

REGISTRATION REPORT

Part B

Section 7

Metabolism and Residues

Detailed summary of the risk assessment

Product code: 3AEY

Product name(s): Mevalone

Chemical active substances:

Eugenol 33 g/L

Geraniol 66 g/L

Thymol 66 g/L

Central Zone

Zonal Rapporteur Member State: Poland

CORE ASSESSMENT

(Authorization for Mevalone product)

Applicant: Eden Research plc

Submission date: 15/07/2021

Updated date: 21/12/2021

MS Finalisation date: April 2022 (initial Core Assessment)

November 2022 (final Core Assessment)

Version history

When	What
July 2021	Authorization of marketing in Central Zone of the plant protection product Mevalone on grapes and pome fruits
December 2021	Update of the GAP table Addition of storage stability final reports for grapes and apples
April 2022	Initial assessment by the zRMS The report in the dRR format has been prepared by the Applicant, therefore all comments, additional evaluations and conclusions of the zRMS are presented in grey commenting boxes. Minor changes are introduced directly in the text and highlighted in grey. Not agreed or not relevant information are struck through and shaded for transparency .
November 2022	Final report (Core Assessment updated following the commenting period). Additional information/assessments included by the zRMS in the report in response to comments received from the CMS and the Applicant are highlighted in yellow. Information no longer relevant is struck through and shaded .

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7 Metabolism and residue data (KCA section 6)

7.1 Summary and zRMS Conclusion

zRMS conclusion:

Mevalone was the representative formulation in the EU review of eugenol, geraniol and thymol. The residue trials in grapes were already addressed during the EU review of eugenol, geraniol and thymol. The GAP supported during the EU review was identical to the GAP supported in this submission.

Eugenol, geraniol and thymol were evaluated in the EU Review and have been included in Annex IV to Regulation 396/2005, for which no maximum residue levels (MRLs) are required. Therefore this means that residue trials are not necessary.

Additional evaluations and conclusions of the zRMS are presented in grey commenting boxes below each point.

7.1.1 Critical GAP(s) and overall conclusion

Selection of critical uses and justification

The critical GAPs with respect to consumer intake and risk assessment for the preparation Mevalone are presented in Table 7.1-1. They have been selected from the individual GAPs in the central zone for grapes and pome fruit. A list of all intended uses within the zone is given in Part B, Section 0.

The same GAP is being supported throughout the zone. The cGAP reflects the highest application rate and the shortest interval between applications.

Overall conclusion

The data available are considered sufficient for risk assessment. Eugenol, geraniol and thymol are provisionally included into Annex IV to Regulation (EC) No. 396/2005 and therefore MRLs are not necessary.

The chronic and the short-term intakes of eugenol, geraniol and thymol residues are unlikely to present a public health concern.

As far as consumer health protection is concerned, the zRMS, Poland agrees with the authorization of the intended use(s).

According to available data, no specific mitigation measures should apply.

Data gaps

There are no data gaps.

Table 7.1-1: Acceptability of critical GAPs

1	2	3	4	5	6	7		8				9			10	11
GAP number (see part B.0)*	Crop and/or situation	Zone	Product code	F, Fn, Fpn, G, Gn, Gpn or I**	Pests or Group of pests controlled	Formulation		Application				Application rate per treatment			PHI (days)	Conclusion
						Type	Conc. of a.s. (g/L)	method kind	growth stage & season	number min max	interval between applications (min)	g as/hL min max	water L/ha min max	g as/ha min max		
1	Grape (<i>Vitis vinifera</i> VITVI)	Central	3AEY	F	Grey mould (<i>Botrytis cinerea</i> BOTRCI)	CS	33 (E) 66 (G) 66 (T)	Foliar. Tractor-mounted air blast sprayer. Hand-held knapsack sprayer.	BBCH 60 - 89	1 - 4	7 days	13.2 (E) 26.4 (G) 26.4 (T)	400 - 1000	52.8 - 132 (E) 106 - 264 (G) 106 - 264 (T)	7	A
2	Pome fruit †	Central	3AEY	F	Post-harvest storage diseases (Example; <i>Phytophthora</i> spp. PHYTSP mainly <i>P. cactorum</i> PHYTCC or <i>P. syringae</i> PHYTSY, ALTESP, <i>Botrytis cinerea</i> BOTRCI)	CS	33 (E) 66 (G) 66 (T)	Foliar. Tractor-mounted air blast sprayer. Hand-held knapsack sprayer.	BBCH 75 - 87	1 - 4	7 days	13.2 (E) 26.4 (G) 26.4 (T)	600 - 1000	79.2 - 132 (E) 158 - 264 (G) 158 - 264 (T)	1	A

* Use number(s) in accordance with the list of all intended GAPs in Part B, Section 0 should be given in column 1

** F: professional field use, Fn: non-professional field use, Fpn: professional and non-professional field use, G: professional greenhouse use, Gn: non-professional greenhouse use, Gpn: professional and non-professional greenhouse use, I: indoor application

† (apple *Malus domestica* MABSD, pear *Pyrus communis* PYUCO, quince *Cydonia oblonga* CYDOB, crab-apple *Malus sylvestris* MABSY, loquat *Eryobotria japonica* EIOJA, medlar *Mespilus germanica* MSPGE, Nashi pear *Pyrus pyrifolia* var. *culta* PYUPC)

Explanation for Column 11 “Conclusion”

A	Exposure acceptable without risk mitigation measures, safe use
R	Further refinement and/or risk mitigation measures required
N	Exposure not acceptable, no safe use

7.1.2 Summary of the evaluation

The preparation Mevalone is composed of eugenol, geraniol and thymol.

Table 7.1-2: Toxicological reference values for the dietary risk assessment of eugenol, geraniol and thymol

Reference value	Source	Year	Value	Study relied upon	Safety factor
Eugenol					
ADI	EFSA	2013	1.0 mg/kg bw/day	Rat developmental study (Wood & McKenzie, 2004) and rabbit developmental study (Wood, 2004)	100
ARfD	EFSA	2013	Not necessary	-	-
Geraniol					
ADI	EFSA	2013	0.5 mg/kg bw/day	JECFA	-
ARfD	EFSA	2013	Not necessary	-	-
Thymol					
ADI	EFSA	2013	0.03 mg/kg bw/day	JECFA	-
ARfD	EFSA	2013	0.08 mg/kg bw/day	Rat repeat dose oral toxicity and reproductive toxicity (gavage dosing) (Matsuura <i>et al.</i>)	100

7.1.2.1 Summary for eugenol

Table 7.1-3: Summary for eugenol

Use-No.*	Crop	Plant metabolism covered?	Sufficient residue trials?	PHI sufficiently supported?	Sample storage covered by stability data?	MRL compliance	Chronic risk for consumers identified?	Acute risk for consumers identified?
1	Grape	N/A	Yes (3)	Yes	Yes	N/A	No	N/A
2	Pome fruit	N/A	Yes (3)	Yes	Yes	N/A		N/A

* Use numbers in accordance with the list of all intended GAPs in Part B, Section 0

Eugenol occurs naturally in variety of fruits, vegetables, herbs and spices. It is used in cosmetics as a fragrance, as a flavouring agent in food, as an analgesic in dentistry, to flavour cigarettes and is also a constituent of oils used in aromatherapy. Due to its ubiquitous natural occurrence, in the EU review it was considered that plant metabolism studies were not necessary.

During the EU review of eugenol it was concluded that MRLs would not be proposed for this active substance because it is found in wide range of plants and consumers are exposed via many different sources. As such monitoring of GAP will not be possible and in any case, it would afford little additional consumer protection.

As the active substance is temporarily included into Annex IV of Regulation (EC) No. 396/2005, it is considered that 3 trials per crop are sufficient. There were no detectable residues of eugenol or methyleugenol in grapes or pome fruit following application of Mevalone according to the cGAP (LOD = 0.003 mg/kg).

As residues of eugenol do not exceed the trigger values defined in Reg (EU) No 283/2013, there is no

need to investigate the effect of industrial and/or household processing.

Residues in succeeding crops are not relevant, since grapes and pome fruit are not grown in rotation.

Considering dietary burden and based on the intended uses, livestock metabolism and feeding studies are not necessary.

The consumer risk assessment is acceptable.

7.1.2.2 Summary for geraniol

Table 7.1-4: Summary for geraniol

Use- No.*	Crop	Plant metabolism covered?	Sufficient residue trials?	PHI sufficiently supported?	Sample storage covered by stability data?	MRL compliance	Chronic risk for consumers identified?	Acute risk for consumers identified?
1	Grape	N/A	Yes (3)	Yes	Yes	N/A	No	N/A
2	Pome fruit	N/A	Yes (3)	Yes	Yes	N/A		N/A

* Use numbers in accordance with the list of all intended GAPs in Part B, Section 0

Geraniol occurs naturally in variety of fruits, vegetables, herbs and spices. It is used in cosmetics, as a flavouring agent in food, in household and laundry cleaning products and in air fresheners and is also a constituent of oils used in aromatherapy. Due to its ubiquitous natural occurrence, in the EU review it was considered that plant metabolism studies were not necessary.

During the EU review of geraniol it was concluded that MRLs would not be proposed for this active substance because it is found in wide range of plants and consumers are exposed via many different sources. As such monitoring of GAP will would not be possible and in any case, it would afford little additional consumer protection.

As the active substance is temporarily included into Annex IV of Regulation (EC) No. 396/2005, it is considered that 3 trials per crop are sufficient. Residues of geraniol were all <LOQ (0.01 mg/kg) or equal to natural background concentrations in grapes and there were no detectable residues (LOD = 0.003 mg/kg) in pome fruit following application of Mevalone according to the cGAP.

As residues of geraniol do not exceed the trigger values defined in Reg (EU) No 283/2013, there is no need to investigate the effect of industrial and/or household processing.

Residues in succeeding crops are not relevant, since grapes and pome fruit are not grown in rotation.

Considering dietary burden and based on the intended uses, livestock metabolism and feeding studies are not necessary.

The consumer risk assessment is acceptable.

7.1.2.3 Summary for thymol

Table 7.1-5: Summary for thymol

Use- No.*	Crop	Plant metabolism covered?	Sufficient residue trials?	PHI sufficiently supported?	Sample storage covered by stability data?	MRL compliance	Chronic risk for consumers identified?	Acute risk for consumers identified?
1	Grape	N/A	Yes (3)	Yes	Yes	N/A	No	No
2	Pome fruit	N/A	Yes (3)	Yes	Yes	N/A		No

* Use numbers in accordance with the list of all intended GAPs in Part B, Section 0

Thymol occurs naturally in variety of fruits, vegetables, herbs and spices. It is used in cosmetics as a fragrance, as a flavouring agent in food, in veterinary and human medicine. The European Medicine Agency Committee for Veterinary Medicinal Products has concluded that thymol residues in animal products are not likely to be of toxicological concern to human and decided that MRLs for edible tissues were not needed. Thymol is also present in mouthwashes and toothpastes. Thyme oil which contains 30 - 50% thymol is used in aromatherapy oils. Due to its ubiquitous natural occurrence, in the EU review it was considered that plant metabolism studies were not necessary.

