL proposal of 80 mg/kg for the proposed use on hops (dried). Adequate analytical enforcement methods are available to control the residues of metrafenone on the commodity under consideration. Based on the risk assessment results, EFSA concludes that the proposed use of metrafenone on hops (dried) will not result in a consumer exposure exceeding the toxicological reference value and therefore is unlikely to pose a consumer health risk.

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#### KEY WORDS

metrafenone, hops (dried), MRL application, Regulation (EC) No 396/2005, consumer risk assessment, aryl phenyl ketone fungicides.

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## SUMMARY

In accordance with Article 6 of Regulation (EC) No 396/2005, Germany, hereafter referred to as the evaluating Member State (EMS), received an application from BASF SE to set a new maximum residue level (MRL) for the active substance metrafenone in hops (dried). In order to accommodate for the intended use of metrafenone, Germany proposed to raise the existing MRL from the limit of quantification (LOQ) of 0.05 mg/kg to 80 mg/kg. Germany drafted an evaluation report in accordance with Article 8 of Regulation (EC) No 396/2005, which was submitted to the European Commission and forwarded to EFSA on 26 May 2014.

EFSA bases its assessment on the evaluation report submitted by the EMS, the Draft Assessment Report (DAR) prepared under Council Directive 91/414/EEC, the Commission Review Report on metrafenone, the conclusion on the peer review of the pesticide risk assessment of the active substance metrafenone as well as the conclusions from previous EFSA opinions on metrafenone.

The toxicological profile of metrafenone was assessed in the framework of the peer review under Directive 91/414/EEC and the data were sufficient to derive an ADI of 0.25 mg/kg bw per day. No ARfD was deemed necessary.

The metabolism of metrafenone in primary crops was investigated in grape and cucumber (fruit crops) and in wheat (cereals). From these studies the peer review concluded to establish the residue definition for enforcement and for risk assessment as metrafenone, limited to the cereal and fruit crop groups only. Since hops belong to the leafy crop group, a metabolism study on a third crop group is in principle required. However, considering the very low contribution of hops to the overall consumer dietary burden and the non-significant transfer of residues expected from hops to processed commodities, EFSA concludes that the residue definitions derived in the course of the peer review are applicable, even if the metabolism of metrafenone has not been sufficiently addressed for the leafy crop group.

EFSA concludes that the submitted supervised residue trials are sufficient to derive a MRL proposal of 80 mg/kg for the proposed use on hops (dried). An adequate analytical enforcement method is available to control the residues of metrafenone in hops at the validated LOQ of 0.01 mg/kg.

Metrafenone was hydrolytically stable under standard hydrolysis conditions and therefore for processed commodities the same residue definition as for raw agricultural commodities (RAC) is applicable. Several processing studies were provided and the data were sufficient to derive the following processing factors, which are recommended to be included in Annex VI of Regulation (EC) No 396/2005:

- Hops/Beer: 0.0005 - Hops/Extracted hops: 1.8 - Hops/Hops draff: 0.24

Since the proposed use is on a permanent crop and since hops and its by-products are normally not fed to livestock, residues in rotational crops and in commodities of animal origin were not assessed in the framework of this application.

The consumer risk assessment was performed with revision 2 of the EFSA Pesticide Residues Intake Model (PRIMo). No long-term consumer intake concerns were identified for any of the European diets incorporated in the EFSA PRIMo. The total calculated intake accounted for up to 2 % of the ADI (German child). The contribution of residues in hops (dried) to the total consumer exposure accounted for a maximum of 0.05 % of the ADI.

EFSA concludes that the proposed use of metrafenone on hops (dried) will not result in a consumer exposure exceeding the toxicological reference value and therefore is unlikely to pose a consumer health risk.

**RECOMMENDATIONS**

<b>Code(a)</b>	<b>Commodity</b>	<b>Existing EU MRL (mg/kg)</b>	<b>Proposed EU MRL (mg/kg)</b>	<b>Comment/Justification</b>
<b>Enforcement residue definition: metrafenone</b>				
0700000	Hops (dried)	0.05*	80	The MRL proposal is sufficiently supported by data and no consumer health risk was identified.

(a): According to Annex I of Regulation (EC) No 396/2005.

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

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## BACKGROUND

Regulation (EC) No 396/2005<sup>3</sup> establishes the rules governing the setting of pesticide MRLs at European Union level. Article 6 of that Regulation lays down that any party having a legitimate interest or requesting an authorisation for the use of a plant protection product in accordance with Council Directive 91/414/EEC<sup>4</sup>, repealed by Regulation (EC) No 1107/2009<sup>5</sup>, shall submit to a Member State, when appropriate, an application to set a MRL in accordance with the provisions of Article 7 of that Regulation.

Germany, hereafter referred to as the evaluating Member State (EMS), received an application from the company BASF SE<sup>6</sup> to modify the existing MRL for the active substance metrafenone in hops (dried). This application was notified to the European Commission and EFSA and was subsequently evaluated by the EMS in accordance with Article 8 of the Regulation.

