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Modification of the existing maximum residue levels for mepanipyrim in blackberries, raspberries and peppers

European Food Safety Authority (EFSA)

Abstract

In accordance with Article 6 of Regulation (EC) No 396/2005, the evaluating Member State (EMS), Spain, received an application from Sipcam Inagra S.A. to modify the existing maximum residue levels (MRLs) for the active substance mepanipyrim in blackberries, raspberries, peppers and cucumbers. In order to accommodate for the intended uses of mepanipyrim, Spain proposed to raise the existing MRLs to 4 mg/kg on raspberries and blackberries, 1 mg/kg on peppers and 0.5 mg/kg on cucumbers. EFSA assessed only the request for cane fruits and peppers since an MRL proposal of 0.5 mg/kg has already been made for cucumbers in a previous Reasoned Opinion considering the same good agricultural practices (GAP). According to EFSA the data are sufficient to derive MRL proposals of 4 mg/kg on raspberries and blackberries and 1.5 mg/kg on peppers. Adequate analytical enforcement methods are available to control the residues of mepanipyrim on the commodities under consideration. Based on the risk assessment results, EFSA concludes that the proposed uses of mepanipyrim on blackberries, raspberries and peppers will not result in a consumer exposure exceeding the toxicological reference values and therefore are unlikely to pose a consumer health risk.

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Keywords: mepanipyrim, blackberries, raspberries, peppers, MRL application, consumer risk assessment

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Summary

In accordance with Article 6 of Regulation (EC) No 396/2005, the evaluating Member State (EMS) Spain, received an application from Sipcam Inagra S.A. to modify the existing maximum residue levels (MRLs) for the active substance mepanipyrim in blackberries, raspberries, peppers and cucumbers. In order to accommodate for the intended uses of mepanipyrim, Spain proposed to raise the existing MRLs from the limit of quantification (LOQ) to 4 mg/kg on raspberries and blackberries, 1 mg/kg on peppers and 0.5 mg/kg on cucumbers. Spain 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 the European Food Safety Authority (EFSA) on 3 June 2015. The MRL request for cucumbers has not been considered in the framework of this MRL application, since an MRL proposal of 0.5 mg/kg has already been made for cucumbers by EFSA in a previous Reasoned Opinion, considering the same good agricultural practices (GAP)

EFSA bases its assessment on the evaluation report, the Draft Assessment Report (DAR) and its addenda prepared under Directive 91/414/EEC, the Commission Review Report on mepanipyrim as well as the conclusions from previous EFSA opinions, including the review of the existing MRLs for mepanipyrim under Article 12 of Regulation (EC) No 396/2005.

The toxicological profile of mepanipyrim was assessed in the framework of the peer review under Directive 91/414/EEC and the data were sufficient to derive an acceptable daily intake (ADI) of 0.02 mg/kg bw per day and an acute reference dose (ARfD) of 0.3 mg/kg bw.

The metabolism of mepanipyrim in primary crops was investigated in the fruit crop group following foliar applications. The review of the existing MRLs performed under Article 12 of Regulation (EC) No 396/2005 concluded on the residue definitions for enforcement and risk assessment as mepanipyrim, which are applicable to the use on the crops under consideration.

According to EFSA the data are sufficient to derive MRL proposals of 4 mg/kg on blackberries and raspberries and 1.5 mg/kg on peppers. Adequate analytical enforcement methods are available to control the residues of mepanipyrim on the commodities under consideration at the validated LOQ of 0.01 mg/kg.

Studies investigating the nature of mepanipyrim assessed in a previous reasoned opinion showed that the active substance is stable under standard hydrolysis conditions. Therefore for processed commodities the same residue definition as for raw agricultural commodities (RAC) is applicable. Processing studies were not provided and are not required.

The occurrence of mepanipyrim residues in rotational crops was investigated in the framework of the peer review and the Article 12 MRL review. Based on the available information, EFSA concludes that significant residue levels are unlikely to occur in rotational crops provided that the active substance is used according to the proposed Good Agricultural Practice (GAP).

Residues of mepanipyrim in commodities of animal origin were not assessed in the framework of this application, since the crops under consideration are normally not fed to livestock.

