

REASONED OPINION

Reasoned opinion on the modification of the existing maximum residue levels (MRLs) for mepanipyrim in tomato, aubergine, strawberry and cucumber¹

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ABSTRACT

In accordance with Article 6 of Regulation (EC) No 396/2005, The Netherlands, hereafter referred to as the evaluating Member State (EMS), received an application from K-I Chemical Europe SA/NV to modify the existing maximum residue levels (MRLs) for the active substance mepanipyrim in strawberries, tomatoes, aubergines, and cucumbers. In order to accommodate for the intended uses of mepanipyrim, the EMS proposed to raise the existing MRLs from 1.5 mg/kg to 3 mg/kg in strawberries, from 0.8 mg/kg to 1.5 mg/kg in tomatoes and aubergines and from 0.01 mg/kg to 0.5 mg/kg in cucumbers. The EMS 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 MRL proposals of 3 mg/kg on strawberries, 1.5 mg/kg on tomatoes (extrapolated to aubergines) and 0.5 mg/kg on cucumbers. Adequate analytical enforcement methods are available to control the residues of mepanipyrim in on the commodities under consideration. Based on the risk assessment results, EFSA concludes that the proposed use of mepanipyrim on strawberry, tomato, aubergine and cucumber will not result in a consumer exposure exceeding the toxicological reference values and therefore is unlikely to pose a consumer health risk.

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KEY WORDS

mepanipyrim, fruit crops, MRL application, Regulation (EC) No 396/2005, consumer risk assessment, anilino-pyrimidine.

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SUMMARY

In accordance with Article 6 of Regulation (EC) No 396/2005, The Netherlands, hereafter referred to as the evaluating Member State (EMS), received an application from K-I Chemical Europe SA/NV to modify the existing maximum residue levels (MRLs) for the active substance mepanipyrim in strawberries, tomatoes, aubergines, and cucumbers. In order to accommodate for the intended uses of mepanipyrim, the EMS proposed to raise the existing MRLs from 1.5 mg/kg to 3 mg/kg in strawberries, from 0.8 mg/kg to 1.5 mg/kg in tomatoes and aubergines and from 0.01 mg/kg to 0.5 mg/kg in cucumbers. The EMS 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 27 May 2014.

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

The toxicological profile of mepanipyrim was assessed in the DAR by the rapporteur Member State Italy and the data were sufficient to derive an ADI of 0.02 mg/kg bw per day and an ARfD of 0.3 mg/kg bw.

The metabolism of mepanipyrim in primary crops was investigated in grape, tomato and apple (fruit crop group). From these studies the peer review concluded to establish the residue definition for enforcement and risk assessment as mepanipyrim. For the use on strawberries, tomatoes, aubergines, and cucumbers, EFSA concludes that the metabolism of mepanipyrim in primary crops is sufficiently addressed and that the residue definitions derived are applicable.

EFSA concludes that the submitted supervised residue trials are sufficient to derive MRL proposals of 3 mg/kg on strawberries, 1.5 mg/kg on tomatoes (extrapolated to aubergines) and 0.5 mg/kg on cucumbers. Adequate analytical enforcement methods are available to control the residues of mepanipyrim in on the commodities under consideration at the validated LOQ of 0.01 mg/kg.

Studies investigating the nature of mepanipyrim residues under standard hydrolysis conditions were submitted in the framework of this MRL application. It was concluded that mepanipyrim is hydrolytically stable under processing conditions representative of pasteurisation, boiling and sterilisation. Therefore for processed commodities the same residue definition as for raw agricultural commodities is applicable. Additional processing studies on strawberry and tomato were provided and therefore, EFSA updated the processing factors (PF) derived for strawberry and tomato in its previous assessments and recommends the inclusion of the following PFs in Annex VI of Regulation (EC) No 396/2005.

– Strawberry/Jam:	0.47	– Tomato/Canned:	0.06
– Strawberry/Canned:	0.60	– Tomato/Paste:	0.92
– Tomato/Juice:	0.15	– Tomato/Puree:	0.62
– Tomato/Ketchup:	0.70		

The occurrence of mepanipyrim residues in rotational crops was investigated in the framework of the peer review and under the Article 12 MRL review. Based on the available information, it was concluded that significant residue levels are unlikely to occur in rotational crops provided that the compound is used on crops under consideration according to the proposed Good Agricultural Practice.