After completion, the evaluation report was submitted to the European Commission who forwarded the application, the evaluation report and the supporting dossier to EFSA on 26 May 2014.

The application was included in the EFSA Register of Questions with the reference number EFSA-Q-2014-00400 and the following subject:

*Metrafenone: Setting of MRL for Metrafenone in hops cones*

Germany proposed to raise the existing MRL of metrafenone in hops (dried) from the limit of quantification of 0.05\* mg/kg to EMS proposed MRL value of 80 mg/kg.

EFSA proceeded with the assessment of the application and the evaluation report as required by Article 10 of the Regulation.

## TERMS OF REFERENCE

In accordance with Article 10 of Regulation (EC) No 396/2005, EFSA shall, based on the evaluation report provided by the evaluating Member State, provide a reasoned opinion on the risks to the consumer associated with the application.

In accordance with Article 11 of that Regulation, the reasoned opinion shall be provided as soon as possible and at the latest within three months (which may be extended to six months where more detailed evaluations need to be carried out) from the date of receipt of the application. Where EFSA requests supplementary information, the time limit laid down shall be suspended until that information has been provided.

In this particular case the deadline for providing the reasoned opinion is 27 August 2014.

<sup>3</sup> Regulation (EC) No 396/2005 of the Parliament and of the Council of 23 February 2005 on maximum residue levels of pesticides in or on food and feed of plant and animal origin and amending Council Directive 91/414/EEC. OJ L 70, 16.03.2005, p. 1-16.

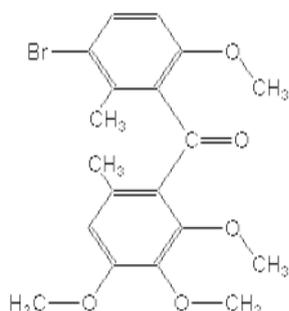
<sup>4</sup> Council Directive 91/414/EEC of 15 July 1991 concerning the placing of plant protection products on the market. OJ L 230, 19.08.1991, p. 1-32.

<sup>5</sup> 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.

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## THE ACTIVE SUBSTANCE AND ITS USE PATTERN

Metrafenone is the ISO common name for 3'-bromo-2,3,4,6'-tetramethoxy-2',6-dimethyl benzophenone (IUPAC). The chemical structure of the compound is reported below.



**Figure 1:** Chemical structure of metrafenone. Molecular weight: 409.3 g/mol

Metrafenone belongs to the group of aryl phenyl ketone fungicides. It inhibits growth of mycelium on the leaf surface, leaf penetration, formation of *haustoria* and sporulation in powdery mildew that is produced, among others, by *Uncinula necator* and *Erysiphe graminis*.

Metrafenone was evaluated in the framework of Council Directive 91/414/EEC with United Kingdom designated as rapporteur Member State (RMS). It was included in Annex I of this Directive by Directive 2007/6/EC<sup>7</sup> which entered into force on 1 February 2007 for use as fungicide only. In accordance with Commission Implementing Regulation (EU) No 540/2011<sup>8</sup> metrafenone is approved under Regulation (EC) No 1107/2009, repealing Council Directive 91/414/EEC.

The representative uses evaluated in the peer review were foliar applications on cereals (wheat and barley) and wine grapes. The Draft Assessment Report (DAR) of metrafenone has been peer reviewed by EFSA (EFSA, 2006).

The EU MRLs for metrafenone are established in Annex IIIA of Regulation (EC) No 396/2005. The review of the existing MRLs was made by EFSA (EFSA, 2013b). The existing EU MRL for metrafenone on hops (dried) is set at the LOQ of 0.05\* mg/kg. No CXLs are established for metrafenone.

The details of the intended GAP on hops (dried) for metrafenone are given in Appendix A.

<sup>7</sup> Commission Directive 2007/6/EC of 14 February 2007 amending Council Directive 91/414/EEC to include metrafenone, *Bacillus subtilis*, spinosad and thiametoxam as active substances. OJ L 43, 15.2.2007, p. 13-18.

<sup>8</sup> Commission Implementing Regulation (EU) No 540/2011 of 23 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, 11.06.2011, p. 1-186.

## ASSESSMENT

EFSA bases its assessment on the evaluation report submitted by the EMS (Germany, 2014), the Draft Assessment Report (DAR) prepared under Council Directive 91/414/EEC (United Kingdom, 2005), the Commission Review Report on metrafenone (EC, 2006), the conclusion on the peer review of the pesticide risk assessment of the active substance metrafenone (EFSA, 2006) as well as the conclusions from previous EFSA opinions on metrafenone (EFSA, 2011, 2013a,b). The assessment is performed in accordance with the legal provisions of the Uniform Principles for the Evaluation and the Authorisation of Plant Protection Products adopted by Commission Regulation (EU) No 546/2011<sup>9</sup> and the currently applicable guidance documents relevant for the consumer risk assessment of pesticide residues (EC, 1996, 1997a-g, 2000, 2010a,b, 2011; OECD, 2011).