The consumer risk assessment was performed with revision 2 of the EFSA Pesticide Residues Intake Model. For the calculation of the chronic exposure, EFSA used the supervised trials median residue (STMR) values derived from the residue trials conducted on raspberries and peppers. The assessment was further refined with the STMR values reported in a previous EFSA reasoned opinion and in the Article 12 MRL review. The acute exposure assessment was performed only with regard to the commodities under consideration. The highest chronic exposure was calculated to be 12 % of the ADI (French, all population) and the highest acute exposure 0.7 % of the ARfD for raspberries.

EFSA concludes that the proposed uses of mepanipyrim on blackberries, raspberries and peppers will not result in a consumer exposure exceeding the toxicological reference values and therefore are unlikely to pose a health risk to consumers.

EFSA proposes to amend the existing MRLs as reported in the summary table below.

Code ^(a)	Commodity	Existing EU MRL (mg/kg)	Proposed EU MRL (mg/kg)	Comment/Justification
Enforcement residue definition: mepanipyrim				
0153010	Blackberries	0.01*	4	Extrapolation from raspberries.
0153030	Raspberries	0.01*	4	Indoor use supported.
0231020	Sweet peppers/Bell peppers	0.01*	1.5	Indoor use supported.

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

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

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Background

Regulation (EC) No 396/2005¹ establishes the rules governing the setting of pesticide maximum residue levels (MRLs) at European Union (EU) level. Article 6 of the 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,² repealed by Regulation (EC) No 1107/2009,³ shall submit to a Member State, when appropriate, an application to modify a MRL in accordance with the provisions of Article 7 of the Regulation.

Spain, hereafter referred to as the evaluating Member State (EMS), received an application from the company Sipcam Inagra S.A.⁴ to modify the existing MRLs for the active substance mepanipyrim in blackberries, raspberries, peppers and cucumbers. This application was notified to the European Commission and the European Food Safety Authority (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 and to EFSA on 3 June 2015.

The application was included in the EFSA Register of Questions with the reference number EFSA-Q-2015-00359 and the following subject:

Mepanipyrim: Setting new MRLs in various crops

Spain proposed to raise the existing MRLs of mepanipyrim in blackberries, raspberries, peppers and cucumbers from the LOQ of 0.01 mg/kg to 4 mg/kg on blackberries and raspberries, 1 mg/kg on peppers and 0.5 mg/kg on cucumbers.

EFSA proceeded with the assessment of the application and the evaluation report as required by Article 10 of the Regulation. In accordance with Article 10 of Regulation (EC) No 396/2005, EFSA shall, based on the evaluation report provided by the EMS, provide a reasoned opinion on the risks to the consumer associated with the application.

In accordance with Article 11 of the 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 if more detailed evaluations need to be carried out) from the date of receipt of the application. If EFSA requests supplementary information, the time limit laid down shall be suspended until that information has been provided.

The active substance and its use pattern

Mepanipyrim is the ISO common name for *N*-(4-methyl-6-prop-1-ynylpyrimidin-2-yl)aniline (IUPAC). The chemical structure of the active substance is reported in Appendix C. Mepanipyrim has been approved for the use as a fungicide.

Mepanipyrim was evaluated in the framework of Directive 91/414/EEC with Italy designated as rapporteur Member State (RMS). It was included in Annex I of this Directive by Directive 2004/62/EC⁵ which entered into force on 01 October 2004 for use as fungicide only. In accordance with Regulation (EU) No 540/2011,⁶ mepanipyrim is approved under Regulation (EC) No 1107/2009, repealing Directive 91/414/EEC. The representative uses evaluated in the peer review were foliar applications on grapes, tomatoes and strawberries. The Draft Assessment Report (DAR) of mepanipyrim was not peer reviewed by EFSA; therefore an EFSA conclusion is not available.

¹ Regulation (EC) No 396/2005 of the Parliament and of the Council of 23 February 2005 on maximum residue levels of pesticides in or on food and feed of plant and animal origin and amending Council Directive 91/414/EEC. OJ L 70, 16.03.2005, 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, 19.08.1991, p. 1–32.

³ Regulation (EC) No 1107/2009 of the European Parliament and of the Council of 21 October 2009 concerning the placing of plant protection products on the market and repealing Council Directives 79/117/EEC and 91/414/EEC. OJ L 309, 24.11.2009, p. 1–50.

⁴ Sipcam Inagra S.A., Prof. Beltrán Báguena, 5, 46022 Valencia, Spain.

⁵ Commission Directive 2004/62/EC of 26 April 2004 amending Council Directive 91/414/EEC to include mepanipyrim as active substance, OJ L 125, 28.04.2004, p. 38–40.