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. In the framework of Article 12 MRL review, a comprehensive long-term consumer exposure assessment was performed, taking into account the existing uses of mepanipyrim at European Union level which are supported by data. EFSA updates the risk assessment performed under the Article 12 MRL review including the median (STMR) and highest (HR) residue levels as derived from the residue trials on strawberry, tomato and cucumber. The highest chronic exposure was calculated to be 12 % of the ADI (FR, all population), and the highest acute exposure 17 % of the ARfD for tomatoes.

EFSA concludes that the proposed use of mepanipyrim on strawberry, tomato, aubergine and cucumber will not result in a consumer exposure exceeding the toxicological reference values and therefore is unlikely to pose a consumer health risk.

Thus EFSA proposes to amend the existing MRL as reported in the summary table.

SUMMARY TABLE

Code number ^(a)	Commodity	Existing EU MRL (mg/kg)	Proposed EU MRL (mg/kg)	Justification for the proposal
Enforcement residue definition: mepanipyrim				
0152000	Strawberries	1.5	3	based on indoor dataset
0231010	Tomatoes	0.8	1.5	based on indoor dataset
0231030	Aubergines	0.8	1.5	Extrapolation from tomatoes
0232010	Cucumbers	0.01*	0.5	based on indoor dataset

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

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

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BACKGROUND

Regulation (EC) No 396/2005³ establishes the rules governing the setting of pesticide maximum residue levels (MRL) at European Union level (EU). 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,⁴ repealed by Regulation (EC) No 1107/2009,⁵ shall submit to a Member State, when appropriate, an application to modify a MRL in accordance with the provisions of Article 7 of that Regulation.

The Netherlands, hereafter referred to as the evaluating Member State (EMS), received an application from the company K-I Chemical Europe SA/NV⁶ to modify the existing MRLs for the active substance mepanipyrim in strawberries, tomatoes, aubergines, and cucumbers. This application was notified to the European Commission (EC) 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 27 May 2014.

The application was included in the EFSA Register of Questions with the reference number EFSA-Q-2014-00396 and the following subject:

Meponipyrim – Application to modify the existing MRLs in strawberry, tomato, aubergine (eggplant) and cucumber

The EMS proposed to raise the existing MRLs of mepanipyrim from 1.5 mg/kg to 3 mg/kg in strawberries, from 0.8 mg/kg to 1.5 mg/kg in tomatoes and aubergines and from 0.01 mg/kg to 0.5 mg/kg in cucumbers.

During the assessment of the application, EFSA identified some data gaps which were essential to conclude on the consumer risk assessment. Thus, EFSA asked for further data which were provided by the applicant and evaluated by the EMS. An addendum to the evaluation report was provided on 17 December 2014. Upon reception of this data, 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.

³ 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.

⁴ 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.

⁵ 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.

⁶ K-I Chemical Europe SA/NV, Avenue Louise 326, Box 3, 1050, Brussels, Belgium.

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).

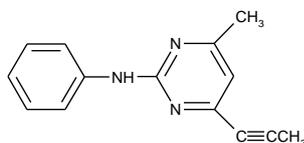


Figure 1: Structure of mepanipyrim. Molecular weight: 223.3 g/mol

Mepanipyrim belongs to the group of anilino-pyrimidine compounds which are used as fungicides. This non-systemic substance is highly active against the mycelial growth and is effective to control several diseases, especially grey mould (*Botrytis cinerea*) of vines and vegetables but also scab (*Venturia sp.*) of apples and pears and brown rot (*Monilinia fructicola*) of peaches.

Mepanipyrim was evaluated in the framework of Council 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/EC,⁷ which entered into force on 01 October 2004 for use as fungicide only. In accordance with Commission Implementing Regulation (EU) No 540/2011⁸ mepanipyrim is approved under Regulation (EC) No 1107/2009, repealing Council Directive 91/414/EEC.

The representative uses evaluated in the peer review/supported by the applicant were foliar applications on grapes, tomatoes and strawberries. The Draft Assessment Report (DAR) of mepanipyrim was not peer reviewed by EFSA; therefore no EFSA conclusion is available.