### 1. Method of analysis

#### 1.1. Methods for enforcement of residues in food of plant origin

During the peer review under Directive 91/414/EEC, an analytical method using GC-ECD and its ILV were evaluated and validated for the determination of parent metrafenone in acidic (grapes) and dry/starch matrices (barley grain) at an LOQ of 0.02 mg/kg (United Kingdom, 2003).

In addition, in the course of the Article 12 MRL review, the multi-residue QuEChERS method in combination with LC-MS/MS detection and its ILV, were concluded to be fully validated for the determination of metrafenone residues in high acid-, high water-, dry/starch and dry/protein matrices at the LOQ of 0.01 mg/kg (EFSA, 2013b). Additional validation data were submitted in the framework of this MRL application to confirm that the QuEChERS method is suitable for the analysis of metrafenone residues in hops (dried cones) at a LOQ of 0.01 mg/kg. A confirmatory method was indeed provided.

Therefore, EFSA concludes that a sufficiently validated analytical method for enforcing the proposed MRL for metrafenone in hops (dried) is available.

#### 1.2. Methods for enforcement of residues in food of animal origin

Analytical methods for the determination of residues in food of animal origin are not assessed in the current application, since hops (dried) is normally not fed to livestock.

### 2. Mammalian toxicology

The toxicological profile of metrafenone was assessed in the framework of the peer review under Directive 91/414/EEC (EFSA, 2006). The data were sufficient to derive toxicological reference values for metrafenone which are compiled in Table 2-1.

**Table 2-1:** Overview of the toxicological reference values

	Source	Year	Value	Study relied upon	Safety factor
<b>Metrafenone</b>					
<b>ADI</b>	EFSA	2006	0.25 mg/kg bw per day	Rat - 2 year study	100
<b>ARfD</b>	EFSA	2006	Not allocated – not necessary		

<sup>9</sup> 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, 11.06.2011, p. 127-175.

### 3. Residues

#### 3.1. Nature and magnitude of residues in plant

##### 3.1.1. Primary crops

###### 3.1.1.1. Nature of residues

The metabolism of metrafenone in primary crops was evaluated by the RMS (United Kingdom, 2005) and reviewed by EFSA (EFSA, 2006) in the framework of the peer review under Directive 91/414/EEC. An additional study performed on cucumbers was also evaluated in the framework of a previous MRL application (EFSA, 2013a). The overview of the metabolism study designs is presented in the table below.

**Table 3-1:** Summary of available metabolism studies in plants

Crop group	Crops	Application	Sampling <sup>(a)</sup> (day, DAT)	Comments
Fruits	Grape	Foliar , 5 × 200 g/ha	19, 35 DAT5	EFSA, 2006
	Cucumber	Foliar , 2 × 200 g/ha	0 (leaf), 14, 17 DAT1	EFSA, 2013a
Cereals	Wheat	Foliar, 2 × 300 + 1 × 200 g/ha	Grain & straw: 35 DAT3	EFSA, 2006

(a): DATx, Days after treatment ×.

The metabolism of metrafenone was investigated after foliar applications on cereals (wheat) and on fruits (grapes), using <sup>14</sup>C-metrafenone labelled on the bromophenyl and the trimethoxyphenyl moieties respectively. The additional metabolism study on cucumbers was conducted using metrafenone labelled on the trimethoxyphenyl moiety only.

The available metabolism studies did not indicate any evidence of a molecular cleavage of the parent compound and it was concluded that similar metabolism of metrafenone can be assumed in the two crop categories investigated (cereals and fruit crop groups). The peer review derived the residue definition for enforcement and risk assessment as metrafenone only, restricted to cereals and fruit crop groups. No general residue definition for commodities of plant origin can be proposed.

Since hops belong to the leafy crop group, a metabolism study on a third crop group is in principle required. However, considering the very low contribution of hops to the overall consumer dietary burden and the non-significant transfer of residues expected from hops to processed commodities (see section 3.1.1.3), this metabolism data can be considered as only desirable as this would provide more certainty on the expectation that the metabolic pattern will not differ in hops (dried). The current residue definition set in Regulation (EC) No 396/2005 is identical to the residue definition for enforcement derived in the peer review.

EFSA concludes that even if the metabolism of metrafenone has not been sufficiently addressed for the leafy crop group, the residue definitions for enforcement and risk assessment agreed in the peer review might be considered applicable.

###### 3.1.1.2. Magnitude of residues

In support of the MRL application, 6 residue trials compliant with the GAP in the northern outdoor zone were provided. Residues in dried cones were in the range of 18.3 to 34 mg/kg and result in an MRL proposal of 80 mg/kg.