During the EU review of thymol it was concluded that MRLs would not be proposed for this active substance because it is found in wide range of plants and consumers are exposed via many different sources. As such monitoring of GAP will would not be possible and in any case, it would afford little additional consumer protection.

As the active substance is temporarily included into Annex IV of Regulation (EC) No. 396/2005, it is considered that 3 trials per crop are sufficient. Residue of thymol in grapes or pome fruit following application of Mevalone according to the cGAP were all below the LOQ (0.01 mg/kg).

As residues of thymol do not exceed the trigger values defined in Reg (EU) No 283/2013, there is no need to investigate the effect of industrial and/or household processing.

Residues in succeeding crops are not relevant, since grapes and pome fruit are not grown in rotation.

Considering dietary burden and based on the intended uses, livestock metabolism and feeding studies are not necessary.

The consumer risk assessment is acceptable.

7.1.2.4 Summary for Mevalone

Table 7.1-6: Information on Mevalone (KCA 6.8)

Crop	PHI for Mevalone proposed by applicant	PHI sufficiently supported for			PHI for Mevalone proposed by zRMS	zRMS Comments (if different PHI proposed)
		Eugenol	Geraniol	Thymol		
Grapes	7 days	Yes	Yes	Yes	7 days	-
Pome fruit	1 day	Yes	Yes	Yes	1 day	-

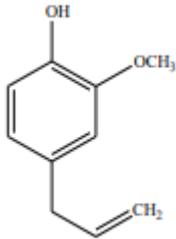
Assessment

The submitted residue trials are sufficient to support the proposed PHI and demonstrate no residues of eugenol, geraniol or thymol at or above the LOQ, or else the same as natural background concentrations. Eugenol, geraniol and thymol are temporarily included into Annex IV of Regulation (EC) No. 396/2005 and as such, MRLs are considered not necessary.

7.2 Eugenol

General data on eugenol are summarized in the table below (last updated 2013/12/01)

Table 7.2-1: General information on eugenol

Active substance (ISO Common Name)	Eugenol (No ISO common name)
IUPAC	4-allyl-2-methoxyphenol
Chemical structure	
Molecular formula	C ₁₀ H ₁₂ O ₂
Molar mass	164.20 g/mol
Chemical group	Plant derived - Plant oil (terpene)
Mode of action (if available)	Prohibits the growth of both Gram-positive and Gram-negative bacteria and fungi. Strong insect repellent
Systemic	Yes
Company	Eden Research plc *
Rapporteur Member State (RMS)	SP, co-RMS: GR (former RMS: UK)
Approval status	Approved Date of (01/12/2013)
Restriction	None
Review Report	SANCO/10577/2013 rev 3 17 May 2013
Current MRL regulation	Reg. (EC) No 839/2008
Peer review of MRLs according to Article 12 of Reg No 396/2005 EC performed	None – not yet scheduled.
EFSA Journal : conclusion on the peer review	Yes - EFSA Journal 2012;10(11):2914
EFSA Journal: conclusion on article 12	No
Current MRL applications on intended uses	Commission Regulation (EC) No 839/2008 of 31 July 2008 amending Regulation (EC) No 396/2005 of the European Parliament and of the Council as regards Annexes II, III and IV on maximum residue levels of eugenol. Submission of MRL application to include eugenol in Annex IV of Regulation (EC) No 396/2005 was submitted at the same time as the AIR dossier on 28 th February 2021.

* Notifier in the EU process to whom the a.s. belongs

7.2.1 Stability of Residues (KCA 6.1)

7.2.1.1 Stability of residues during storage of samples

Available data

Table 7.2-2: Summary of stability data achieved at $\leq -18^{\circ}\text{C}$ (unless stated otherwise)

Matrix	Characteristics of the matrix	Acceptable Maximum Storage duration	Reference
Data relied on in EU			
Plant products			
Grapes – surface extractable residues	High water content	Not stable	DAR, UK, 2012
Grapes – total residues	High water content	28 days*	DAR, UK, 2012
Animal Products			
Not required			
New data			
Plant products			
Grapes	High water content	154 days	Driss, 2021, S20-06526
Apples	High water content	112 days	Driss, 2021, S20-06527
Animal Products			
Not required			

* Study was ongoing at the time of the EU Review and final study is included with this submission and demonstrates 12 months' storage stability

Conclusion on stability of residues during storage

Surface extractable residues are not stable under storage. Residues on whole grapes are stable for at least 12 months. Residues on homogenised whole grapes are stable for at least 154 days.

Residues on homogenised apples are stable for at least 112 days.

zRMS comments:

In the EFSA Journal 2012;10(11):2914 it is stated that EFSA was unable to conclude on the storage stability of residues of eugenol in grapes within 1 month of storage based on the submitted studies as the results were shown to be contradictory. The acceptability of these trials is therefore pending the outcome of new storage stability data to cover the maximum storage time interval of eugenol in the samples from the residue trials, and a data gap is identified.

Three new stability studies have been submitted by the Applicant in the framework of this application:

1. Brown, D. 2012; Report No. AF/12351/ED

Stability of eugenol residues in grapes (whole grapes) has been demonstrated for storage intervals of up to twelve months under frozen conditions.

2. Driss, F. 2021a; Report No. S20-06526

Stability of eugenol residues in grapes (homogenised grapes) has been demonstrated for storage intervals of up to 154 days and stability of methyleugenol residues – up to 278 days under frozen conditions.

3. Driss, F. 2021b; Report No. S20-06527

Stability of eugenol residues in apples has been demonstrated for storage intervals of up to 112 days and stability of methyleugenol residues – up to 285 days under frozen conditions.

The studies on the magnitude of residues are valid with regard to storage stability.

No additional data are required.

7.2.1.2 Stability of residues in sample extracts (KCA 6.1)

Available data

In the grape residue trials, the maximum duration between extraction and analysis was 7 days and stability of extracts was demonstrated for 7 days in study S20-06528 by Driss, 2021 – please refer to dRR Part B5 for further details.

In the apple residue trials, the maximum duration between extraction and analysis was 7 days and stability of extracts was demonstrated for 15 days in study S20-06529 by Driss, 2021 – please refer to dRR Part B5 for further details.

Conclusion on stability of residues in sample extracts

Stability of extracts is demonstrated.

zRMS comments:

Information submitted by Applicant is sufficient and accepted.
No further data are required.

7.2.2 Nature of residues in plants, livestock and processed commodities

7.2.2.1 Nature of residue in primary crops (KCA 6.2.1)

Mevalone was the representative formulation in the EU review of eugenol. The metabolism in plants was already addressed during the EU review and no additional studies are required.

Plant metabolism studies are not necessary, due to the natural occurrence of eugenol in a variety of fruits, vegetables, herbs and spices. Limited information from the published literature was submitted as part of the EU Review.

No new data submitted in the framework of this application.

zRMS comments:

EFSA concluded (EFSA, 2012) that plant metabolism studies were not submitted as eugenol occurs naturally in plants and very limited information from the published literature was reported in the DAR. Data on the natural background levels of eugenol in grapes from retail samples were also submitted and gave indication of residue levels far below 0.05 mg/kg (validated LOQ of the method). EFSA is of the opinion that no metabolism data are required to conduct a reliable consumer risk assessment with regard to the eugenol residues if the submitted residue trials are considered as acceptable.

No additional metabolism studies are necessary to support the intended uses for Mevalone.

Definition:

According to the EFSA Journal 2012;10(11):2914:

The residue definition for enforcement and for risk assessment for plant is not required.

Regulation (EC) 839/2008 included eugenol in Annex IV of the reg. (EC) 396/2005 as an active substance for which MRL are not required.

No further data are required to support the proposed uses.

7.2.2.2 Nature of residue in rotational crops (KCA 6.6.1)

Rotational crop studies are not relevant, since grapes and pome fruit are not grown in rotation.

No new data submitted in the framework of this application.

zRMS comments:

Information submitted by Applicant is sufficient and accepted.
No additional data are necessary to support the intended uses for Mevalone.

7.2.2.3 Nature of residues in processed commodities (KCA 6.5.1)

As residues of eugenol do not exceed the trigger values defined in Reg (EU) No 283/2013, studies on the nature of the residue in processed commodities are not required.

No new data submitted in the framework of this application.

zRMS comments:

Information submitted by Applicant is sufficient and accepted.
No additional data are necessary to support the intended uses for Mevalone.

7.2.2.4 Conclusion on the nature of residues in commodities of plant origin (KCA 6.7.1)

Studies on the nature of the residue in commodities of plant origin are not required.

zRMS comments:

According to the EFSA Journal 2012;10(11):2914:

Table 7.2-3: Summary of the nature of residues in commodities of plant origin

Endpoints	
Plant groups covered	Currently not required ⁽¹⁾
Rotational crops covered	Data not required.
Metabolism in rotational crops similar to metabolism in primary crops?	N/A
Processed commodities	Data not required
Residue pattern in processed commodities similar to pattern in raw commodities?	N/A
Plant residue definition for monitoring	Not required ⁽¹⁾
Plant residue definition for risk assessment	Not required ⁽¹⁾
Conversion factor from enforcement to RA	N/A

⁽¹⁾: Additional metabolism data and residue definitions not required pending the acceptability of the residue trials.

7.2.2.5 Nature of residues in livestock (KCA 6.2.2-6.2.5)

Mevalone was the representative formulation in the EU review of eugenol. The metabolism in livestock was already addressed during the EU review and no additional studies are required.

Livestock metabolism studies are not necessary, due to the natural occurrence of eugenol in a variety of fruits, vegetables, herbs and spices. Furthermore, livestock dietary intake calculations demonstrate that the dietary intake is below the trigger of 0.004 mg/kg bw/day.

No new data submitted in the framework of this application.

zRMS comments:

Information submitted by Applicant is sufficient and accepted. It is not required to investigate the metabolism of eugenol in livestock.
No additional data are necessary to support the intended uses for Mevalone.

7.2.2.6 Conclusion on the nature of residues in commodities of animal origin

(KCA 6.7.1)

Studies on the nature of the residue in commodities of animal origin are not required.

zRMS comments:

According to the EFSA Journal 2012;10(11):2914:

Table 7.2-4: Summary of the nature of residues in commodities of animal origin

Endpoints	
Animals covered	Data not required.
Time needed to reach a plateau concentration	N/A
Animal residue definition for monitoring	Not required
Animal residue definition for risk assessment	Not required
Conversion factor	N/A
Metabolism in rat and ruminant similar	N/A
Fat soluble residue	N/A

7.2.3 Magnitude of residues in plants (KCA 6.3)

7.2.3.1 Summary of European data and new data supporting the intended uses

New studies on the magnitude of residue have been submitted by the applicant in the framework of this application. These studies are summarized in the Table below. The detailed assessment of these studies is presented in Appendix 2.