The EU MRLs for mepanipyrim are established in Annexes II and IIIB of Regulation (EC) No 396/2005. Existing MRLs for mepanipyrim were reviewed by EFSA according to Article 12 (EFSA, 2011) which were considered in Regulation (EU) No 777/2013⁹. The existing EU MRLs for mepanipyrim on tomato, aubergine, strawberry and cucumber are set at 0.8, 0.8, 1.5 and 0.01 mg/kg respectively. No CXLs are established for mepanipyrim.

The details of the intended good agricultural practices (GAPs) for mepanipyrim are given in Appendix A.

⁷ 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.

⁸ 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.

⁹ Commission Regulation (EU) No 777/2013 of 12 August 2013 amending Annexes II, III and V to Regulation (EC) No 396/2005 of the European Parliament and of the Council as regards maximum residue levels for clodinafop, clomazone, diuron, ethalfluralin, ioxynil, iprovalicarb, maleic hydrazide, mepanipyrim, metconazole, prosulfocarb and tepraloxym in or on certain products. OJ L 221, 17.8.2013, p. 1–48.

ASSESSMENT

EFSA bases its assessment on the evaluation report submitted by the EMS (The Netherlands, 2014a, 2014b), the Draft Assessment Report (DAR) (and its addendum/addenda) prepared under Council Directive 91/414/EEC (Italy, 2000, 2002, 2003), the Commission Review Report on mepanipyrim (EC, 2004) as well as the conclusions from previous EFSA opinions (EFSA, 2009, 2011). 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 546/2011¹⁰ and the currently applicable guidance documents relevant for the consumer risk assessment of pesticide residues (EC, 1996, 1997a, 1997b, 1997c, 1997d, 1997e, 1997f, 1997g, 2000, 2010a, 2010b, 2011; OECD, 2011).

1. Method of analysis

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

The availability of the analytical enforcement methods for the determination of residues of mepanipyrim in commodities of plant origin was investigated in the framework of the review of the existing MRLs under Article 12 of Regulation (EC) No 396/2005 (EFSA, 2011). It was concluded that there are adequate analytical enforcement methods available to monitor mepanipyrim residues in high water, high acid content commodities and in dry commodities with an LOQ validated at 0.01 mg/kg (EFSA, 2011).

Under this application, a new UPLC-MS/MS method was provided for the quantification of mepanipyrim and metabolite KIF-3535-M-31 in grapes, strawberries, tomatoes, and their processed commodities. This method was validated at an LOQ of 0.01 mg/kg. No ILV is available.

Since the commodities under consideration belong to the group of high water and high acid commodities, EFSA concludes that sufficiently validated analytical methods for enforcing the proposed MRLs for mepanipyrim on the tomato, aubergine, strawberry and cucumber are 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 tomato, aubergine, strawberry and cucumber 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 (EC, 2004). The data were sufficient to derive toxicological reference values for mepanipyrim which are compiled in Table 2-1.

Table 2-1: Overview of the toxicological reference values

	Source	Year	Value	Study relied upon	Uncertainty factor
mepanipyrim					
ADI	EC	2004	0.02 mg/kg bw per d	Rat, 2 years	100
ARfD	EC	2004	0.30 mg/kg bw	Rabbit, developmental	100

¹⁰ 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

In the framework of the Article 12 MRL review EFSA assessed the available metabolism studies of mepanipyrim in fruits (grapes, tomatoes and apples) (EFSA, 2011). EFSA confirmed to define the residue for both enforcement and risk assessment as mepanipyrim as proposed during the peer review (EFSA, 2011; EC, 2004).

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

Group group	Crop	Application and sampling details				
		Method	Rate (g/ha)	No	Sampling (DAT)	Remarks
Fruit	Grapes	Foliar	500	3	At each treatment (0, 44 and 74 DAT), and harvest (30 days after the last treatment)	
		Foliar	0.9 g	3	At each treatment time (0, 47, 77 DAT) and harvest (30 days after the last treatment)	
	Tomato	Foliar	500	3	0 and 36 days after the last treatment	
		Foliar	500	3	14, 40 and 76 days after the last treatment	
	Apple	Foliar	500	3	0 and 16 days after the last treatment	

The current residue definition set in Regulation (EC) No 396/2005 is identical to the residue definition for enforcement derived in the peer review.