The results of the residue trials, the related risk assessment input values (highest residue, median residue) and the MRL proposal are summarised in Table 3-2.

In the framework of the peer review, storage stability of metrafenone was demonstrated at -20 °C for a period of 18 months in acidic commodities (grapes) and 24 months in dry commodities (cereals) (EFSA, 2006). An additional study evaluated in the framework of the MRL application on table and wine grapes, demonstrated the storage stability of metrafenone in commodities with high water content (tomatoes) for a period of 15 months (EFSA, 2011). In the framework of this application, additional storage stability data demonstrated the frozen storage stability of metrafenone at  $\leq 20$  °C for up to 24 months in matrices with high water- (wheat whole plant, tomato), high acid- (grapes), high oil content (soya bean) as well as in dry matrices (wheat grain, dried peas). As the hops samples were stored frozen for a maximum period of 5 to 8 months prior to analysis, it is concluded that the residue data are valid with regard to storage stability.

According to the EMS, the analytical method used to analyse the supervised residue trial samples has been sufficiently validated and was proven to be fit for the purpose (Germany, 2014).

EFSA concludes that the data are sufficient to derive a MRL proposal of 80 mg/kg for the intended use on hops (dried).

**Table 3-2:** Overview of the available residues trials data

<b>Crop</b> (Trial GAPs)	<b>Region/ Indoor</b> (a)	<b>Residue levels (mg/kg) observed in the supervised residue trials relevant to the supported GAPs</b> (b)	<b>Recommendations/comments</b> (c)	<b>MRL proposals</b> (mg/kg)	<b>HR</b> (mg/kg) (d)	<b>STMR</b> (mg/kg) (e)
Hops (dried)	NEU	18.3, 19.7, 21.3, 22.8, 33, 34	MRL <sub>OECD</sub> : 75/80	80	34	22.05

(a): NEU (Northern Europe), SEU (Southern Europe), EU (i.e. indoor use) or Import (country code) (EC, 2011).

(b): Individual residue levels considered for MRL calculation are reported in ascending order as following:  $3 \times <0.01$ , 0.01,  $6 \times 0.02$ , 0.04, 0.08,  $2 \times 0.10$ , 0.15, 0.17

(c): Any information/comment supporting the decision and OECD MRL calculation (e.g. MRL<sub>OECD</sub>: 0.82/0.9; unrounded/rounded values)

(d) HR: Highest value of the individual trial results according to the residue definition for risk assessment.

(e): STMR: Median value of the individual trial results according to residue definition for risk assessment

### 3.1.1.3. Effect of industrial processing and/or household preparation

The effect of processing on the nature of metrafenone was investigated under standard hydrolysis conditions. The studies were reported in the DAR and in the conclusion on the peer review (United Kingdom, 2005; EFSA, 2006). EFSA concluded that the compound is hydrolytically stable under the representative processing conditions. Thus, for processed commodities the same residue definition as for raw agricultural commodities (RAC) is applicable (EFSA, 2006).

Three studies investigating the transfer of residues from hops to different processed products were assessed in support of this MRL application (Germany, 2014). Processing study results are summarised in Table 3-3 below.

**Table 3-3:** Overview of the available processing studies

Processed commodity	Number of studies	PF <sup>(a)</sup> (individual PF) Median	Median CF <sup>(b)</sup>	Comments
<b>Enforcement residue definition: metrafenone</b>				
Beer	3	(0.0005, 0.0005, 0.0006) <b>0.0005</b>	n.a.	Residue levels in beer were all < 0.01 mg/kg
Extracted hops	3	(1.8, 1.8, 1.8) <b>1.8</b>	n.a.	
Hops draff	3	(0.24, 0.24, 0.25) <b>0.24</b>	n.a.	

(a): The median processing factor is obtained by calculating the median of the individual processing factors of each processing study.

(b): The median conversion factor for enforcement to risk assessment is obtained by calculating the median of the individual conversion factors of each processing study (n.a.: not applicable).

EFSA recommends the inclusion of the derived processing factors for processed products in Annex VI of Regulation (EC) No 396/2005.

### 3.1.2. Rotational crops

#### 3.1.2.1. Preliminary considerations

Since the proposed use of metrafenone is on a permanent crop, investigations of residues in rotational crops are not required.

### 3.2. Nature and magnitude of residues in livestock

Since hops cones and its by-products are not normally fed to livestock, the nature and magnitude of metrafenone residues in livestock is not assessed in the framework of this application (EC, 1996).

## 4. Consumer risk assessment

The consumer risk assessment was performed with revision 2 of the EFSA Pesticide Residues Intake Model (PRIMo). This exposure assessment model contains the relevant European food consumption data for different sub-groups of the EU population<sup>10</sup> (EFSA, 2007).