Table 7.2-5: Summary of EU reported and new data supporting the intended uses of Mevalone and conformity to existing MRL

Commodity	Source	Residue zone (N-EU, S-EU, EU, outside EU)	Evaluation GAP Residue levels (mg/kg) E = according to enforcement residue definition RA = according to risk assessment residue definition	STMR (mg/kg)	HR (mg/kg)	Unrounded OECD calculator MRL (mg/kg)	Current EU MRL (mg/kg) *	MRL compliance
Grapes	New trials	N-EU	Trials GAP: 4 x 4.0 L product/ha, PHI 7d, outdoor E & RA: 3 x ND (eugenol) 3 x ND (methyleugenol)					
	Overall supporting data for cGAP	N-EU	E & RA: 3 x ND (eugenol) 3 x ND (methyleugenol)	ND (eugenol) ND (methyleugenol)	ND (eugenol) ND (methyleugenol)	Eugenol is temporarily included into Annex IV to Regulation (EC) No. 396/2005 and therefore MRLs are not required.		
Pome fruit	New trials	N-EU	Trials GAP: 4 x 4.0 L product/ha, PHI 1d, outdoor E & RA: 3 x ND (eugenol) 3 x ND (methyleugenol)					
	Overall supporting data for cGAP	N-EU	E & RA: 3 x ND (eugenol) 3 x ND (methyleugenol)	ND (eugenol) ND (methyleugenol)	ND (eugenol) ND (methyleugenol)	Eugenol is temporarily included into Annex IV to Regulation (EC) No. 396/2005 and therefore MRLs are not required.		

* Eugenol is temporarily included into Annex IV to Regulation (EC) No. 396/2005
 ND: not detected (<0.003 mg/kg)

7.2.3.2 Conclusion on the magnitude of residues in plants

According to the available data, the intended uses on grapes and pome fruit are considered acceptable, for outdoor uses.

Eugenol is temporarily included into Annex IV to Regulation (EC) No. 396/2005 and therefore MRLs are not applicable. There were no detectable residues of eugenol or methyleugenol in grapes or apples (LOD = 0.003 mg/kg).

According to appendix D of EU guidelines, extrapolation to all of the pome fruit crop group is possible with trials on apples. Taking into account the no residue situation, 3 trials are considered to be sufficient for the extrapolation.

The uses are considered acceptable.

zRMS comments:

Mevalone was the representative formulation in the EU review of eugenol, geraniol and thymol. The residue trials in grapes were already addressed during the EU review of eugenol, geraniol and thymol. The GAP supported during the EU review was identical to the GAP supported in this submission. According to the EFSA Journal 2012;10(11):2914 *Sufficient residue trials on grapes in compliance with the representative use were submitted and demonstrated that the use of eugenol as a plant protection product did not result in residue levels higher than the LOQ of the analytical method (0.05 mg/kg) both in the treated and control samples.*

All data were considered adequate and thus the studies are not described in detail in this document.

Regulation (EC) 839/2008 included eugenol in Annex IV of the reg. (EC) 396/2005 as an active substance for which MRL are not required. Therefore this means that residue trials are not necessary.

In EFSA Journal 2012; 10(11): 2914 it was stated that data were required to address the levels of methyl-eugenol in grapes. This issue was subsequently closed off by the response to the EFSA Conclusion Report and is no longer an issue in the Commission Review Report (SANCO/10577/2013 rev. 3 of 17 May 2013). The response from the RMS-UK is available on the CIRCA website:

“(…) A data gap has been set to determine the occurrence of methyl-eugenol in grapes. We do not consider this is necessary, since residue trials have been submitted which show a zero residue situation, even immediately after application. Application of 3AEY does not increase the levels of eugenol above background concentrations. (...)Furthermore, low levels of eugenol have been demonstrated to be present naturally in grapes (<LOQ). If there were metabolism from eugenol to methyl-eugenol in grapes, this would occur with eugenol that is naturally present. Since there is no increase in eugenol above background, there is no increased risk of metabolism to methyl-eugenol compared to untreated grapes and therefore no increased risk to the consumer. The risk assessment is therefore adequately addressed.”

Two new residue studies have been submitted by the Applicant in the framework of this application.

1. Determination of residues of eugenol, methyl eugenol, geraniol and thymol after 4 foliar applications of Mevalone (3AEY / EDN-004) to **grapevine**, 3 trials in N EU (3 x DEC) and 3 trials in S EU (3 x DEC), 2020 - Chadwick, G. 2021a Report No. S20-06337

Three residue trials were conducted on grape during 2020 in NEU. Four applications of Mevalone were applied at nominal rates of 264 g ai/ha thymol; 264 g ai/ha geraniol and 132 g ai/ha eugenol. Samples of ~~apple-fruit~~ **grape** from the treated plots were taken by hand 0, 1, 2, 3 and 7 days after the final application.

There were no detectable residues of eugenol or methyl-eugenol in grapes (LOD = 0.003 mg/kg) **at 7 days after last application.**

2. Determination of residues of eugenol, methyl eugenol, geraniol and thymol after 4 foliar applications of Mevalone (3AEY / EDN-004) to **apple**, 3 trials in N EU (3 x DEC) and 3 trials in S EU (3 x DEC), 2020. Chadwick, G. 2021b Report No. S20-06361

Three residue trials were conducted on apples during 2020 in NEU. Four applications of Mevalone were applied at nominal rates of 264 g ai/ha thymol; 264 g ai/ha geraniol and 132 g ai/ha eugenol. Samples of apple fruit from the treated plots were taken by hand 0, 1, 2, 3 and 7 days after the final application.

There were no detectable residues of eugenol and methyl-eugenol in apples samples (LOD = 0.003 mg/kg) **collected at I DALA.**

In zero residue situation (no detectable residues (< limit of detection (LOD))), three trials shall be performed for

major crops.
 According to SANTE/2019/12752 trials on apples can be extrapolated to the whole of the pome fruit group.
 No further data are required to support the proposed uses.

7.2.4 Magnitude of residues in livestock

7.2.4.1 Dietary burden calculation

To assess the livestock dietary burden of eugenol for EU livestock, the residues trials values (STMR and HR) supporting the cGAP for the raw agricultural commodities (RAC) for apples were used as input into the ‘Animal model 2017’. Values used in the livestock dietary intake calculator are shown in the table below. The calculation is worst-case, since there were no detectable residues of eugenol or methyleugenol in apples (LOD = 0.003 mg/kg), but the calculation is performed using the LOQ (0.01 mg/kg) as the input value.

It should be noted that in the case of apples, livestock are not typically fed the raw agricultural commodity (RAC). Instead, livestock are routinely fed the processed by-products of apples (pomace). Usually, a processing factor would be applied to the residue value of the RAC, however, as the residues in the treated apples are less than the LOQ (<0.01 mg/kg), a processing factor does not need to be applied. The PF value was adjusted to 1 in the model. A conversion factor is not necessary.

Table 7.2-6: Input values for the dietary burden calculation (considering the uses under consideration)

Feed commodity	Median dietary burden		Maximum dietary burden	
	(mg/kg)	Comment	(mg/kg)	Comment
Eugenol				
Apple pomace, wet	0.01	STMR	0.01	STMR
Methyleugenol				
Apple pomace, wet	0.01	STMR	0.01	STMR

Table 7.2-7: Results of the dietary burden calculation

Animal species	Median dietary burden (mg/kg bw/d)	Maximum dietary burden (mg/kg bw/d)	Highest contributing commodity	Max dietary burden (mg/kg DM)	Trigger exceeded (Y/N)
Eugenol					
Beef cattle*	0.0006	0.0006	Apple (pomace, wet)	0.03	N
Dairy cattle*	0.0005	0.0005	Apple (pomace, wet)	0.01	N
Ram/ewe	0.0004	0.0004	Apple (pomace, wet)	-	N
Lamb	0.0005	0.0005	Apple (pomace, wet)	-	N
Breeding swine	-	-	-	-	N
Finishing swine*	-	-	-	-	N
Broiler poultry	-	-	-	-	N
Layer poultry*	-	-	-	-	N
Turkey	-	-	-	-	N
Methyleugenol					
Beef cattle*	0.0006	0.0006	Apple (pomace, wet)	0.03	N
Dairy cattle*	0.0005	0.0005	Apple (pomace, wet)	0.01	N
Ram/ewe	0.0004	0.0004	Apple (pomace, wet)	-	N
Lamb	0.0005	0.0005	Apple (pomace, wet)	-	N
Breeding swine	-	-	-	-	N
Finishing swine*	-	-	-	-	N
Broiler poultry	-	-	-	-	N
Layer poultry*	-	-	-	-	N
Turkey	-	-	-	-	N

* These categories correspond to those (formerly) assessed at EU level.

7.2.4.2 Livestock feeding studies (KCA 6.4.1-6.4.3)

Livestock feeding studies are not triggered.

No new data were submitted in the framework of this application.

zRMS comments:

Information presented by Applicant are sufficient.

The median and maximum dietary burdens were calculated for different groups of livestock using the EFSA Animal model 2017.

The calculated dietary burdens for eugenol and methyl-eugenol for all groups of livestock were found to be below the trigger value of 0.004 mg/kg bw per day for all animal species. Further investigation of residues in animal commodities is therefore not required.

7.2.5 Magnitude of residues in processed commodities (Industrial Processing and/or Household Preparation) (KCA 6.5.2-6.5.3)

7.2.5.1 Available data for all crops under consideration

No new data were submitted in the framework of this application.

7.2.5.2 Conclusion on processing studies

Processing studies are not triggered.

zRMS comments:

Information submitted by Applicant is sufficient and accepted.
No additional data are necessary to support the intended uses for Mevalone.

7.2.6 Magnitude of residues in representative succeeding crops

Crops under evaluation are not expected to be grown in rotation. Further investigation of residues in rotational crops is therefore not required.

7.2.6.1 Field rotational crop studies (KCA 6.6.2)

No new data submitted in the framework of this application.

zRMS comments:

Information submitted by Applicant is sufficient and accepted.
No additional data are necessary to support the intended uses for Mevalone.

7.2.7 Other / special studies (KCA6.10, 6.10.1)

The available data for the active substance sufficiently address aspects of the residue situation that might arise from the use of Mevalone. Therefore, other special studies are not needed.

According to SANTE/11956/2016, grapes and pome fruit may be foraged by bees. For grapes the timing of application (BBCH 60-69) is such that bees may potentially forage the crop following application. However, the timing of application for pome fruit (BBCH 75-87) is after the flowering stage (BBCH 60-69) and therefore the bees will not forage blossoms following application of Mevalone. Furthermore, eugenol is not persistent and therefore potential exposure in subsequent seasons will not occur.