For the uses on tomato, aubergine, strawberry and cucumber, EFSA concludes that the metabolism of mepanipyrim is sufficiently addressed and the residue definitions for enforcement and risk assessment agreed in the peer review are applicable.

3.1.1.2. Magnitude of residues

a. Strawberries

In support of the intended GAPs the applicant submitted eight NEU outdoor trials, eight SEU outdoor trials and eight indoor trials conducted in compliance with the proposed GAPs. These trials were performed during the growing seasons 2009, 2010 and 2011 in Belgium, Germany, the Netherlands the United Kingdom, France, Greece, Italy and Spain.

A MRL proposal of 3 mg/kg is derived for strawberries from the indoor dataset. This MRL proposal covers the outdoor uses of mepanipyrim according to the proposed GAPs.

b. Tomatoes and aubergines

The applicant submitted eight GAP-compliant trials on tomatoes conducted indoor during the growing seasons 2009 and 2010. Residue levels in the range of 0.19 to 0.86 mg/kg result in a MRL proposal of 1.5 mg/kg for tomatoes grown under indoor conditions.

This MRL proposal can be extrapolated to aubergines since the same GAP has been reported for both tomatoes and aubergines (EC, 2011).

c. Cucumber

In support of the intended indoor GAP the applicant submitted eight GAP compliant trials conducted indoor during the growing seasons 2008, 2009 and 2010. A MRL proposal of 0.5 mg/kg is derived from the submitted dataset.

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

The storage stability of mepanipyrim in primary crops was investigated in the DAR under Directive 91/414/EEC (Italy, 2000). Residues of mepanipyrim were found to be stable at ≤ -20 °C for up to 19 and 12 months in matrices with high acid-, and high water-content respectively. As the supervised residue trial samples were stored at *ca.* -18 °C to -20 °C for a period of 1 to 10 months prior to analyses, it is concluded that the residue data are valid with regard to storage stability.

According to the EMS, the analytical methods used to analyse the supervised residue trial samples have been sufficiently validated and were proven to be fit for the purpose (The Netherlands, 2014a, 2014b).

EFSA concludes that the data are sufficient to derive MRL proposals of 3.0 mg/kg for strawberries, 1.5 mg/kg for tomatoes and aubergines and 0.5 mg/kg for cucumbers.

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

Commodity	Residue region ^(a)	Individual trial results (mg/kg) ^(b)	Recommendations/comments ^(c)	MRL proposals (mg/kg)	HR (mg/kg) (d)	STMR (mg/kg) (e)
		Enforcement and Risk assessment: mepanipyrin				
Strawberry	NEU	0.11; 0.13; 0.27; 0.33 ^(f) ; 0.47; 0.49; 0.58; 0.59	MRL proposal derived from the indoor data set. NEU: MRL _{OECD} = 1.1/1.5 SEU: MRL _{OECD} = 2.0/2 Indoor: MRL _{OECD} = 2.7/3	-	0.59	0.40
	SEU	2 × 0.19; 0.25; 0.39; 0.51; 0.65; 0.74; 1.33		-	1.33	0.45
	Indoor	0.11; 0.26 ^(f) ; 0.31; 0.39; 0.42 ^(f) ; 0.95; 1.18; 1.57		3	1.57	0.41
Tomato	Indoor	0.19; 0.22; 0.29; 0.30 ^(g) ; 0.32; 0.49; 0.52; 0.86 ^(g)	MRL _{OECD} = 1.3/1.5 Extrapolation to aubergines	1.5	0.86	0.31
Cucumber	Indoor	0.09; 0.096; 0.14; 0.15 ^(f) ; 0.16; 0.19; 0.22; 0.23	MRL _{OECD} = 0.48/0.5	0.5	0.23	0.16

(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 (EC, 2011).

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

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

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

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

(f): Result at PHI 3 since it was higher than at PHI.

(g): Residue trials performed with cherry tomatoes.

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

3.1.1.3. Effect of industrial processing and/or household preparation

Standard hydrolysis studies have not been provided by the applicant in the course of the peer review or during the Article 12 MRL review. Such studies were submitted in the framework of this MRL application. Under the different hydrolysis conditions, 99.7 % to 105.3 % of the applied radioactivity was recovered as parent mepanipyrim and it was therefore, concluded that mepanipyrim is hydrolytically stable under conditions representative of pasteurisation, boiling and sterilisation. Thus, for processed commodities the same residue definition as for raw agricultural commodities (RAC) is applicable.