For the calculation of the chronic exposure, EFSA used STMR values as derived from the residue trials on hops (dried) (see Table 3-2), the median residue values reported in the framework of the review of the existing EU MRLs (EFSA, 2013b). For the remaining commodities of plant and animal

<sup>10</sup> The calculation of the long-term exposure (chronic exposure) is based on the mean consumption data representative for 22 national diets collected from MS surveys plus 1 regional and 4 cluster diets from the WHO GEMS Food database; for the acute exposure assessment the most critical large portion consumption data from 19 national diets collected from MS surveys is used. The complete list of diets incorporated in EFSA PRIMo is given in its reference section (EFSA, 2007).

origin, the existing MRLs as established in Annexes IIIA of Regulation (EC) No 396/2005 were used as input values.

The model assumptions for the long-term exposure assessment are considered to be sufficiently conservative for a first tier exposure assessment, assuming that all food items consumed have been treated with the active substance under consideration. In reality, it is not likely that all food consumed will contain residues at the MRL or at levels of the median residue values identified in supervised field trials. However, if this first tier exposure assessment does not exceed the toxicological reference value for long-term exposure (i.e. the ADI), a consumer health risk can be excluded with a high probability.

No acute consumer exposure assessment was performed, due to the low acute toxicity of the active substance.

The input values used for the dietary exposure calculation are summarised in Table 4-1.

**Table 4-1:** Input values for the consumer dietary exposure assessment

Commodity	Chronic exposure assessment	
	Input value (mg/kg)	Comment
<b>Risk assessment residue definition: metrafenone</b>		
Table grapes	1.08	STMR (EFSA, 2013b)
Wine grapes	0.24	STMR*PF*YF <sup>(a)</sup> (EFSA, 2013b)
Strawberries	0.13	STMR (EFSA, 2013b)
Tomatoes	0.1	STMR (EFSA, 2013b)
Peppers	0.12	STMR (EFSA, 2013b)
Aubergines	0.1	STMR (EFSA, 2013b)
Cucurbits – edible peel	0.03	STMR (EFSA, 2013b)
Cucurbits – inedible peel	0.04	STMR (EFSA, 2013b)
Cultivated fungi	0.11	STMR (EFSA, 2013b)
Barley & oats grain	0.09	STMR (EFSA, 2013b)
Wheat & rye grain	0.01	STMR (EFSA, 2013b)
Hops (dried)	22.05	STMR
Other plant and animal commodities	EC MRL	MRLs in Regulation (EU) 500/2013 <sup>11</sup>

(a): Consumption figure in the PRIMo model is expressed for the raw commodity (e.g. grape, olive...). A yield factor (YF) is therefore considered to estimate the consumption figure for the processed commodity (e.g. wine, oil...).

The estimated exposure was then compared with the toxicological reference value derived for metrafenone (see Table 2-1). The results of the intake calculation are presented in Appendix B to this reasoned opinion.

No long-term consumer intake concerns were identified for any of the European diets incorporated in the EFSA PRIMo. The total calculated intake accounted for up to 2 % of the ADI (German child). The

<sup>11</sup> Commission Regulation (EU) No 500/2013 of 30 May 2013 amending Annexes II, III and IV to Regulation (EC) No 396/2005 of the European Parliament and of the Council as regards maximum residue levels for acetamiprid, Adoxophyes orana granulovirus strain BV-0001, azoxystrobin, clothianidin, fenpyrazamine, heptamaloxylglucan, metrafenone, Paecilomyces lilacinus strain 251, propiconazole, quizalofop-P, spiromesifen, tebuconazole, thiamethoxam and zucchini yellow mosaic virus - weak strain in or on certain products Text with EEA relevance. OJ L 151, 4.6.2013, p. 1–32.

contribution of residues in hops (dried) to the total consumer exposure accounted for less than 0.05 % of the ADI.

EFSA concludes that the intended use of metrafenone on hops (dried) will not result in a consumer exposure exceeding the toxicological reference value and therefore is unlikely to pose a public health concern.

## CONCLUSIONS AND RECOMMENDATIONS

### CONCLUSIONS

The toxicological profile of metrafenone was assessed in the framework of the peer review under Directive 91/414/EEC and the data were sufficient to derive an ADI of 0.25 mg/kg bw per day. No ARfD was deemed necessary.

The metabolism of metrafenone in primary crops was investigated in grape and cucumber (fruit crops) and in wheat (cereals). From these studies the peer review concluded to establish the residue definition for enforcement and for risk assessment as metrafenone, limited to the cereal and fruit crop groups only. Since hops belong to the leafy crop group, a metabolism study on a third crop group is in principle required. However, considering the very low contribution of hops to the overall consumer dietary burden and the non-significant transfer of residues expected from hops to processed commodities, EFSA concludes that the residue definitions derived in the course of the peer review are applicable, even if the metabolism of metrafenone has not been sufficiently addressed for the leafy crop group.