⁶ 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.

The EU MRLs for mepanipyrim are established in Annex II of Regulation (EC) No 396/2005. Since the entry into force of this Regulation, EFSA has issued a total of three reasoned opinions on the modification of MRLs for mepanipyrim. The proposals from two of these reasoned opinions have already been considered in the EU legislation. The MRL changes that were reported in the EU legislation are summarised in Table 1.

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

Procedure ^(a)	Considered by Regulation	Remarks
Art. 10 (EFSA, 2009)	(EC) No 1050/2009	Courgette
Art. 12 (EFSA, 2011)	(EU) No 777/2013	Review of all existing MRLs
Art. 10 (EFSA, 2015)	Not yet implemented	Tomato, aubergine, strawberry, cucumber

(a): Art. 10: Assessment of MRL application according to Article 6 to 10 of Regulation (EC) No 396/2005.
 Art. 12: Review of the existing MRLs according to Article 12 of Regulation (EC) No 396/2005.

EFSA has recently issued a reasoned opinion on the modification of the existing MRLs for mepanipyrim in tomatoes, aubergines, strawberries and cucumbers (EFSA, 2015). The modifications of the MRLs recommended have not yet been considered in the EU legislation. Since, based on the same indoor GAP and residue data submitted by Spain, an MRL of 0.5 mg/kg on cucumbers was proposed in this reasoned opinion, the use on cucumbers requested in the present MRL application is nowadays obsolete and will not be assessed in this reasoned opinion.

Codex Alimentarius has not established Codex maximum residue limits for mepanipyrim.

The details of the intended GAPs for mepanipyrim are given in Appendix A. The GAP on cucumbers will not be assessed in this reasoned opinion.

Assessment

EFSA bases its assessment on the evaluation report submitted by the EMS (Spain, 2014), the draft assessment report (DAR) and its addenda prepared under Directive 91/414/EEC (Italy, 2000, 2002, 2003), the Commission review report on mepanipyrim (European Commission, 2004) and the conclusions from previous EFSA opinions on mepanipyrim, including the review of the existing MRLs according to Article 12 of Regulation (EC) No 396/2005 (EFSA, 2009, 2011, 2015). 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 546/2011⁷ and the currently applicable guidance documents relevant for the consumer risk assessment of pesticide residues (European Commission, 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

The review of the existing MRLs according to Article 12 of Regulation (EC) No 396/2005 concluded that analytical multi-residue QuEChERS methods (CEN, 2008) is available to enforce mepanipyrim in food of plant origin at the LOQ of 0.01 mg/kg in high water, high acid matrices and dry/starch commodities (EFSA, 2011).

Since the crops under consideration belongs to the group of high water and high acid content, EFSA concludes that sufficiently validated analytical methods are available to enforce the proposed MRLs for mepanipyrim in blackberries, raspberries and peppers.

⁷ Commission Regulation (EU) No 546/2011 of 10 June 2011 implementing Regulation (EC) No 1107/2009 of the European Parliament and of the Council as regards uniform principles for evaluation and authorisation of plant protection products. OJ L 155, 11.06.2011, p. 127–175.

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 blackberries, raspberries and peppers are normally not fed to livestock.

2. Mammalian toxicology

The toxicological profile of the active substance mepanipyrim was assessed in the framework of the peer review under Directive 91/414/EEC (European Commission, 2004). The data were sufficient to derive the toxicological reference values compiled in Table 2.

Table 2: Overview of the toxicological reference values

	Source	Year	Value	Study	Safety factor
Mepanipyrim					
ADI	European	2004	0.02 mg/kg bw per day	Rat, 2-year	100
ARfD	Commission	2004	0.30 mg/kg bw	Rabbit, teratogenesis	100

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 mepanipyrim in primary crops was evaluated in the fruit crop group in the framework of the peer review under Directive 91/414/EEC and the Article 12 MRL review (Italy, 2000; EFSA, 2011). The overview of the metabolism study designs, which are reported in details in previous EFSA opinions, is presented in Table 3.

Table 3: Summary of available metabolism studies in plants

Crop group	Crops	Application ^(a)	Sampling ^(b)	Comments
Fruit	Grape	Foliar, 3× 500 g/ha	0, 44, 74 DAT _{1/2} , 30 DALA	
		Foliar, 3× 0.9 g (dose/ha not reported)		
	Tomato	Foliar, 3× 500 g/ha	0, 36 DALA	
		Foliar, 3× 500 g/ha	14, 40, 76 DALA	
	Apple	Foliar, 3× 500 g/ha	0, 16 DALA	

(a): Mepanipyrim was radio-labelled in the aniline and/or the pyrimidine ring.