Studies investigating the effect of processing on the magnitude of mepanipyrim residues in processed strawberry and tomato products were assessed in the DAR and several processing factors (PF) were established in the framework of the peer review of the active substance (Italy, 2000). Additional studies on strawberry and tomato were provided in support of this MRL application and therefore, EFSA updates the initial PFs, considering these additional data. An overview of all available processing studies in tomato and strawberry, including the studies evaluated in the DAR (Italy, 2000) are reported in table 3-3.

Table 3-3: Overview of the available processing studies

Processed commodity	Number of studies	Processing Factors (PF) ^(a)		Comments
		individual values	Median	
Strawberry/Jam	8	<u>0.16</u> , <u>0.21</u> ; <u>0.32</u> , 0.45, 0.48, 0.50, 0.54, <u>0.59</u>	0.47	PFs derived from the additional studies submitted in the framework of this MRL application are <u>underlined</u> . Other values (Italy 2000).
Strawberry/Canned	8	<u>0.15</u> , <u>0.25</u> , <u>0.35</u> , <u>0.50</u> , 0.70, 0.88, 1.00, 1.07	0.60	
Tomato/Juice	8	0.03, 0.04, <u>0.08</u> , <u>0.15</u> , 0.15, <u>0.21</u> , 0.45, <u>0.60</u>	0.15	
Tomato/Ketchup	4	<u>0.42</u> , <u>0.60</u> , <u>0.80</u> , <u>1.25</u>	0.70	
Tomato/Canned	8	0.03, 0.04, 0.05, 0.05, <u>0.06</u> , <u>0.06</u> , <u>0.08</u> , <u>0.10</u>	0.06	
Tomato/Paste	3	0.71, 0.92, 1.33	0.92	
Tomato/Puree	11	0.28, 0.42, 0.52, 0.55, 0.56, 0.62, <u>0.73</u> , <u>0.76</u> , 0.90, <u>1.22</u> , <u>1.25</u>	0.62	

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

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

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 Review EFSA concluded that no significant residues might be expected in rotational crops even after four applications at a rate of 400 g/ha (EFSA, 2011).

Considering that the uses supported in this MRL application are limited to a total of two treatments at a rate of 396 g/kg, EFSA concludes that relevant residue levels are unlikely to occur in rotational crops provided that the compound is used on crops under consideration according to the proposed GAP.

3.2. Nature and magnitude of residues in livestock

Since 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 (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 population¹¹ (EFSA, 2007).

In the framework of Article 12 MRL review a comprehensive long-term consumer exposure assessment was performed, taking into account the existing uses of mepanipyrin at EU level which are supported by data (EFSA, 2011). Those food commodities, for which no uses of mepanipyrin were reported in the framework of Article 12 of Regulation (EC) No 396/2005, were excluded from the exposure calculation, assuming that there is no use on these crops. EFSA now updates the risk assessment performed in the Article 12 MRL review, including the median residue levels (STMR) as derived from the residue trials on tomato, strawberry and cucumber (see Table 3-2).

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.

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 highest residue level (HR) as observed in supervised field trials. A variability factor accounting for the inhomogeneous distribution on the individual items consumed was included in the calculation, when required (EFSA, 2007).

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		Acute exposure assessment	
	Input value (mg/kg)	Comment	Input value (mg/kg)	Comment
Risk assessment residue definition: mepanipyrin				
Strawberry	0.41	STMR (Table 3-2)	1.57	HR (table 3-2)
Tomato	0.31	STMR (Table 3-2)	0.86	HR (table 3-2)
Aubergine	0.31	STMR (Table 3-2)	0.86	HR (table 3-2)
Cucumber	0.16	STMR (Table 3-2)	0.23	HR (table 3-2)
Other commodities of food and animal origin	STMR	See Table 4-1 in EFSA, 2011.	Acute risk assessment was undertaken only with regard to the crops under consideration.	

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

¹¹ 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).

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 12 % of the ADI (FR all population). The contribution of residues in tomato, aubergine, strawberry and cucumber to the total consumer exposure accounted for a maximum of 5 % of the ADI (WHO Cluster diet B).