Exposure of bees to eugenol residues will be negligible following the proposed representative uses of Mevalone on grapes and pome fruit. Residue trials have demonstrated that eugenol levels in treated crops are below the trigger of 0.05 mg/kg on the day of application. Eugenol is temporarily included into Annex IV of Regulation (EC) No. 396/2005 meaning that MRLs are not necessary.

For both grapes and pome fruit, the timing of application is such that application may occur during the period April to September i.e. when in-field weeds or adjacent crops may be flowering. However, eugenol is found in a wide variety of plants. Since it is naturally occurring in the flowers of plants, it may be expected that bees will naturally be exposed to eugenol when foraging. Furthermore, products containing eugenol may be used for the control of varroa mite on bees.

Eugenol is rapidly degraded in soil with a $DT_{90} < 3$ days (please refer to MCP Part B8 for further details). Therefore, residues in succeeding crops and weeds are not applicable. Furthermore, grapes and pome fruit are not grown in rotation.

Eugenol is not intended to be used in forestry and therefore potential exposure to honeydew from plant sucking insects is not relevant.

It is concluded that studies on the residue level in pollen and bee products are not required. Residues of eugenol were always below the trigger of 0.05 mg/kg. It is considered that MRLs are also not necessary for honey. Eugenol is naturally occurring in a wide variety of plants, on which bees forage, including many flowers to which bees are attracted. Therefore, any residues found in bee products, including honey could not necessarily be concluded to be due to plant protection product use.

zRMS comments:

Information submitted by Applicant is sufficient and accepted.
No other data are necessary to support the intended uses for Mevalone.

7.2.8 Estimation of exposure through diet and other means (KCA 6.9)

Toxicological reference values relevant for dietary risk assessment are reported in the summary of the evaluation (see 7.1.2).

As ARfD was not deemed necessary, acute risk assessment is not relevant.

7.2.8.1 Input values for the consumer risk assessment

Table 7.2-8: Input values for the consumer risk assessment

Commodity	Chronic risk assessment	
	Input value (mg/kg)	Comment
Grapes	0.01*	Default value [†]
Apples	0.01*	Default value [†]
All other commodities listed within Regulation (EU) 2018/62	0.01*	Default value
All products of livestock origin (as listed within Regulation (EU) 2018/62)	0.01*	Default value

[†] There were no detectable residues (LOD = 0.003 mg/kg)

7.2.8.2 Conclusion on consumer risk assessment

Extensive calculation sheets are presented in Appendix 3. The calculation is worst-case, since there were no detectable residues of eugenol or methyleugenol in grapes or apples (LOD = 0.003 mg/kg), but the calculation is performed using the LOQ (0.01 mg/kg) as the input value.

Table 7.2-9: Consumer risk assessment

TMDI (% ADI) according to EFSA PRIMo	0.1 % (based on NL, toddler)
IEDI (% ADI) according to EFSA PRIMo	Not required
IESTI (% ARfD) according to EFSA PRIMo	Not required
NTMDI (% ADI)	Not required
NEDI (% ADI)	Not required
NESTI (% ARfD)	Not required

The proposed uses of eugenol in the formulation Mevalone do not represent unacceptable chronic risks for the consumer.

zRMS comment:

EFSA (EFSA Journal 2012;10(11):2914) performed a provisional consumer risk assessment with regard to eugenol residues and no intake concern was identified (<1% of the ADI). Nevertheless, the overall consumer exposure cannot be concluded with regard to the genotoxic carcinogenic methyl-eugenol and this issue was identified as a critical area of concern.

The response from the RMS-UK is available on the CIRCA website:

“Consumer exposure data generated in the DAR addendum showed that the maximum consumer intake was predicted from the NESTI calculation (UK and German diet databases giving very similar results) of infants/children consuming table grapes with exposure levels of eugenol approximately 0.003 mg/kg/bw/day. Using a worst case scenario of 0.1% methyl-eugenol present in eugenol, maximum consumer exposure to methyl-eugenol is 0.000003 mg/kg/bw/day, giving rise to >300,000 fold safety factor to the lowest threshold as described by EMEA”.

Methyl-eugenol does not form part of the residue definition for risk assessment.

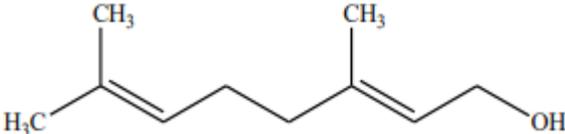
According to the Eugenol - SANCO/10577/2013 rev. 3, 17 May 2013:
The following reference values have been finalised as part of this evaluation:
ADI: 1.0 mg/kg bw per day
ARfD: Not necessary

Information given by the Applicant is sufficient. The proposed uses of eugenol in the product Mevalone do not represent unacceptable chronic risk for the consumer.
No further data are required to support the proposed use.

7.3 Geraniol

General data on geraniol are summarized in the table below (last updated 2013/12/01)

Table 7.3-1: General information on geraniol

Active substance (ISO Common Name)	Geraniol (No ISO common name)
IUPAC	(E) 3,7-dimethyl-2,6-octadien-1-ol
Chemical structure	
Molecular formula	C ₁₀ H ₁₈ O
Molar mass	154.25 g/mol
Chemical group	Plant derived - Plant oil (terpene)
Mode of action (if available)	Believed to disrupt the cell walls, membranes and organelles of micro-organisms
Systemic	Yes
Company (ies)	Eden Research plc *
Rapporteur Member State (RMS)	SP, co-RMS: GR (former RMS: UK)
Approval status	Approved Date of (01/12/2013)
Restriction	None
Review Report	SANCO/10579/2013 rev 3 17 May 2013
Current MRL regulation	Reg. (EU) 2015/896
Peer review of MRLs according to Article 12 of Reg No 396/2005 EC performed	None – not yet scheduled.
EFSA Journal : conclusion on the peer review	Yes - EFSA Journal 2012;10(11):2915
EFSA Journal: conclusion on article 12	No
Current MRL applications on intended uses	Commission Regulation (EU) 2015/896 of 11 June 2015 amending Annex IV to Regulation (EC) No 396/2005 of the European Parliament and of the Council as regards maximum residue levels for geraniol. Submission of MRL application to include geraniol in Annex IV of Regulation (EC) No 396/2005 was submitted at the same time as the AIR dossier on 28 th February 2021.

* Notifier in the EU process to whom the a.s. belongs

7.3.1 Stability of Residues (KCA 6.1)

7.3.1.1 Stability of residues during storage of samples

Available data

Table 7.3-2: Summary of stability data achieved at ≤ - 18°C (unless stated otherwise)

Matrix	Characteristics of the matrix	Acceptable Maximum Storage duration	Reference
Data relied on in EU			
Plant products			
Grapes – surface extractable residues	High water content	Not stable	DAR UK, 2012
Grapes – total residues	High water content	28 days*	DAR UK, 2012

Matrix	Characteristics of the matrix	Acceptable Maximum Storage duration	Reference
Animal Products			
Not required			
New data			
Plant products			
Grapes	High water content	278 days	Driss, 2021, S20-06526
Apples	High water content	161 days	Driss, 2021, S20-06527
Animal Products			
Not required			

* Study was ongoing at the time of the EU Review and final study demonstrates 12 months' storage stability

Conclusion on stability of residues during storage

Surface extractable residues are not stable under storage. Residues on whole grapes are stable for at least 12 months. Residues on homogenised whole grapes are stable for at least 278 days.

Residues on homogenised apples are stable for at least 161 days.

zRMS comments:

In the EFSA Journal 2012;10(11):2915 it is stated that EFSA was unable to conclude on the storage stability of residues of geraniol in grapes within 1 month of sample storage based on the submitted studies as the results were shown to be contradictory. A data gap was identified to provide new storage stability data to cover the maximum storage time interval of geraniol in the samples from the residue trials in order to consider these trials as acceptable.

Three new stability studies have been submitted by the Applicant in the framework of this application.

1. Brown, D. 2012; Report No. AF/12351/ED

Stability of geraniol residues in grapes (whole grapes) has been demonstrated for storage intervals of up to twelve months under frozen conditions.

2. Driss, F. 2021a; Report No. S20-06526

Stability of geraniol residues in grapes (homogenised grapes) has been demonstrated for storage intervals of up to 278 days under frozen conditions.

3. Driss, F. 2021b; Report No. S20-06527

Stability of geraniol residues in apples (homogenised apples) has been demonstrated for storage intervals of up to 161 days under frozen conditions.

The studies on the magnitude of residues are valid with regard to storage stability.

No additional data are required.

7.3.1.2 Stability of residues in sample extracts (KCA 6.1)

Available data

In the grape residue trials, the maximum duration between extraction and analysis was 7 days and stability of extracts was demonstrated for 7 days in study S20-06528 by Driss, 2021 – please refer to dRR Part B5 for further details.

In the apple residue trials, the maximum duration between extraction and analysis was 7 days and stability of extracts was demonstrated for 15 days in study S20-06529 by Driss, 2021 – please refer to dRR Part B5 for further details.

Conclusion on stability of residues in sample extracts

Stability of extracts is demonstrated.

zRMS comments:

Information submitted by Applicant is sufficient and accepted.
No further data are required.

7.3.2 Nature of residues in plants, livestock and processed commodities

7.3.2.1 Nature of residue in primary crops (KCA 6.2.1)

Mevalone was the representative formulation in the EU review of geraniol. The metabolism in plants was already addressed during the EU review and no additional studies are required.

Plant metabolism studies are not necessary, due to the natural occurrence of geraniol in a variety of fruits, vegetables, herbs and spices. Limited information from the published literature was submitted as part of the EU Review.

No new data submitted in the framework of this application.

zRMS comments:

EFSA concluded (EFSA, 2012) that plant metabolism studies were not submitted as geraniol occurs naturally in plants but information from the published literature was reported in the DAR. Data on the natural background levels of geraniol in grapes from retail samples were also submitted and gave indication of residue levels between <0.05-0.31 mg/kg. These data demonstrated that the use of geraniol as a plant protection product will not result in higher residue levels than the natural background levels recovered in grapes. No additional metabolism data are therefore required to conduct a reliable consumer risk assessment. This assessment should be reconsidered pending the acceptability of the residue trials.

No additional metabolism studies are necessary to support the intended uses for Mevalone.

Definition:

According to the EFSA Journal 2012;10(11):2915:

The residue definition for enforcement and for risk assessment for plant is not required.

Regulation (EU) 2015/896 included geraniol in Annex IV of the reg. (EC) 396/2005 as an active substance for which MRL are not required.

No further data are required to support the proposed uses.

7.3.2.2 Nature of residue in rotational crops (KCA 6.6.1)

Rotational crop studies are not relevant, since grapes and pome fruit are not grown in rotation.