(b): DALA: days after last treatment; DAT₁ and DAT₂: day after first and second treatment.

The review of the existing MRLs for mepanipyrim performed under Article 12 of Regulation (EC) No 396/2005 concluded on the residue definition for enforcement and risk assessment as mepanipyrim for fruit crops (EFSA, 2011). The current residue definition for enforcement set in Regulation (EC) No 396/2005 in plants is identical to the agreed residue definition.

EFSA concludes that the metabolism of mepanipyrim in fruit crops is sufficiently addressed and the residue definition for enforcement and risk assessment as parent compound is applicable to the crops under consideration.

3.1.1.2. Magnitude of residues

In support of the MRL application, residue trials on raspberries and peppers were submitted.

a. Blackberries, raspberries

Four GAP compliant residue trials on raspberries with two applications at 7 days interval were submitted. Extrapolation from four trials on raspberries to blackberries is possible (European Commission, 2011). EFSA concludes that the data are sufficient to derive a MRL proposal of 4 mg/kg.

b. Peppers

Eight GAP compliant residue trials on peppers with two applications at 14 days interval were submitted. EFSA concludes that the data are sufficient to derive a MRL proposal of 1.5 mg/kg.⁸

The results of the residue trials, the related risk assessment input values (HR, STMR) and the MRL proposals are summarised in Table 4.

The storage stability of mepanipyrim in primary crops was investigated in the DAR under Directive 91/414/EEC (Italy, 2000; EFSA, 2011). Residues of mepanipyrim were found to be stable at -20°C for up to 19 and 12 months in high acid and high water content matrices, respectively. According to the EMS, the trial samples were stored in compliance with the above reported storage conditions and analysed using sufficiently validated analytical methods (Spain, 2014).

EFSA concludes that the data are sufficient to derive the following MRL proposals:

- 4 mg/kg blackberries and raspberries, indoor use.
- 1.5 mg/kg peppers, indoor use.

⁸ The EMS proposed the MRL of 1 mg/kg based on the OECD methodology and same set of data (Spain, 2014).

Table 4: Overview of the available residues trials data

Crop (GAPs)	Region/ Indoor ^(a)	Residue levels observed in the supervised residue trials ^(b) (mg/kg)	Recommendations/comments ^(c)	MRL proposal (mg/kg)	HR ^(d) (mg/kg)	STMR ^(e) (mg/kg)
Raspberries (2× 400 g/ha, PHI 3 d)	Indoor	0.83; 1.03; 1.34; 2.24	MRL _{OECD} : 4.1/4.0 Extrapolation from raspberries to blackberries.	4	2.24	1.19
Peppers (2× 400 g/ha, PHI 1 d)	Indoor	0.15; 0.19; <u>0.21</u> ; 0.22; 0.27; 0.37; 0.62; 0.63	<u>Underlined value</u> : higher residue measured at PHI 0 days. MRL _{OECD} : 1.10/1.50	1.5	0.63	0.25

(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): Individual residue levels considered for MRL calculation are reported in ascending order.

(c): Any information/comment supporting the decision and OECD MRL calculation (unrounded/rounded values).

(d): HR: Highest residue level according to the residue definition for risk assessment.

(e): STMR: Median residue level according to residue definition for risk assessment.

3.1.1.3. Effect of industrial processing and/or household preparation

Standard hydrolysis studies simulating the effect on the nature of mepanipyrim residues under processing conditions representative of pasteurisation, boiling and sterilisation were assessed in the framework of a previous reasoned opinion and it was concluded that the compound is hydrolytically stable under the representative conditions (EFSA, 2015). Thus, for processed commodities the same residue definition as for RAC is applicable.

Processing studies on grape (juice, wine, raisins), strawberry (jam, canned) and tomato (juice, paste, puree, ketchup, canned) processed products are available and processing factors were recommended for inclusion in Annex VI of Regulation (EC) No 396/2005 (EFSA, 2011, 2015).

Studies investigating the magnitude of mepanipyrim residues in the preparation of cane fruit juice were not provided. Due to the low contribution of residues in these fruits to the total consumer exposure, they are not expected to affect the outcome of the consumer risk assessment.