No acute consumer risk was identified in relation to the MRL proposals for tomato, aubergine, strawberry and cucumber. The calculated maximum exposure in percentage of the ARfD was 17 % for tomatoes (BE, child).

EFSA concludes that the intended use of mepanipyrin on tomato, aubergine, strawberry and cucumber will not result in a consumer exposure exceeding the toxicological reference values and therefore is unlikely to pose a public health concern.

CONCLUSIONS AND RECOMMENDATIONS

CONCLUSIONS

The toxicological profile of mepanipyrim was assessed in the DAR by the rapporteur Member State Italy and the data were sufficient to derive an ADI of 0.02 mg/kg bw per day and an ARfD of 0.3 mg/kg bw.

The metabolism of mepanipyrim in primary crops was investigated in grape, tomato and apple (fruit crop group). From these studies the peer review concluded to establish the residue definition for enforcement and risk assessment as mepanipyrim. For the use on strawberries, tomatoes, aubergines, and cucumbers, EFSA concludes that the metabolism of mepanipyrim in primary crops is sufficiently addressed and that the residue definitions derived are applicable.

EFSA concludes that the submitted supervised residue trials are sufficient to derive MRL proposals of 3 mg/kg on strawberries, 1.5 mg/kg on tomatoes (extrapolated to aubergines) and 0.5 mg/kg on cucumbers. Adequate analytical enforcement methods are available to control the residues of mepanipyrim in on the commodities under consideration at the validated LOQ of 0.01 mg/kg.

Studies investigating the nature of mepanipyrim residues under standard hydrolysis conditions were submitted in the framework of this MRL application. It was concluded that mepanipyrim is hydrolytically stable under processing conditions representative of pasteurisation, boiling and sterilisation. Therefore for processed commodities the same residue definition as for raw agricultural commodities is applicable. Additional processing studies on strawberry and tomato were provided and therefore, EFSA updated the processing factors (PF) derived for strawberry and tomato in its previous assessments and recommends the inclusion of the following PFs in Annex VI of Regulation (EC) No 396/2005.

– Strawberry/Jam:	0.47	– Tomato/Canned:	0.06
– Strawberry/Canned:	0.60	– Tomato/Paste:	0.92
– Tomato/Juice:	0.15	– Tomato/Puree:	0.62
– Tomato/Ketchup:	0.70		

The occurrence of mepanipyrim residues in rotational crops was investigated in the framework of the peer review and under the Article 12 MRL review. Based on the available information, it was concluded that significant residue levels are unlikely to occur in rotational crops provided that the compound is used on crops under consideration according to the proposed Good Agricultural Practice.

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. In the framework of Article 12 MRL review, a comprehensive long-term consumer exposure assessment was performed, taking into account the existing uses of mepanipyrim at European Union level which are supported by data. EFSA updates the risk assessment performed under the Article 12 MRL review including the median (STMR) and highest (HR) residue levels as derived from the residue trials on strawberry, tomato and cucumber. The highest chronic exposure was calculated to be 12 % of the ADI (FR, all population), and the highest acute exposure 17 % of the ARfD for tomatoes.

EFSA concludes that the proposed use of mepanipyrim on strawberry, tomato, aubergine and cucumber will not result in a consumer exposure exceeding the toxicological reference values and therefore is unlikely to pose a consumer health risk.

RECOMMENDATIONS

Code number^(a)	Commodity	Existing EU MRL (mg/kg)	Proposed EU MRL (mg/kg)	Justification for the proposal
Enforcement residue definition: mepanipyrin				
0152000	Strawberries	1.5	3	based on indoor dataset
0231010	Tomatoes	0.8	1.5	based on indoor dataset
0231030	Aubergines	0.8	1.5	Extrapolation from tomatoes
0232010	Cucumbers	0.01*	0.5	based on indoor dataset

(a): According to Annex I of Regulation (EC) No 396/2005, based on indoor dataset

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

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APPENDICES

Appendix A. Good Agricultural Practice (GAPs)