No new data submitted in the framework of this application.

zRMS comments:

Information submitted by Applicant is sufficient and accepted.

No additional data are necessary to support the intended uses for Mevalone.

7.3.2.3 Nature of residues in processed commodities (KCA 6.5.1)

As residues of geraniol do not exceed the trigger values defined in Reg (EU) No 283/2013, studies on the nature of the residue in processed commodities are not required.

No new data submitted in the framework of this application.

zRMS comments:

Information submitted by Applicant is sufficient and accepted.

No additional data are necessary to support the intended uses for Mevalone.

7.3.2.4 Conclusion on the nature of residues in commodities of plant origin (KCA 6.7.1)

Studies on the nature of the residue in commodities of plant origin are not required.

zRMS comments:

According to the EFSA Journal 2012;10(11):2915:

Table 7.3-3: Summary of the nature of residues in commodities of plant origin

Endpoints	
Plant groups covered	Currently not required ⁽¹⁾
Rotational crops covered	Data not required.
Metabolism in rotational crops similar to metabolism in primary crops?	N/A
Processed commodities	Data not required
Residue pattern in processed commodities similar to pattern in raw commodities?	N/A
Plant residue definition for monitoring	Not required ⁽¹⁾
Plant residue definition for risk assessment	Not required ⁽¹⁾
Conversion factor from enforcement to RA	N/A

⁽¹⁾: Additional metabolism data and residue definitions not required pending the acceptability of the residue trials.

7.3.2.5 Nature of residues in livestock (KCA 6.2.2-6.2.5)

Mevalone was the representative formulation in the EU review of geraniol. The metabolism in livestock was already addressed during the EU review and no additional studies are required.

Livestock metabolism studies are not necessary, due to the natural occurrence of geraniol in a variety of fruits, vegetables, herbs and spices. Furthermore, livestock dietary intake calculations demonstrate that the dietary intake is below the trigger of 0.004 mg/kg bw/day.

No new data submitted in the framework of this application.

zRMS comments:

Information submitted by Applicant is sufficient and accepted. It is not required to investigate the metabolism of geraniol in livestock.

No additional data are necessary to support the intended uses for Mevalone.

7.3.2.6 Conclusion on the nature of residues in commodities of animal origin (KCA 6.7.1)

Studies on the nature of the residue in commodities of animal origin are not required.

zRMS comments:

According to the EFSA Journal 2012;10(11):2915:

Table 7.3-4: Summary of the nature of residues in commodities of animal origin

Endpoints	
Animals covered	Data not required.
Time needed to reach a plateau concentration	N/A

Animal residue definition for monitoring	Not required
Animal residue definition for risk assessment	Not required
Conversion factor	N/A
Metabolism in rat and ruminant similar	N/A
Fat soluble residue	N/A

7.3.3 Magnitude of residues in plants (KCA 6.3)

7.3.3.1 Summary of European data and new data supporting the intended uses

New studies on the magnitude of residue have been submitted by the applicant in the framework of this application. These studies are summarized in the Table below. The detailed assessment of these studies is presented in Appendix 2.

Table 7.3-5: Summary of EU reported and new data supporting the intended uses of Mevalone and conformity to existing MRL

Commodity	Source	Residue zone (N-EU, S-EU, EU, outside EU)	Evaluation GAP Residue levels (mg/kg) E = according to enforcement residue definition RA = according to risk assessment residue definition	STMR (mg/kg)	HR (mg/kg)	Unrounded OECD calculator MRL (mg/kg)	Current EU MRL (mg/kg) *	MRL compliance
Grapes	New trials	N-EU	Trials GAP: 4 x 4.0 L product/ha, PHI 7d, outdoor E & RA: <0.01, 0.03 [†] , 0.04 [†]					
	Overall supporting data for cGAP	N-EU	E & RA: <0.01, 0.03 [†] , 0.04 [†]	0.03 [†]	0.04 [†]	Geraniol is temporarily included into Annex IV to Regulation (EC) No. 396/2005 and therefore MRLs are not required.		
Pome fruit	New trials	N-EU	Trials GAP: 4 x 4.0 L product/ha, PHI 1d, outdoor E & RA: 3 x ND					
	Overall supporting data for cGAP	N-EU	E & RA: 3 x ND	ND	ND	Geraniol is temporarily included into Annex IV to Regulation (EC) No. 396/2005 and therefore MRLs are not required.		

* Geraniol is temporarily included into Annex IV to Regulation (EC) No. 396/2005

† The residue is the same as the natural background concentration. There is no increase over natural background concentrations.

ND: not detected (<0.003 mg/kg)

7.3.3.2 Conclusion on the magnitude of residues in plants

According to the available data, the intended uses on grapes and pome fruit are considered acceptable, for outdoor uses.

Geraniol is temporarily included into Annex IV to Regulation (EC) No. 396/2005 and therefore MRLs are not applicable. Natural background levels of geraniol were found in grapes and the trials demonstrated no increase over natural background concentrations. There were no detectable residues of geraniol in apples.

According to appendix D of EU guidelines, extrapolation to all of the pome fruit crop group is possible with trials on apples. Taking into account the no residue situation, 3 trials are considered to be sufficient for the extrapolation.

The uses are considered acceptable.

zRMS comments:

Mevalone was the representative formulation in the EU review of eugenol, geraniol and thymol. The residue trials in grapes were already addressed during the EU review of eugenol, geraniol and thymol. The GAP supported during the EU review was identical to the GAP supported in this submission. According to the EFSA Journal 2012;10(11):2915 *Residue trials on grapes were submitted where samples were analysed for geraniol in compliance with the representative use and achieving a LOQ of 0.05 mg/kg both in the treated and control samples.*

All data were considered adequate and thus the studies are not described in detail in this document.

Regulation (EU) 2015/896 included geraniol in Annex IV of the reg. (EC) 396/2005 as an active substance for which MRL are not required. Therefore this means that residue trials are not necessary.

Two new residue studies have been submitted by the Applicant in the framework of this application.

1. Determination of residues of eugenol, methyl eugenol, geraniol and thymol after 4 foliar applications of Mevalone (3AEY / EDN-004) to **grapevine**, 3 trials in N EU (3 x DEC) and 3 trials in S EU (3 x DEC), 2020 - Chadwick, G. 2021a Report No. S20-06337

Three residue trials were conducted on grape during 2020 in NEU. Four applications of Mevalone were applied at nominal rates of 264 g ai/ha thymol; 264 g ai/ha geraniol and 132 g ai/ha eugenol. Samples of ~~apple fruit~~ **grape** from the treated plots were taken by hand 0, 1, 2, 3 and 7 days after the final application.

Residues of geraniol in grapes samples taken 7 days after last application were \leq 0.01 mg/kg, 0.03 mg/kg, 0.04 mg/kg. The residue is the same as the natural background concentration. There is no increase over natural background concentrations.

2. Determination of residues of eugenol, methyl eugenol, geraniol and thymol after 4 foliar applications of Mevalone (3AEY / EDN-004) to **apple**, 3 trials in N EU (3 x DEC) and 3 trials in S EU (3 x DEC), 2020. Chadwick, G. 2021b Report No. S20-06361

Three residue trials were conducted on apples during 2020 in NEU. Four applications of Mevalone were applied at nominal rates of 264 g ai/ha thymol; 264 g ai/ha geraniol and 132 g ai/ha eugenol. Samples of apple fruit from the treated plots were taken by hand 0, 1, 2, 3 and 7 days after the final application.

There were no detectable residues of geraniol in apples samples (LOD = 0.003 mg/kg) **at 1 day after last application.**

In zero residue situation (no detectable residues (< limit of detection (LOD))), three trials shall be performed for major crops.

According to SANTE/2019/12752 trials on apples can be extrapolated to the whole of the pome fruit group.

No further data are required to support the proposed uses.

7.3.4 Magnitude of residues in livestock

7.3.4.1 Dietary burden calculation

To assess the livestock dietary burden of geraniol for EU livestock, the residues trials values (STMR and HR) supporting the cGAP for the raw agricultural commodities (RAC) for apples were used as input into the 'Animal model 2017'. Values used in the livestock dietary intake calculator are shown in the table below. The calculation is worst-case, since there were no detectable residues of geraniol in apples (LOD = 0.003 mg/kg), but the calculation is performed using the LOQ (0.01 mg/kg) as the input value.

It should be noted that in the case of apples, livestock are not typically fed the raw agricultural

commodity (RAC). Instead, livestock are routinely fed the processed by-products of apples (pomace). Usually, a processing factor would be applied to the residue value of the RAC, however, as the residues in the treated apples are less than the LOQ (<0.01 mg/kg), a processing factor does not need to be applied. The PF value was adjusted to 1 in the model. A conversion factor is not necessary.

Table 7.3-6: Input values for the dietary burden calculation (considering the uses under consideration)

Feed commodity	Median dietary burden		Maximum dietary burden	
	(mg/kg)	Comment	(mg/kg)	Comment
Apple pomace, wet	0.01	STMR	0.01	STMR

Table 7.3-7: Results of the dietary burden calculation

Animal species	Median dietary burden (mg/kg bw/d)	Maximum dietary burden (mg/kg bw/d)	Highest contributing commodity	Max dietary burden (mg/kg DM)	Trigger exceeded (Y/N)
Beef cattle*	0.0006	0.0006	Apple (pomace, wet)	0.03	N
Dairy cattle*	0.0005	0.0005	Apple (pomace, wet)	0.01	N
Ram/ewe	0.0004	0.0004	Apple (pomace, wet)	-	N
Lamb	0.0005	0.0005	Apple (pomace, wet)	-	N
Breeding swine	-	-	-	-	N
Finishing swine*	-	-	-	-	N
Broiler poultry	-	-	-	-	N
Layer poultry*	-	-	-	-	N
Turkey	-	-	-	-	N

* These categories correspond to those (formerly) assessed at EU level.

7.3.4.2 Livestock feeding studies (KCA 6.4.1-6.4.3)

Livestock feeding studies are not triggered.

No new data were submitted in the framework of this application.

zRMS comments:

Information presented by Applicant are sufficient.

The median and maximum dietary burdens were calculated for different groups of livestock using the EFSA Animal model 2017.

The calculated dietary burdens for geraniol for all groups of livestock were found to be below the trigger value of 0.004 mg/kg bw per day for all animal species. Further investigation of residues in animal commodities is therefore not required.

7.3.5 Magnitude of residues in processed commodities (Industrial Processing and/or Household Preparation) (KCA 6.5.2-6.5.3)

7.3.5.1 Available data for all crops under consideration

No new data were submitted in the framework of this application.

7.3.5.2 Conclusion on processing studies

Processing studies are not triggered.

zRMS comments:

Information submitted by Applicant is sufficient and accepted.

No additional data are necessary to support the intended uses for Mevalone.