EFSA concludes that the submitted supervised residue trials are sufficient to derive a MRL proposal of 80 mg/kg for the proposed use on hops (dried). An adequate analytical enforcement method is available to control the residues of metrafenone in hops at the validated LOQ of 0.01 mg/kg.

Metrafenone was hydrolytically stable under standard hydrolysis conditions and therefore for processed commodities the same residue definition as for raw agricultural commodities (RAC) is applicable. Several processing studies were provided and the data were sufficient to derive the following processing factors, which are recommended to be included in Annex VI of Regulation (EC) No 396/2005:

- Hops/Beer: 0.0005 - Hops/Extracted hops: 1.8 - Hops/Hops draff: 0.24

Since the proposed use is on a permanent crop and since hops and its by-products are normally not fed to livestock, residues in rotational crops and in commodities of animal origin were not assessed in the framework of this application.

The consumer risk assessment was performed with revision 2 of the EFSA Pesticide Residues Intake Model (PRIMO). No long-term consumer intake concerns were identified for any of the European diets incorporated in the EFSA PRIMo. The total calculated intake accounted for up to 2 % of the ADI (German child). The contribution of residues in hops (dried) to the total consumer exposure accounted for a maximum of 0.05 % of the ADI.

EFSA concludes that the proposed use of metrafenone on hops (dried) will not result in a consumer exposure exceeding the toxicological reference value and therefore is unlikely to pose a consumer health risk.

## RECOMMENDATIONS

Code(a)	Commodity	Existing EU MRL (mg/kg)	Proposed EU MRL (mg/kg)	Comment/Justification
<b>Enforcement residue definition: metrafenone</b>				
0700000	Hops (dried)	0.05*	80	The MRL proposal is sufficiently supported by data and no consumer health risk was identified.

(a): According to Annex I of Regulation (EC) No 396/2005.

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

## REFERENCES

- EC (European Commission), 1996. Appendix G. Livestock Feeding Studies. 7031/VI/95-rev.4.
- EC (European Commission), 1997a. Appendix A. Metabolism and distribution in plants. 7028/IV/95-rev.3.
- EC (European Commission), 1997b. Appendix B. General recommendations for the design, preparation and realisation of residue trials. Annex 2. Classification of (minor) crops not listed in the Appendix of Council Directive 90/642/EEC. 7029/VI/95-rev.6.
- EC (European Commission), 1997c. Appendix C. Testing of plant protection products in rotational crops. 7524/VI/95-rev.2.
- EC (European Commission), 1997d. Appendix E. Processing studies. 7035/VI/95-rev.5.
- EC (European Commission), 1997e. Appendix F. Metabolism and distribution in domestic animals. 7030/VI/95-rev.3.
- EC (European Commission), 1997f. Appendix H. Storage stability of residue samples. 7032/VI/95-rev.5.
- EC (European Commission), 1997g. Appendix I. Calculation of maximum residue level and safety intervals. 7039/VI/95.
- EC (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.
- EC (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.
- EC (European Commission), 2010b. Residue analytical methods. For post-registration control. SANCO/825/00-rev.8.1.
- EC (European Commission), 2011. Appendix D. Guidelines on comparability, extrapolation, group tolerances and data requirements for setting MRLs. 7525/VI/95-rev.9.
- EFSA (European Food Safety Authority), 2006. Conclusion on the peer review of the pesticide risk assessment of the active substance metrafenone. The EFSA Journal 2006, 58r, 1-72. Available online: <http://www.efsa.europa.eu/it/efsajournal/doc/58r.pdf>
- EFSA (European Food Safety Authority), 2007. Reasoned opinion on the potential chronic and acute risk to consumers' health arising from proposed temporary EU MRLs. The EFSA Journal 2007, 32r, 1-1141. Available online: <http://www.efsa.europa.eu/en/efsajournal/doc/32r.pdf>
- EFSA (European Food Safety Authority), 2011. Reasoned opinion on the modification of the existing MRLs for metrafenone in table and wine grapes. EFSA Journal 2011;9(1):1979, 23 pp. doi:10.2903/j.efsa.2011.1979

- EFSA (European Food Safety Authority), 2013a. Reasoned opinion on the modification of the existing MRLs for metrafenone in various crops. EFSA Journal 2013;11(1):3075, 30 pp. doi:10.2903/j.efsa.2013.3075
- EFSA (European Food Safety Authority), 2013b. Reasoned opinion on the review of the existing maximum residue levels (MRLs) for metrafenone according to article 12 of Regulation (EC) No 396/2005. EFSA Journal 2013; 11(12):3498, 43 pp. doi:10.2903/j.efsa.2013.3498
- Germany, 2014. Evaluation report on the setting of MRL for metrafenone in hop cones prepared by the evaluating Member State Germany under Article 8 of Regulation (EC) No 396/2005, 06 May 2014, 46 pp.
- Meier U, 2001. Growth Stages of mono- and dicotyledonous plants. BBCH Monograph, 2nd Ed., Federal Biological Research Centre of Agriculture and Forestry, Braunschweig, Germany, 2001.
- 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.
- United Kingdom, 2005. Draft assessment report on the active substance metrafenone prepared by the rapporteur Member State United Kingdom in the framework of Council Directive 91/414/EEC, October 2003.