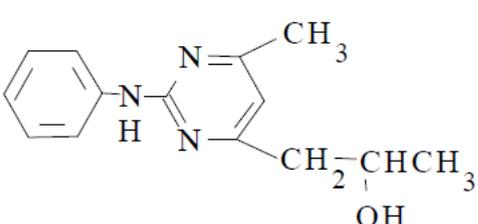
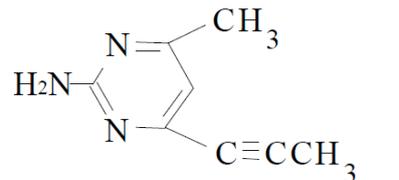
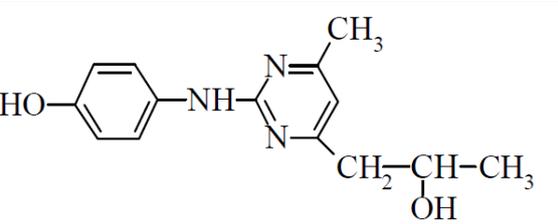
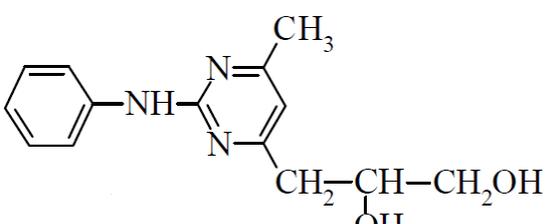
Crop and/or situation (a)	MS	F G or I (b)	Pest or group of pests controlled (c)	Formulation		Application				Application rate per treatment			PHI (days) (l)	Remarks (m)
				type (d-f)	conc. a.s. (i)	method kind (f-h)	growth stage & season (j)	number (k)	interval min max	g as/hL min-max	water L/ha min max	g a.s /ha max		
Strawberry	NL	F	<i>Botryotinia fuckeliana</i> Powdery	SC	440 g/l	Foliar spray	BBCH 10-85 (Apr-Oct.)	1-2	7 days	70-130	300 -600	396	1	a) 2 applications per crop cycle and year b) 1.8 L/ha per season
	NL	G	Mildew (<i>Sphaerotheca aphansis</i>)	SC	440 g/l	Foliar spray	BBCH 10-85 (Jan-Dec)	1-2	7 days	70-130	600 -1200	396	1	
strawberry substrate	NL	G	<i>Botryotinia fuckeliana</i>	SC	440 g/l	Foliar pray	BBCH 10-85 (Jan-Dec)	1-2	7 days	30-40	1100 -1400	396	1	
Tomato and aubergine	NL	G	Powdery Mildew (<i>Leveillula taurica</i> , <i>Oidium spp.</i>)	SC	440 g/l	Foliar spray	beginning of infection BBCH 11 – 89 (Jan-Dec)	1-2	7 days	30-80	500 -1500	396	1	a) 2 applications per crop cycle and year b) 1.8 L/ha per season c) A spreader should be added to the spray solution. Adjust volume to prevent dripping off and loss of product.
Cucumber	NL	G	Powdery mildew (<i>Spaerotheca spp.</i>)	SC	440 g/l	Foliar spray	beginning of infection BBCH 11 – 89 (Jan-Dec)	1-2	7 days	0.03-0.08	500 -1500	396	1	a) 2 applications per crop cycle; 3 crop cycles per year; 6 applications/year. Keep × weeks/month interval between the last application in the previous crop cycle and the first one in the present. b) 5.4 l/ha per year c) A spreader should be added to the spray solution. Adjust spray volume to prevent dripping off and loss of product

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, 4th 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 (Growth stages of mono-and dicotyledonous plants. BBCH Monograph, 2nd Ed., 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)