3.1.2. Rotational crops

The crops under consideration can be grown in rotation with other plants and therefore the possible occurrence of residues in succeeding crops resulting from the use on primary crops has to be assessed.

Under the Article 12 MRL review, EFSA concluded that significant residues are not expected in rotational crops when the active substance is applied on primary crops up to four applications at 400 g/ha (EFSA, 2011).

Since the uses supported in this MRL application are limited to a maximum of two applications at 400 g/kg, EFSA concludes that relevant residue levels are unlikely to occur in rotational crops provided that the compound is used on blackberries, raspberries and peppers according to the proposed GAPs.

3.2. Nature and magnitude of residues in livestock

As the crops under consideration are not normally fed to livestock, the nature and magnitude of mepanipyrim residues in livestock is not assessed in the framework of this application (European Commission, 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 (EFSA, 2007).

To calculate the chronic exposure, EFSA used the STMRs derived from the residue trials conducted on raspberries and peppers for the crops under consideration in this MRL application and reported in Table 4. The assessment was further refined with the STMR values reported in a previous EFSA reasoned opinion (EFSA, 2015) and in the Article 12 MRL review (EFSA, 2011). The food commodities, for which no uses were reported in the framework of the Article 12 review, were excluded from the exposure calculation, assuming that there is no use of mepanipyrim on these crops.

The acute exposure assessment was performed only with regard to the commodities under consideration assuming the consumption of a large portion of the food items as reported in the national food surveys and that these items contained residues at the HR as observed in supervised field trials (see Table 4). A variability factor accounting for the inhomogeneous distribution on the individual items consumed was included in the calculation for peppers (EFSA, 2007).

The input values used for the dietary exposure calculation are summarised in Table 5.

Table 5: Input values for the consumer dietary exposure assessment

Commodity	Chronic exposure assessment		Acute exposure assessment	
	Input (mg/kg)	Comment	Input (mg/kg)	Comment
Risk assessment residue definition: mepanipyrin				
Blackberries, raspberries	1.19	STMR (indoor, raspberries)	2.24	HR (indoor, raspberries)
Peppers	0.25	STMR (indoor)	0.63	HR (indoor)
Table, wine grapes	0.53	STMR (EFSA, 2011)	Acute risk assessment undertaken only with regard to the crops under consideration.	
Strawberries	0.45	STMR (EFSA, 2015)		
Tomatoes, aubergines	0.31	STMR (EFSA, 2015)		
Cucumbers	0.16	STMR (EFSA, 2015)		
Courgettes	0.13	STMR (EFSA, 2009, 2011)		

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

A long-term consumer intake concern was not identified for any of the European diets incorporated in the EFSA PRIMo. The total chronic intake calculated accounted for up to 12 % of the ADI (French, all population). The contribution of residues in the crops under consideration to the total consumer exposure accounted for a maximum of 0.7 % of the ADI for raspberries (Dutch child).

An acute consumer risk was not identified in relation to the MRL proposals for crops under consideration. The highest acute consumer exposure was calculated to be 13 % of the ARfD for peppers.

EFSA concludes that the intended uses of mepanipyrin on peppers, blackberries, raspberries and cucumbers will not result in a consumer exposure exceeding the toxicological reference values and therefore are unlikely to pose a concern for public health.

Conclusions and recommendations

The information submitted was sufficient to propose the MRLs summarised in the table below:

Code ^(a)	Commodity	Existing EU MRL (mg/kg)	Proposed EU MRL (mg/kg)	Comment/Justification
Enforcement residue definition: mepanipyrin				
0153010	Blackberries	0.01*	4	Extrapolation from raspberries.
0153030	Raspberries	0.01*	4	Indoor use supported.
0231020	Sweet peppers/Bell peppers	0.01*	1.5	Indoor use supported.