7.3.6 Magnitude of residues in representative succeeding crops

Crops under evaluation are not expected to be grown in rotation. Further investigation of residues in rotational crops is therefore not required.

7.3.6.1 Field rotational crop studies (KCA 6.6.2)

No new data submitted in the framework of this application.

zRMS comments:

Information submitted by Applicant is sufficient and accepted.
No additional data are necessary to support the intended uses for Mevalone.

7.3.7 Other / special studies (KCA6.10, 6.10.1)

The available data for the active substance sufficiently address aspects of the residue situation that might arise from the use of Mevalone. Therefore, other special studies are not needed.

According to SANTE/11956/2016, grapes and pome fruit may be foraged by bees. For grapes the timing of application (BBCH 60-69) is such that bees may potentially forage the crop following application. However, the timing of application for pome fruit (BBCH 75-87) is after the flowering stage (BBCH 60-69) and therefore the bees will not forage blossoms following application of Mevalone. Furthermore, geraniol is not persistent and therefore potential exposure in subsequent seasons will not occur.

Exposure of bees to geraniol residues will be negligible following the proposed representative uses of Mevalone on grapes and pome fruit. In grapes, in one residue trial, residues were reported above the trigger of 0.05 mg/kg. However, geraniol is found to be naturally occurring in grapes and if the corresponding control residue level is subtracted, all residues due to plant protection product use are below the trigger. For apples, residue trials have demonstrated that geraniol levels in treated crops are below the trigger of 0.05 mg/kg on the day of application. Geraniol is temporarily included into Annex IV of Regulation (EC) No. 396/2005 meaning that MRLs are not necessary.

For both grapes and pome fruit, the timing of application is such that application may occur during the period April to September i.e. when in-field weeds or adjacent crops may be flowering. However, geraniol is found in a wide variety of plants. Since it is naturally occurring in the flowers of plants, it may be expected that bees will naturally be exposed to geraniol when foraging.

Geraniol is rapidly degraded in soil with a $DT_{90} < 3$ days (please refer to dRR Part B8 for further details). Therefore, residues in succeeding crops and weeds are not applicable. Furthermore, grapes and pome fruit are not grown in rotation.

Geraniol is not intended to be used in forestry and therefore potential exposure to honeydew from plant sucking insects is not relevant.

It is concluded that studies on the residue level in pollen and bee products are not required due to application not increasing residues above natural background concentrations for grapes or above the LOQ for apples. It is considered that MRLs are also not necessary for honey. Geraniol is naturally occurring in a wide variety of plants, on which bees forage, including many flowers to which bees are attracted. Therefore, any residues found in bee products, including honey could not necessarily be concluded to be due to plant protection product use.

zRMS comments:

Information submitted by Applicant is sufficient and accepted.
No other data are necessary to support the intended uses for Mevalone.

7.3.8 Estimation of exposure through diet and other means (KCA 6.9)

Toxicological reference values relevant for dietary risk assessment are reported in the summary of the evaluation (see 7.1.2).

As ARfD was not deemed necessary, acute risk assessment is not relevant.

7.3.8.1 Input values for the consumer risk assessment

Table 7.3-8: Input values for the consumer risk assessment

Commodity	Chronic risk assessment	
	Input value (mg/kg)	Comment
Grapes	0.01 *	Default value [#]
Apples	0.01 *	Default value [†]
All other commodities listed within Regulation (EU) 2018/62	0.01 *	Default value
All products of livestock origin (as listed within Regulation (EU) 2018/62)	0.01 *	Default value

[#] Residues in trials were all the same as the control samples and so a default value is used to represent residues from plant protection product use.

[†] There were no detectable residues (LOD = 0.003 mg/kg)

7.3.8.2 Conclusion on consumer risk assessment

Extensive calculation sheets are presented in Appendix 3. The calculation is worst-case, since there were no detectable residues of geraniol in apples (LOD = 0.003 mg/kg) and for grapes the residues were identical to natural background concentrations i.e. there is no increase in residues due to plant protection product use. The STMR/HR were therefore not used for the consumer risk assessment since there is no increase over natural background concentrations following the treatment. The calculation is performed using the default value of 0.01 mg/kg as the input value.

Table 7.3-9: Consumer risk assessment

TMDI (% ADI) according to EFSA PRIMo	0.2 % (based on NL, toddler)
IEDI (% ADI) according to EFSA PRIMo	Not required
IESTI (% ARfD) according to EFSA PRIMo	Not required
NTMDI (% ADI)	Not required
NEDI (% ADI)	Not required
NESTI (% ARfD)	Not required

The proposed uses of geraniol in the formulation Mevalone do not represent unacceptable chronic risks for the consumer.

zRMS comment:

EFSA (EFSA Journal 2012;10(11):2915) concluded that no consumer risk assessment with regard to the geraniol residues could be conducted since the toxicological database was insufficient to derive reference values.

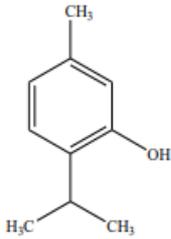
According to the Geraniol - SANCO/10579/2013 rev. 3, 17 May 2013:
 The following reference values have been derived as part of this evaluation:
 ADI: 0.5 mg/kg bw per day (Group ADI set by JECFA (2003))
 ARfD: Not necessary

Information given by the Applicant is sufficient. The proposed uses of geraniol in the product Mevalone do not represent unacceptable chronic risk for the consumer.
 No further data are required to support the proposed use.

7.4 Thymol

General data on thymol are summarized in the table below (last updated 2013/12/01)

Table 7.4-1: General information on thymol

Active substance (ISO Common Name)	Thymol (No ISO common name)
IUPAC	5-methyl-2-propan-2-yl-phenol
Chemical structure	
Molecular formula	C ₁₀ H ₁₄ O
Molar mass	150.22 g/mol
Chemical group	Plant derived - Plant oil (terpene)
Mode of action (if available)	Contact, GABAergic activity and also repels vertebrate pests by a non-toxic mode of action but is toxic to micro-organisms
Systemic	Yes
Company (ies)	Eden Research plc *
Rapporteur Member State (RMS)	SP, co-RMS: GR (former RMS: UK)
Approval status	Approved Date of (01/12/2013)
Restriction	None.
Review Report	SANCO/10581/2013 rev 3 17 May 2013
Current MRL regulation	Reg. (EU) 2015/896
Peer review of MRLs according to Article 12 of Reg No 396/2005 EC performed	None – not yet scheduled.
EFSA Journal : conclusion on the peer review	Yes - EFSA Journal 2012;10(11):2916
EFSA Journal: conclusion on article 12	No
Current MRL applications on intended uses	Commission Regulation (EU) 2015/896 of 11 June 2015 amending Annex IV to Regulation (EC) No 396/2005 of the European Parliament and of the Council as regards maximum residue levels for thymol. Submission of MRL application to include thymol in Annex IV of Regulation (EC) No 396/2005 was submitted at the same time as the AIR dossier on 28 th February 2021.

* Notifier in the EU process to whom the a.s. belongs

7.4.1 Stability of Residues (KCA 6.1)
7.4.1.1 Stability of residues during storage of samples
Available data

Table 7.4-2: Summary of stability data achieved at $\leq -18^{\circ}\text{C}$ (unless stated otherwise)

Matrix	Characteristics of the matrix	Acceptable Maximum Storage duration	Reference
Data relied on in EU			
Plant products			
Grapes – surface extractable residues	High water content	Not stable	DAR UK, 2012
Grapes – total residues	High water content	28 days*	DAR UK, 2012
Animal Products			
Not required			
New data			
Plant products			
Grapes	High water content	280 days	Driss, 2021, S20-06526
Apples	High water content	161 days	Driss, 2021, S20-06527
Animal Products			
Not required			

* Study was ongoing at the time of the EU Review and final study demonstrates 12 months' storage stability

Conclusion on stability of residues during storage

Surface extractable residues are not stable under storage. Residues on whole grapes are stable for at least 12 months. Residues on homogenised whole grapes are stable for at least 280 days. Residues on homogenised apples are stable for at least 161 days.

zRMS comments:

In the EFSA Journal 2012;10(11):2916 it is stated that EFSA was unable to conclude on the storage stability of residues of thymol in grapes within 1 month of sample storage based on the submitted studies as the results were shown to be contradictory. A data gap was identified to provide new storage stability data to cover the maximum storage time interval of thymol in the samples from the residue trials in order to consider whether these trials are acceptable.

Three new stability studies have been submitted by the Applicant in the framework of this application.

1. Brown, D. 2012; Report No. AF/12351/ED

Stability of thymol residues in grapes (whole grapes) has been demonstrated for storage intervals of up to twelve months under frozen conditions.

2. Driss, F. 2021a; Report No. S20-06526

Stability of thymol residues in grapes (homogenised grapes) has been demonstrated for storage intervals of up to 280 days under frozen conditions

3. Driss, F. 2021b; Report No. S20-06527

Stability of thymol residues in apples (homogenised apples) has been demonstrated for storage intervals of up to 161 days under frozen conditions.

The studies on the magnitude of residues are valid with regard to storage stability.

No additional data are required.

7.4.1.2 Stability of residues in sample extracts (KCA 6.1)

Available data

In the grape residue trials, the maximum duration between extraction and analysis was 7 days and stability of extracts was demonstrated for 7 days in study S20-06528 by Driss, 2021 – please refer to dRR Part B5 for further details.

In the apple residue trials, the maximum duration between extraction and analysis was 7 days and stability of extracts was demonstrated for 15 days in study S20-06529 by Driss, 2021 – please refer to dRR Part B5 for further details.

Conclusion on stability of residues in sample extracts

Stability of extracts is demonstrated.

zRMS comments:

Information submitted by Applicant is sufficient and accepted.
No further data are required.

7.4.2 Nature of residues in plants, livestock and processed commodities

7.4.2.1 Nature of residue in primary crops (KCA 6.2.1)

Mevalone was the representative formulation in the EU review of thymol. The metabolism in plants was already addressed during the EU review and no additional studies are required.

Plant metabolism studies are not necessary, due to the natural occurrence of thymol in a variety of fruits, vegetables, herbs and spices. Limited information from the published literature was submitted as part of the EU Review.

No new data submitted in the framework of this application.

zRMS comments:

EFSA concluded (EFSA, 2012) that Plant metabolism studies were not submitted as thymol occurs naturally in plants and very limited information from the published literature was reported in the DAR. Data on the natural background levels of thymol in grapes from retail samples were also submitted and gave indication of residue levels far below 0.05 mg/kg (validated LOQ of the method). EFSA is of the opinion that no metabolism data are required to conduct a reliable consumer risk assessment if the submitted residue trials are considered as acceptable. No additional metabolism studies are necessary to support the intended uses for Mevalone.

Definition:

According to the EFSA Journal 2012;10(11):2916:

The residue definition for enforcement and for risk assessment for plant is not required.