Acute risk assessment /children - refined calculations						Acute risk assessment / adults / general population - refined calculations						
The acute risk assessment is based on the ARfD.												
For each commodity the calculation is based on the highest reported MS consumption per kg bw and the corresponding unit weight from the MS with the critical consumption. If no data on the unit weight was available from that MS an average European unit weight was used for the IESTI calculation.												
In the IESTI 1 calculation, the variability factors were 10, 7 or 5 (according to JMPR manual 2002), for lettuce a variability factor of 5 was used.												
In the IESTI 2 calculations, the variability factors of 10 and 7 were replaced by 5. For lettuce the calculation was performed with a variability factor of 3.												
Threshold MRL is the calculated residue level which would leads to an exposure equivalent to 100 % of the ARfD.												
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):		
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	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)	Highest % of ARfD/ADI	Commodities	pTMRL/ threshold MRL (mg/kg)
	16.7	Tomatoes	0.86 / -	12.1	Tomatoes	0.86 / -	7.1	Aubergines (egg)	0.86 / -	7.1	Aubergines (egg plants)	0.86 / -
8.2	Strawberries	1.57 / -	8.2	Strawberries	1.57 / -	4.4	Tomatoes	0.86 / -	3.5	Tomatoes	0.86 / -	
7.2	Aubergines (egg)	0.86 / -	7.2	Aubergines (egg)	0.86 / -	2.8	Strawberries	1.57 / -	2.8	Strawberries	1.57 / -	
4.5	Cucumbers	0.23 / -	4.5	Cucumbers	0.23 / -	1.5	Cucumbers	0.23 / -	1.5	Cucumbers	0.23 / -	
No of critical MRLs (IESTI 1)						No of critical MRLs (IESTI 2)						
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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:		
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	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)	Highest % of ARfD/ADI	Processed commodities	***) pTMRL/ threshold MRL (mg/kg)
8.7	Tomato juice	1.5 / -				1.0	Tomato (preserved-	1.5 / -				
*) 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.												
**) pTMRL: provisional temporary MRL												
***) pTMRL: provisional temporary MRL for unprocessed commodity												
Conclusion:												
For Mepanipirim 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.												
For processed commodities, no exceedance of the ARfD/ADI was identified.												

Appendix C. List of metabolites and related structural formula

Common name	IUPAC name	Structural formula
M31	2-anilino-4-(2-hydroxypropyl)-6-methylpyrimidine	 <p>The structure shows a pyrimidine ring with a methyl group at position 6, a 2-hydroxypropyl group at position 4, and an anilino group at position 2. The anilino group consists of a benzene ring attached to the nitrogen at position 2 of the pyrimidine ring.</p>
M41	2-amino-4-methyl-6-(1-propynyl)pyrimidine	 <p>The structure shows a pyrimidine ring with a methyl group at position 4, a propynyl group (C≡CCH₃) at position 6, and an amino group (H₂N) at position 2.</p>
M45	2-(4-hydroxyanilino)-4-(2-hydroxypropyl)-6-methylpyrimidine	 <p>The structure shows a pyrimidine ring with a methyl group at position 6, a 2-hydroxypropyl group at position 4, and a 4-hydroxyanilino group at position 2. The 4-hydroxyanilino group consists of a benzene ring with a hydroxyl group (HO-) at the para position relative to the attachment point to the pyrimidine ring.</p>
M36	2-anilino-4-(2,3-dihydroxypropyl)-6-methylpyrimidine	 <p>The structure shows a pyrimidine ring with a methyl group at position 6, a 2,3-dihydroxypropyl group at position 4, and an anilino group at position 2. The 2,3-dihydroxypropyl group has hydroxyl groups on both the second and third carbons of the propyl chain.</p>

ABBREVIATIONS

a.s.	active substance
ADI	acceptable daily intake
ARfD	acute reference dose
BBCH	growth stages of mono- and dicotyledonous plants
bw	body weight
CF	conversion factor for enforcement to risk assessment residue definition
CXL	codex maximum residue limit
d	day
DAR	Draft Assessment Report (prepared under Council Directive 91/414/EEC)
EC	European Commission
EEC	European Economic Community
EFSA	European Food Safety Authority
EMS	evaluating Member State
EU	European Union
GAP	good agricultural practice
GEMS	Global Environment Monitoring System
ha	hectare
hL	hectolitre
ILV	independent laboratory validation
ISO	International Organisation for Standardization
IUPAC	International Union of Pure and Applied Chemistry
IT	Italy
kg	kilogram
L	litre
LOQ	limit of quantification
mg	milligram
MRL	maximum residue level
MS	Member States
MS/MS	tandem mass spectrometry
NEU	northern European Union
NL	Netherlands
OECD	Organisation for Economic Co-operation and Development
OJ	Official Journal
PF	processing factor
PHI	pre-harvest interval
PRIMo	(EFSA) Pesticide Residues Intake Model

RAC	raw agricultural commodity
RMS	rappporteur Member State
SC	suspension concentrate
SEU	sorthern European Union
STMR	supervised trials median residue
UPLC	ultra performance liquid chromatography
WHO	World Health Organization