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

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

References

- CEN (European Committee for Standardisation), 2008. Foods of plant origin – Determination of pesticide residues using GC-MS and/or LC-MS/MS following acetonitrile extraction/partitioning and clean-up by dispersive SPE. QuEChERS-method. EN 15662.2008. November 2008.
- European Commission, 1996. Appendix G. Livestock Feeding Studies. 7031/VI/95-rev.4.
- European Commission, 1997a. Appendix A. Metabolism and distribution in plants. 7028/IV/95-rev.3.
- 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.
- European Commission, 1997c. Appendix C. Testing of plant protection products in rotational crops. 7524/VI/95-rev.2.
- European Commission, 1997d. Appendix E. Processing studies. 7035/VI/95-rev.5.
- European Commission, 1997e. Appendix F. Metabolism and distribution in domestic animals. 7030/VI/95-rev.3.
- European Commission, 1997f. Appendix H. Storage stability of residue samples. 7032/VI/95-rev.5.
- European Commission, 1997g. Appendix I. Calculation of maximum residue level and safety intervals. 7039/VI/95.
- 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, 2004. Review report for the active substance mepanipyrim. Finalised in the Standing Committee on the Food Chain and Animal Health at its meeting on 30 March 2004 in view of the inclusion of mepanipyrim in Annex I of Council Directive 91/414/EEC. SANCO/1412/2001/01-Final, 29 March 2004, 27 pp.
- 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.
- 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), 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. doi:10.2903/j.efsa.2007.32r
- EFSA (European Food Safety Authority), 2009. Reasoned opinion on the modification of the existing MRL for mepanipyrim in courgettes. The EFSA Journal 2009, 266r, 1–21. doi:10.2903/j.efsa.2009.266r
- EFSA (European Food Safety Authority), 2011. Reasoned opinion on the review of the existing MRL(s) for mepanipyrim according to Article 12 of Regulation (EC) No 396/2005. EFSA Journal 2011;9(8):2342, 31 pp. doi:102903/j.efsa.2011.2342
- EFSA (European Food Safety Authority), 2015. Reasoned opinion on the modification of the existing maximum residue levels (MRLs) for mepanipyrim in in tomato, aubergine, strawberry and cucumber. EFSA Journal 2015;13(3):4037, 24 pp. doi:102903/j.efsa.2015.4037
- Italy, 2000. Draft assessment report on the active substance mepanipyrim prepared by the rapporteur Member State Italy in the framework of Council Directive 91/414/EEC, July 2000.

- Italy, 2002. Addendum to the draft assessment report on the active substance mepanipyrim prepared by the rapporteur Member State Italy in the framework of Council Directive 91/414/EEC, June 2002.
- Italy, 2003. Addendum to the draft assessment report on the active substance mepanipyrim prepared by the rapporteur Member State Italy in the framework of Council Directive 91/414/EEC, June 2003.
- OECD (Organisation for Economic Co-operation and Development), 2008. OECD Test Guideline 508: Magnitude of the pesticide residues in processed commodities. Series on testing and assessment Number 96, 29 July 2008. Available online: <http://www.oecd.org>
- 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>
- Spain, 2014. Evaluation report on the modification of MRLs for mepanipyrim in peppers, blackberries, raspberries and cucumbers prepared by the evaluating Member State Spain under Article 8 of Regulation (EC) No 396/2005, July 2014, 41 pp.

Abbreviations

a.s.	active substance
ADI	acceptable daily intake
ARfD	acute reference dose
BBCH	growth stages of mono- and dicotyledonous plants
bw	body weight
CEN	European Committee for Standardisation (Comité Européen de Normalisation)
CIPAC	Collaborative International Pesticide Analytical Council
DALA	days after last application
DAR	draft assessment report
DAT	days after treatment
EMS	evaluating Member State
FAO	Food and Agriculture Organization of the United Nations
GAP	good agricultural practice
GCPF	Global Crop Protection Federation (formerly International Group of National Associations of Manufacturers of Agrochemical Products (GIFAP))
HR	highest residue
ISO	International Organization for Standardization
IUPAC	International Union of Pure and Applied Chemistry
LOQ	limit of quantification
MRL	maximum residue level
NEU	northern Europe
OECD	Organisation for Economic Co-operation and Development
PHI	pre-harvest interval
PRIMo	(EFSA) Pesticide Residues Intake Model
QuEChERS	Quick, Easy, Cheap, Effective, Rugged, and Safe (analytical method)
RAC	raw agricultural commodity
RMS	rapporteur Member State
SANCO	European Commission's Directorate-General for Health and Consumers
SEU	southern Europe
STMR	supervised trials median residue
TMDI	theoretical maximum daily intake
WHO	World Health Organization
WP	wettable powder

Appendix A – Good Agricultural Practice (GAPs)