Regulation (EU) 2015/896 included thymol in Annex IV of the reg. (EC) 396/2005 as an active substance for which MRL are not required.

No further data are required to support the proposed uses.

7.4.2.2 Nature of residue in rotational crops (KCA 6.6.1)

Rotational crop studies are not relevant, since grapes and pome fruit are not grown in rotation.

No new data submitted in the framework of this application.

zRMS comments:

Information submitted by Applicant is sufficient and accepted.
No additional data are necessary to support the intended uses for Mevalone.

7.4.2.3 Nature of residues in processed commodities (KCA 6.5.1)

As residues of thymol do not exceed the trigger values defined in Reg (EU) No 283/2013, studies on the nature of the residue in processed commodities are not required.

No new data submitted in the framework of this application.

zRMS comments:

Information submitted by Applicant is sufficient and accepted.
No additional data are necessary to support the intended uses for Mevalone.

7.4.2.4 Conclusion on the nature of residues in commodities of plant origin (KCA 6.7.1)

Studies on the nature of the residue in commodities of plant origin are not required.

zRMS comments:

According to the EFSA Journal 2012;10(11):2916:

Table 7.4-3: Summary of the nature of residues in commodities of plant origin

Endpoints	
Plant groups covered	Data not required ⁽¹⁾
Rotational crops covered	Data not required.
Metabolism in rotational crops similar to metabolism in primary crops?	N/A
Processed commodities	Data not required
Residue pattern in processed commodities similar to pattern in raw commodities?	N/A
Plant residue definition for monitoring	Not required ⁽¹⁾
Plant residue definition for risk assessment	Not required ⁽¹⁾
Conversion factor from enforcement to RA	N/A

⁽¹⁾: Additional metabolism data and residue definitions not required pending the acceptability of the residue trials.

7.4.2.5 Nature of residues in livestock (KCA 6.2.2-6.2.5)

Mevalone was the representative formulation in the EU review of thymol. The metabolism in livestock was already addressed during the EU review and no additional studies are required.

Livestock metabolism studies are not necessary, due to the natural occurrence of thymol in a variety of fruits, vegetables, herbs and spices. Furthermore, livestock dietary intake calculations demonstrate that the dietary intake is below the trigger of 0.004 mg/kg bw/day.

No new data submitted in the framework of this application.

zRMS comments:

Information submitted by Applicant is sufficient and accepted. It is not required to investigate the metabolism of thymol in livestock.
No additional data are necessary to support the intended uses for Mevalone.

7.4.2.6 Conclusion on the nature of residues in commodities of animal origin (KCA 6.7.1)

Studies on the nature of the residue in commodities of animal origin are not required.

zRMS comments:

According to the EFSA Journal 2012;10(11):2916:

Table 7.4-4: Summary of the nature of residues in commodities of animal origin

Endpoints	
Animals covered	Data not required.
Time needed to reach a plateau concentration	N/A
Animal residue definition for monitoring	Not required
Animal residue definition for risk assessment	Not required
Conversion factor	N/A
Metabolism in rat and ruminant similar	N/A
Fat soluble residue	N/A

7.4.3 Magnitude of residues in plants (KCA 6.3)

7.4.3.1 Summary of European data and new data supporting the intended uses

New studies on the magnitude of residue have been submitted by the applicant in the framework of this application. These studies are summarized in the Table below. The detailed assessment of these studies is presented in Appendix 2.

Table 7.4-5: Summary of EU reported and new data supporting the intended uses of Mevalone and conformity to existing MRL

Commodity	Source	Residue zone (N-EU, S-EU, EU, outside EU)	Evaluation GAP Residue levels (mg/kg) E = according to enforcement residue definition RA = according to risk assessment residue definition	STMR (mg/kg)	HR (mg/kg)	Unrounded OECD calculator MRL (mg/kg)	Current EU MRL (mg/kg) *	MRL compliance
Grapes	New trials	N-EU	Trials GAP: 4 x 4.0 L product/ha, PHI 7d, outdoor E & RA: 2 x ND, <0.01 (thymol)					
	Overall supporting data for cGAP	N-EU	E & RA: 2 x ND, <0.01 (thymol)	ND (thymol)	<0.01 (thymol)	Thymol is temporarily included into Annex IV to Regulation (EC) No. 396/2005 and therefore MRLs are not required.		
Pome fruit	New trials	N-EU	Trials GAP: 4 x 4.0 L product/ha, PHI 1d, outdoor E & RA: ND, 2 x <0.01 (thymol)					
	Overall supporting data for cGAP	N-EU	E & RA: ND, 2 x <0.01 (thymol)	<0.01 (thymol)	<0.01 (thymol)	Thymol is temporarily included into Annex IV to Regulation (EC) No. 396/2005 and therefore MRLs are not required.		

* Thymol is temporarily included into Annex IV to Regulation (EC) No. 396/2005
 ND: not detected (<0.003 mg/kg)

7.4.3.2 Conclusion on the magnitude of residues in plants

According to the available data, the intended uses on grapes and pome fruit are considered acceptable, for outdoor uses.

Thymol temporarily included into Annex IV to Regulation (EC) No. 396/2005 and therefore MRLs are not applicable. Natural background levels of thymol were found in grapes and apples, but results were below the LOQ (0.01 mg/kg) for both the test and control samples. The trials demonstrated no increase over natural background concentrations.

According to appendix D of EU guidelines, extrapolation to all of the pome fruit crop group is possible with trials on apples. Taking into account no increase over natural concentrations, 3 trials are considered to be sufficient for the extrapolation.

The uses are considered acceptable.

zRMS comments:

Mevalone was the representative formulation in the EU review of eugenol, geraniol and thymol. The residue trials in grapes were already addressed during the EU review of eugenol, geraniol and thymol. The GAP supported during the EU review was identical to the GAP supported in this submission. According to the EFSA Journal 2012;10(11):2916 sufficient residue trials on grapes in compliance with the representative use were submitted and demonstrated that the use of thymol as a plant protection product did not result in residue levels higher than the LOQ of the analytical method (0.05 mg/kg) both in the treated and control samples.

All data were considered adequate and thus the studies are not described in detail in this document.

Regulation (EU) 2015/896 included thymol in Annex IV of the reg. (EC) 396/2005 as an active substance for which MRL are not required. Therefore this means that residue trials are not necessary.

Two new residue studies have been submitted by the Applicant in the framework of this application.

1. Determination of residues of eugenol, methyl eugenol, geraniol and thymol after 4 foliar applications of Mevalone (3AEY / EDN-004) to **grapevine**, 3 trials in N EU (3 x DEC) and 3 trials in S EU (3 x DEC), 2020 - Chadwick, G. 2021a Report No. S20-06337

Three residue trials were conducted on grape during 2020 in NEU. Four applications of Mevalone were applied at nominal rates of 264 g ai/ha thymol; 264 g ai/ha geraniol and 132 g ai/ha eugenol. Samples of ~~apple fruit~~ **grape** from the treated plots were taken by hand 0, 1, 2, 3 and 7 days after the final application.

Residues of thymol in grapes samples taken 7 days after last application were below LOQ (0.01 mg/kg). The trials demonstrated no increase over natural background concentrations.

2. Determination of residues of eugenol, methyl eugenol, geraniol and thymol after 4 foliar applications of Mevalone (3AEY / EDN-004) to **apple**, 3 trials in N EU (3 x DEC) and 3 trials in S EU (3 x DEC), 2020. Chadwick, G. 2021b Report No. S20-06361

Three residue trials were conducted on apples during 2020 in NEU. Four applications of Mevalone were applied at nominal rates of 264 g ai/ha thymol; 264 g ai/ha geraniol and 132 g ai/ha eugenol. Samples of apple fruit from the treated plots were taken by hand 0, 1, 2, 3 and 7 days after the final application.

Residues of thymol in apples samples were below LOQ (0.01 mg/kg) **at 1 day after last application**. The trials demonstrated no increase over natural background concentrations.

According to SANTE/2019/12752 trials on apples can be extrapolated to the whole of the pome fruit group.

No further data are required to support the proposed uses.

7.4.4 Magnitude of residues in livestock

7.4.4.1 Dietary burden calculation

To assess the livestock dietary burden of thymol for EU livestock, the residues trials values (STMR and HR) supporting the cGAP for renewal for the raw agricultural commodities (RAC) for apples were used as input into the 'Animal model 2017'. Values used in the livestock dietary intake calculator are shown in the table below. The calculation is worst-case, since there were no residues of thymol in apples at or above the LOQ, but the calculation is performed using the LOQ (0.01 mg/kg) as the input value.

It should be noted that in the case of apples, livestock are not typically fed the raw agricultural commodity (RAC). Instead, livestock are routinely fed the processed by-products of apples (pomace). Usually, a processing factor would be applied to the residue value of the RAC, however, as the residues in the treated apples are less than the LOQ (<0.01 mg/kg), a processing factor does not need to be applied. The PF value was adjusted to 1 in the model. A conversion factor is not necessary.

Table 7.4-6: Input values for the dietary burden calculation (considering the uses under consideration)

Feed commodity	Median dietary burden		Maximum dietary burden	
	(mg/kg)	Comment	(mg/kg)	Comment
Apple pomace, wet	0.01	STMR	0.01	STMR

Table 7.4-7: Results of the dietary burden calculation

Animal species	Median dietary burden (mg/kg bw/d)	Maximum dietary burden (mg/kg bw/d)	Highest contributing commodity	Max dietary burden (mg/kg DM)	Trigger exceeded (Y/N)
Beef cattle*	0.0006	0.0006	Apple (pomace, wet)	0.03	N
Dairy cattle*	0.0005	0.0005	Apple (pomace, wet)	0.01	N
Ram/ewe	0.0004	0.0004	Apple (pomace, wet)	-	N
Lamb	0.0005	0.0005	Apple (pomace, wet)	-	N
Breeding swine	-	-	-	-	N
Finishing swine*	-	-	-	-	N
Broiler poultry	-	-	-	-	N
Layer poultry*	-	-	-	-	N
Turkey	-	-	-	-	N

* These categories correspond to those (formerly) assessed at EU level.

7.4.4.2 Livestock feeding studies (KCA 6.4.1-6.4.3)

Livestock feeding studies are not triggered.

No new data were submitted in the framework of this application.

zRMS comments:

Information presented by Applicant are sufficient.

The median and maximum dietary burdens were calculated for different groups of livestock using the EFSA Animal model 2017.

The calculated dietary burdens for thymol for all groups of livestock were found to be below the trigger value of 0.004 mg/kg bw per day for all animal species. Further investigation of residues in animal commodities is therefore not required.

7.4.5 Magnitude of residues in processed commodities (Industrial Processing and/or Household Preparation) (KCA 6.5.2-6.5.3)

7.4.5.1 Available data for all crops under consideration

No new data were submitted in the framework of this application.