## APPENDICES

### APPENDIX A. GOOD AGRICULTURAL PRACTICE (GAPS)

Crop and/or situation (a)	Member State or Country	F G or I (b)	Pest or group of pests controlled (c)	Formulation		Application				Application rate per treatment		PHI (days) (l)	Remarks (m)
				type (d-f)	conc. a.s. (i)	Method kind (f-h)	Growth stage & season (j)	number (k)	interval min-max	Water L/ha min-max	g a.s./ha min-max		
Hops	DE	F	Powdery mildew ( <i>Sphaerotheca macularis</i> )	SC	500	Spraying or fine spraying (low volume spraying)	BBCH 32-81 (crop stage), in case of danger of infection and/or notice of warning service, up to 3 days prior to harvest.	2	7-12	BBCH 32-37: 800-1500 BBCH 37-55: 1500-2200; BBCH 55-81: 2200-3300	<BBCH 37: 150 <BBCH 55: 220 >BBCH 55: 330	3	

#### Remarks:

- (a) For crops, EU or other classifications, e.g. Codex, should be used; where relevant, the use situation should be described (e.g. fumigation of a structure)
- (b) Outdoor or field use (F), glasshouse application (G) or indoor application (I)
- (c) e.g. biting and sucking insects, soil born insects, foliar fungi, weeds
- (d) e.g. wettable powder (WP), emulsifiable concentrate (EC), granule (GR)
- (e) GCPF Technical Monograph No 2, 4<sup>th</sup> Ed., 1999 or other codes, e.g. OECD/CIPAC, should be used
- (f) All abbreviations used must be explained
- (g) Method, e.g. high volume spraying, low volume spraying, spreading, dusting, drench
- (h) Kind, e.g. overall, broadcast, aerial spraying, row, individual plant, between the plants - type of equipment used must be indicated
- (i) g/kg or g/l
- (j) Growth stage at last treatment (Meier, 2001), including where relevant, information on season at time of application
- (k) The minimum and maximum number of application possible under practical conditions of use must be provided
- (l) PHI - minimum pre-harvest interval
- (m) Remarks may include: Extent of use/economic importance/restrictions (i.e. feeding, grazing)