Crop ^(a)	NEU /EU 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 min-max ^(k)	Interval min-max	g/hL max	Water L/ha max	g/ha max		
Blackberry, Raspberry	EU (Spain)	G, I	<i>Botrytis cinerea</i>	WP	500 g/kg	Foliar	BBCH 89	1-2		40	1000	400	3	
Pepper	EU (Spain)	G, I	<i>Botrytis cinerea</i>	WP	500 g/kg	Foliar	BBCH 89	1-2		40	1000	400	1	
Cucumber	EU (Spain)	G, I	<i>Botrytis cinerea</i>	WP	500 g/kg	Foliar	BBCH 89	1-2		40	1000	400	1	Use not considered in this MRL application since already assessed by EFSA (EFSA, 2015)

Remarks:

- (a) For crops, EU or other classifications, e.g. Codex, should be used; where relevant, the usage 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), water soluble granule (WG)
- (e) GCPF Codes – GIFAP Technical Monograph No 2, 1989
- (f) all abbreviations must be explained
- (g) Method, e.g. high volume spraying, low volume spraying, spreading, dusting, drench
- (h) Kind, eg. overall, broadcast, aerial spraying, row, individual plant, between the plants. type of equipment used must be indicated
- (i) g/kg or µg/L
- (j) Growth stage at last treatment (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), 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

Appendix B – Pesticide Residue Intake Model (PRIMO)

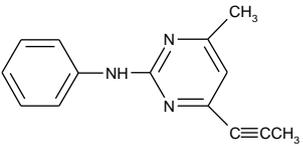
Mepanipyrin								
Status of the active substance: approved			Code no.:					
LOQ (mg/kg bw):			proposed LOQ:					
Toxicological end points								
ADI (mg/kg bw/day): 0.02			ARfD (mg/kg bw): 0.3					
Source of ADI: EC			Source of ARfD: EC					
Year of evaluation: 2004			Year of evaluation: 2004					
Chronic risk assessment - refined calculations								
			TMDI (range) in % of ADI minimum - maximum					
			1 12					
			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	pTMRs at LOQ (in % of ADI)
12	FR all population	11	Wine grapes	0.7	Tomatoes	0.3	Table grapes	
12	WHO Cluster diet B	5	Tomatoes	4.7	Wine grapes	0.9	Table grapes	
9	PT General population	7	Wine grapes	1.4	Tomatoes	0.7	Table grapes	
7	DE child	3	Table grapes	1.5	Tomatoes	1.1	Strawberries	
7	IE adult	3	Wine grapes	0.7	Blackberries	0.7	Table grapes	
6	WHO cluster diet E	4	Wine grapes	0.8	Tomatoes	0.4	Table grapes	
5	DK adult	4	Wine grapes	0.6	Tomatoes	0.2	Cucumbers	
5	NL child	2	Table grapes	1.0	Tomatoes	0.7	Raspberries	
4	UK Adult	3	Wine grapes	0.7	Tomatoes	0.1	Table grapes	
4	UK vegetarian	2	Wine grapes	1.0	Tomatoes	0.2	Table grapes	
4	WHO cluster diet D	2	Tomatoes	1.0	Wine grapes	0.5	Table grapes	
4	FR toddler	1	Strawberries	1.2	Tomatoes	0.6	Table grapes	
3	NL general	2	Wine grapes	0.7	Tomatoes	0.6	Table grapes	
3	WHO regional European diet	2	Tomatoes	0.6	Wine grapes	0.4	Table grapes	
3	WHO Cluster diet F	2	Wine grapes	1.1	Tomatoes	0.3	Table grapes	
3	DK child	1	Cucumbers	0.8	Tomatoes	0.5	Table grapes	
3	IT kids/toddler	2	Tomatoes	0.3	Table grapes	0.3	Strawberries	
3	UK Toddler	1	Tomatoes	0.7	Table grapes	0.6	Raspberries	
3	ES adult	1	Tomatoes	1.1	Wine grapes	0.2	Peppers	
3	IT adult	2	Tomatoes	0.3	Table grapes	0.2	Aubergines (egg plants)	
3	PL general population	1	Tomatoes	0.8	Table grapes	0.1	Peppers	
2	SE general population 90th percentile	1	Tomatoes	0.4	Strawberries	0.3	Cucumbers	
2	ES child	2	Tomatoes	0.2	Strawberries	0.1	Peppers	
2	FI adult	1	Wine grapes	0.7	Tomatoes	0.2	Cucumbers	
2	FR infant	1	Strawberries	0.4	Courgettes	0.2	Tomatoes	
2	LT adult	1	Tomatoes	0.3	Cucumbers	0.1	Strawberries	
1	UK Infant	1	Tomatoes	0.5	Strawberries	0.1	Table grapes	
<p>Conclusion: The estimated Theoretical Maximum Daily Intakes (TMDI), based on pTMRs were below the ADI. A long-term intake of residues of Mepanipyrin is unlikely to present a public health concern.</p>								

(n)

Acute risk assessment /children - refined calculations			Acute risk assessment / adults / general population - refined calculations						
<p>The acute risk assessment is based on the ARfD.</p> <p>For each commodity the calculation is based on the highest reported MS consumption per kg bw and the corresponding unit weight from the MS with the critical consumption. If no data on the unit weight was available from that MS an average European unit weight was used for the IESTI calculation.</p> <p>In the IESTI 1 calculation, the variability factors were 10, 7 or 5 (according to JMPR manual 2002), for lettuce a variability factor of 5 was used.</p> <p>In the IESTI 2 calculations, the variability factors of 10 and 7 were replaced by 5. For lettuce the calculation was performed with a variability factor of 3.</p> <p>Threshold MRL is the calculated residue level which would leads to an exposure equivalent to 100 % of the ARfD.</p>									
Unprocessed commodities	No of commodities for which ARfD/ADI is exceeded (IESTI 1):		No of commodities for which ARfD/ADI is exceeded (IESTI 2):		No of commodities for which ARfD/ADI is exceeded (IESTI 1):		No of commodities for which ARfD/ADI is exceeded (IESTI 2):		
	---		---		---		---		
	IESTI 1 *) **)		IESTI 2 *) **)		IESTI 1 *) **)		IESTI 2 *) **)		
	Highest % of ARfD/ADI	Commodities	pTMRL/ threshold MRL (mg/kg)	Highest % of ARfD/ADI	Commodities	pTMRL/ threshold MRL (mg/kg)	Highest % of ARfD/ADI	Commodities	pTMRL/ threshold MRL (mg/kg)
	13	Peppers	0.63 / -	9	Peppers	0.63 / -	3	Peppers	0.63 / -
8	Blackberries	2.24 / -	8	Blackberries	2.24 / -	3	Raspberries	2.24 / -	
4	Raspberries	2.24 / -	4	Raspberries	2.24 / -	2	Blackberries	2.24 / -	
No of critical MRLs (IESTI 1)			No of critical MRLs (IESTI 2)			---			
Processed commodities	No of commodities for which ARfD/ADI is exceeded:		No of commodities for which ARfD/ADI is exceeded:		No of commodities for which ARfD/ADI is exceeded:		No of commodities for which ARfD/ADI is exceeded:		
	---		---		---		---		
	****)		****)		****)		****)		
	Highest % of ARfD/ADI	Processed commodities	pTMRL/ threshold MRL (mg/kg)	Highest % of ARfD/ADI	Processed commodities	pTMRL/ threshold MRL (mg/kg)	Highest % of ARfD/ADI	Processed commodities	pTMRL/ threshold MRL (mg/kg)
	1.83	Grape juice	0.1665 / -	0.30	Raisins	2.2089 / -	0.75	Tomato juice	0.129 / -
0.30	Grapes (raisins)	2.2089 / -	0.12	Wine	0.0901 / -	0.01	Wine	0.0901 / -	
<p>*) The results of the IESTI calculations are reported for at least 5 commodities. If the ARfD is exceeded for more than 5 commodities, all IESTI values > 90% of ARfD are reported.</p> <p>**) pTMRL: provisional temporary MRL</p> <p>***) pTMRL: provisional temporary MRL for unprocessed commodity</p>									
<p>Conclusion:</p> <p>For Mepanipyrin IESTI 1 and IESTI 2 were calculated for food commodities for which pTMRLs were submitted and for which consumption data are available. No exceedance of the ARfD/ADI was identified for any unprocessed commodity.</p> <p>For processed commodities, no exceedance of the ARfD/ADI was identified.</p>									

Appendix C – Used compound code

Code/Trivial name	Chemical name	Structural formula
mepanipyrim	<i>N</i> -(4-methyl-6-prop-1-ynylpyrimidin-2-yl)aniline	 <p>The chemical structure shows a benzene ring attached to an NH group, which is further attached to a pyrimidine ring. The pyrimidine ring has a methyl group (CH₃) at the 4-position and a prop-1-ynyl group (C≡CCH₃) at the 6-position.</p>