**APPENDIX B. PESTICIDE RESIDUE INTAKE MODEL (PRIMO)**

Metrafenone									
Status of the active substance: <b>Included</b>					Code no.				
LOQ (mg/kg bw):					proposed LOQ: 0.01				
Toxicological end points									
ADI (mg/kg bw/day): <b>0.25</b>					ARfD (mg/kg bw): <b>n.n.</b>				
Source of ADI: <b>EFSA</b>					Source of ARfD: <b>EFSA</b>				
Year of evaluation: <b>2006</b>					Year of evaluation: <b>2006</b>				
<div style="border: 1px solid black; padding: 5px; display: inline-block;">Prepare workbook for refined calculations</div> <div style="border: 1px solid black; padding: 5px; display: inline-block; margin-top: 10px;">Undo refined calculations</div>									
Chronic risk assessment									
TMDI (range) in % of ADI minimum - maximum 0 - 2									
No of diets exceeding ADI: ---									
Highest calculated TMDI values in % of ADI	MS Diet	Highest contributor to MS diet (in % of ADI)	Commodity / group of commodities	2nd contributor to MS diet (in % of ADI)	Commodity / group of commodities	3rd contributor to MS diet (in % of ADI)	Commodity / group of commodities	pTMRLs at LOQ (in % of ADI)	
1.7	DE child	0.5	Table grapes	0.5	PRODUCTS OF ANIMAL ORIGIN	0.3	Pome fruit		
1.6	NL child	0.7	PRODUCTS OF ANIMAL ORIGIN	0.3	Table grapes	0.1	Pome fruit		
1.4	FR toddler	0.9	PRODUCTS OF ANIMAL ORIGIN	0.2	Root and tuber vegetables	0.1	Table grapes		
1.4	UK Toddler	0.5	PRODUCTS OF ANIMAL ORIGIN	0.5	SUGAR PLANTS	0.1	Table grapes		
1.4	UK Infant	0.8	PRODUCTS OF ANIMAL ORIGIN	0.2	SUGAR PLANTS	0.1	Root and tuber vegetables		
1.1	WHO Cluster diet B	0.2	Wine grapes	0.2	Table grapes	0.1	PRODUCTS OF ANIMAL ORIGIN		
0.9	FR infant	0.5	PRODUCTS OF ANIMAL ORIGIN	0.1	Root and tuber vegetables	0.1	Pome fruit		
0.9	IE adult	0.1	Wine grapes	0.1	PRODUCTS OF ANIMAL ORIGIN	0.1	Table grapes		
0.8	DK child	0.4	PRODUCTS OF ANIMAL ORIGIN	0.1	Table grapes	0.1	Root and tuber vegetables		
0.8	WHO cluster diet E	0.2	Wine grapes	0.1	PRODUCTS OF ANIMAL ORIGIN	0.1	Root and tuber vegetables		
0.7	SE general population 90th percentile	0.4	PRODUCTS OF ANIMAL ORIGIN	0.1	Root and tuber vegetables	0.0	Miscellaneous fruit (inedible peel,		
0.7	FR all population	0.4	Wine grapes	0.1	PRODUCTS OF ANIMAL ORIGIN	0.0	Table grapes		
0.7	ES child	0.4	PRODUCTS OF ANIMAL ORIGIN	0.0	Citrus fruit	0.0	Root and tuber vegetables		
0.6	PT General population	0.2	Wine grapes	0.1	Table grapes	0.1	Brassica vegetables		
0.6	WHO regional European diet	0.2	PRODUCTS OF ANIMAL ORIGIN	0.1	Root and tuber vegetables	0.1	Table grapes		
0.6	WHO cluster diet D	0.1	PRODUCTS OF ANIMAL ORIGIN	0.1	Root and tuber vegetables	0.1	Table grapes		
0.6	NL general	0.2	PRODUCTS OF ANIMAL ORIGIN	0.1	Table grapes	0.1	Root and tuber vegetables		
0.6	WHO Cluster diet F	0.1	PRODUCTS OF ANIMAL ORIGIN	0.1	Root and tuber vegetables	0.1	Wine grapes		
0.5	UK Adult	0.1	Wine grapes	0.1	PRODUCTS OF ANIMAL ORIGIN	0.1	SUGAR PLANTS		
0.5	UK vegetarian	0.1	Wine grapes	0.1	SUGAR PLANTS	0.1	PRODUCTS OF ANIMAL ORIGIN		
0.5	DK adult	0.2	PRODUCTS OF ANIMAL ORIGIN	0.1	Wine grapes	0.0	Root and tuber vegetables		
0.4	ES adult	0.2	PRODUCTS OF ANIMAL ORIGIN	0.0	Wine grapes	0.0	Tomatoes		
0.3	PL general population	0.1	Table grapes	0.1	Root and tuber vegetables	0.0	Pome fruit		
0.3	LT adult	0.1	PRODUCTS OF ANIMAL ORIGIN	0.1	Root and tuber vegetables	0.0	Pome fruit		
0.3	FI adult	0.1	PRODUCTS OF ANIMAL ORIGIN	0.0	Root and tuber vegetables	0.0	Wine grapes		
0.3	IT kids/toddler	0.1	Tomatoes	0.0	Table grapes	0.0	Wheat		
0.2	IT adult	0.1	Table grapes	0.0	Tomatoes	0.0	Pome fruit		
<b>Conclusion:</b>									
The estimated Theoretical Maximum Daily Intakes (TMDI), based on pTMRLs were below the ADI.									
A long-term intake of residues of Metrafenone is unlikely to present a public health concern.									

**ABBREVIATIONS**

ADI	acceptable daily intake
ARfD	acute reference dose
a.s.	active substance
BBCH	growth stages of mono- and dicotyledonous plants
bw	body weight
CF	conversion factor for enforcement to risk assessment residue definition
cGAP	critical GAP
CIPAC	
CXL	Codex Maximum Residue Limit (Codex MRL)
d	day
DAR	Draft Assessment Report
DAT	days after treatment
EC	European Community
EMS	evaluating Member State
EU	European Union
GAP	good agricultural practice
GCPF	Global Crop Protection Federation (former GIFAP)
GS	growth stage
ha	hectare
hL	hectolitre
HR	highest residue
ILV	independent laboratory validation
ISO	International Organisation for Standardisation
IUPAC	International Union of Pure and Applied Chemistry
JMPR	Joint FAO/WHO Meeting on Pesticide Residues
kg	kilogram
L	litre
LOQ	limit of quantification
MRL	maximum residue level
MS	Member States
NEU	Northern Europe
OECD	Organisation for Economic Co-operation and Development
PF	processing factor
PHI	pre-harvest interval
PRIMo	(EFSA) Pesticide Residues Intake Model
QuEChERS	Quick, Easy, Cheap, Effective, Rugged, and Safe (method)
RAC	raw agricultural commodity

RD	residue definition
RMS	rapporteur Member State
SEU	southern Europe
STMR	supervised trials median residue
TMDI	theoretical maximum daily intake
TRR	total radioactive residue
WHO	World Health Organization
wk	week
YF	yield factor
yr	year
SC	suspension concentrate
HPLC	high performance liquid chromatography
MS/MS	tandem mass spectrometry