7.4.5.2 Conclusion on processing studies

Processing studies are not triggered.

zRMS comments:

Information submitted by Applicant is sufficient and accepted.

No additional data are necessary to support the intended uses for Mevalone.

7.4.6 Magnitude of residues in representative succeeding crops

Crops under evaluation are not expected to be grown in rotation. Further investigation of residues in rotational crops is therefore not required.

7.4.6.1 Field rotational crop studies (KCA 6.6.2)

No new data submitted in the framework of this application.

zRMS comments:

Information submitted by Applicant is sufficient and accepted.
No additional data are necessary to support the intended uses for Mevalone.

7.4.7 Other / special studies (KCA6.10, 6.10.1)

The available data for the active substance sufficiently address aspects of the residue situation that might arise from the use of Mevalone. Therefore, other special studies are not needed.

According to SANTE/11956/2016, grapes and pome fruit may be foraged by bees. For grapes the timing of application (BBCH 60-69) is such that bees may potentially forage the crop following application. However, the timing of application for pome fruit (BBCH 75-87) is after the flowering stage (BBCH 60-69) and therefore the bees will not forage blossoms following application of Mevalone. Furthermore, thymol is not persistent and therefore potential exposure in subsequent seasons will not occur.

Exposure of bees to thymol residues will be negligible following the proposed representative uses of Mevalone on grapes and pome fruit. Residue trials have demonstrated that thymol levels in treated crops are below the trigger of 0.05 mg/kg on the day of application. Thymol is temporarily included into Annex IV of Regulation (EC) No. 396/2005 meaning that MRLs are not necessary.

For both grapes and pome fruit, the timing of application is such that application may occur during the period April to September i.e. when in-field weeds or adjacent crops may be flowering. However, thymol is found in a wide variety of plants. Since it is naturally occurring in the flowers of plants, it may be expected that bees will naturally be exposed to thymol when foraging. Furthermore, products containing thymol may be used for the control of varroa mite on bees.

Thymol is rapidly degraded in soil with a $DT_{90} < 3$ days (please refer to dRR Part B8 for further details). Therefore, residues in succeeding crops and weeds are not applicable. Furthermore, grapes and pome fruit are not grown in rotation.

Thymol is not intended to be used in forestry and therefore potential exposure to honeydew from plant sucking insects is not relevant.

It is concluded that studies on the residue level in pollen and bee products are not required. Residues of thymol were always below the trigger of 0.05 mg/kg. It is considered that MRLs are also not necessary for honey. Thymol is naturally occurring in a wide variety of plants, on which bees forage, including many flowers to which bees are attracted. Therefore, any residues found in bee products, including honey could not necessarily be concluded to be due to plant protection product use.

zRMS comments:

Information submitted by Applicant is sufficient and accepted.
No other data are necessary to support the intended uses for Mevalone.

7.4.8 Estimation of exposure through diet and other means (KCA 6.9)

Toxicological reference values relevant for dietary risk assessment are reported in the summary of the evaluation (see 7.1.2).

7.4.8.1 Input values for the consumer risk assessment

Table 7.4-8: Input values for the consumer risk assessment

Commodity	Chronic risk assessment		Acute risk assessment	
	Input value (mg/kg)	Comment	Input value (mg/kg)	Comment
Grapes	0.01*	Default value [†]	0.01*	Default value [†]
Apples	0.01*	Default value [†]	0.01*	Default value [†]
All other commodities listed within Regulation (EU) 2018/62	0.01*	Default value	0.01*	Default value
All products of livestock origin (as listed within Regulation (EU) 2018/62)	0.01*	Default value	0.01*	Default value

[†] Residues in all residue trials were <LOQ (0.01 mg/kg)

7.4.8.2 Conclusion on consumer risk assessment

Extensive calculation sheets are presented in Appendix 3. The calculation is worst-case, there were no residues of thymol in grapes or apples at or above the LOQ, but the calculation is performed using the LOQ (0.01 mg/kg) as the input value.

Table 7.4-9: Consumer risk assessment

TMDI (% ADI) according to EFSA PRIMo	4% (based on NL, toddler)
IEDI (% ADI) according to EFSA PRIMo	Not required
UESTI (% ARfD) according to EFSA PRIMo	2% (based on potatoes)
NTMDI (% ADI)	Not required
NEDI (% ADI)	Not required
NESTI (% ARfD)	Not required

The proposed uses of thymol in the formulation Mevalone do not represent unacceptable acute or chronic risks for the consumer.

zRMS comment:

EFSA (EFSA Journal 2012;10(11):2916) concluded that the consumer risk assessment could not be conducted since the toxicological database was insufficient to derive reference values.

According to the Thymol - SANCO/10581/2013 rev. 3, 17 May 2013:
 The following reference values have been derived as part of this evaluation:
 ADI: 0.03 mg/kg bw per day (Group ADI set by JECFA (2003))
 ARfD: 0.08 mg/kg bw

Information given by the Applicant is sufficient. The proposed uses of thymol in the product Mevalone do not represent unacceptable chronic and acute risks for the consumer.

No further data are required to support the proposed use.

7.5 Combined exposure and risk assessment

From a scientific point of view, it is regarded necessary to take into account potential combination effects. However, the evaluation of cumulative or synergistic effects as requested by Art. 4 (3b) of Regulation (EC) No. 1107/2009 should only be performed when harmonised “scientific methods accepted by the

Authority to assess such effects are available.”

Currently, no EU-harmonized guidance is available on the risk assessment of combined exposure to multiple active substances; this approach is not mandatory at EU level.

7.5.1 Acute consumer risk assessment from combined exposure

The product is a mixture of three active substances, but for only one of them has an acute reference dose been allocated and therefore combined exposure cannot be assessed.

7.5.2 Chronic consumer risk assessment from combined exposure

The uses under consideration provide only a minor contribution to the overall chronic exposure of consumers to pesticide residues. The issue requires a more universal consideration and possibly the generic usage of monitoring data. A harmonised approach is not yet available, and currently no specific consideration is warranted in the scope of this evaluation.

zRMS comments:

From a scientific point of view it is regarded necessary to take into account potential combination effects. However, the evaluation of cumulative or synergistic effects as requested by Art. 4 (3b) of Regulation (EC) No. 1107/2009 should only be performed when harmonised “scientific methods accepted by the Authority to assess such effects are available.”

Currently, no EU-harmonized guidance is available on the risk assessment of combined exposure to multiple active substances; this approach is not mandatory at EU level.

7.6 References

United Kingdom, 2011. Draft Assessment Report (DAR) on the active substance eugenol prepared by the rapporteur Member State the United Kingdom in the framework of Directive 91/414/EEC, June 2011.

United Kingdom, 2012. Final Addendum to Draft Assessment Report on eugenol, compiled by EFSA, June 2012.

EFSA (European Food Safety Authority), 2012a. Conclusion on the peer review of the pesticide risk assessment of the active substance thymol. *EFSA Journal* 2012;10(11):2916.

DOI:10.2903/j.efsa.2012.2916. Available online: www.efsa.europa.eu/efsajournal

EFSA (European Food Safety Authority), 2012b. Conclusion on the peer review of the pesticide risk assessment of the active substance geraniol. *EFSA Journal* 2012;10(11):2915.

DOI: 10.2903/j.efsa.2012.2915. Available online: www.efsa.europa.eu/efsajournal

EFSA (European Food Safety Authority), 2012c. Conclusion on the peer review of the pesticide risk assessment of the active substance eugenol. *EFSA Journal* 2012;10(11):2914.

DOI: 10.2903/j.efsa.2012.2914. Available online: www.efsa.europa.eu/efsajournal

Appendix 1 Lists of data considered in support of the evaluation

List of data submitted by the applicant and relied on

These studies have also been submitted within the AIR dossier submitted 28th February 2021 (RMS: Spain).

Data point	Author(s)	Year	Title Company Report No. Source (where different from company) GLP or GEP status Published or not	Vertebrate study Y/N	Owner
KCP 8.1/01	Brown, D.	2012	To determine the stability of thymol, eugenol and geraniol residues in grape specimens following storage at ca. -18°C for 0, 1, 3, 7, 14 and 28 days, 3, 6 and 12 months after treatment with 3AEY (6.4% w/w geraniol, 3.2% w/w eugenol and 6.4% w/w thymol) Eurofins Agrosience Services Report No. AF/12351/ED GLP Unpublished	N	Eden Research plc
KCP 8.1/02	Driss, F.	2021a	Storage Stability of Eugenol, Geraniol, Thymol and Methyl Eugenol in Grape under Deep Freeze Conditions Eurofins Agrosience Services Report No. S20-06526 GLP Unpublished	N	Eden Research plc
KCP 8.1/03	Driss, F.	2021b	Storage Stability of Eugenol, Methyl Eugenol, Geraniol and Thymol in Apple under Deep Freeze Conditions Eurofins Agrosience Services Report No. S20-06527 GLP Unpublished	N	Eden Research plc
KCP 8.3/01	Chadwick, G.	2021a	Determination of residues of eugenol, methyl eugenol, geraniol and thymol after 4 foliar applications of Mevalone (3AEY / EDN-004) to grapevine, 3 trials in N EU (3 x DEC) and 3 trials in S EU (3 x DEC), 2020 Eurofins Agrosience Services Report No. S20-06337 GLP Unpublished	N	Eden Research plc
KCP 8.3/02	Chadwick, G.	2021b	Determination of residues of eugenol, methyl eugenol, geraniol and thymol after 4 foliar applications of Mevalone (3AEY / EDN-004) to apple, 3 trials in N EU (3 x DEC) and 3 trials in S EU (3 x DEC), 2020 Eurofins Agrosience Services Report No. S20-06361 GLP Unpublished	N	Eden Research plc

List of data submitted or referred to by the applicant and relied on, but already evaluated at EU peer review

Data point	Author(s)	Year	Title Company Report No. Source (where different from company) GLP or GEP status Published or not	Vertebrate study Y/N	Owner
-	-	-	-	-	-

List of data submitted by the applicant and not relied on

Data point	Author(s)	Year	Title Company Report No. Source (where different from company) GLP or GEP status Published or not	Vertebrate study Y/N	Owner
-	-	-	-	-	-

List of data relied on and not submitted by the applicant but necessary for evaluation

Data point	Author(s)	Year	Title Company Report No. Source (where different from company) GLP or GEP status Published or not	Vertebrate study Y/N	Owner
-	-	-	-	-	-

Appendix 2 Detailed evaluation of the additional studies relied upon

A 2.1.1 Stability of residues

A 2.1.1.1 Stability of residues during storage of samples

A 2.1.1.1.1 Storage stability of residues in plant products

A 2.1.1.1.1.1 Study 1

The following study was considered in the original EU Review of eugenol, geraniol and thymol but only the one-month interim report was submitted. Now the final 1-year report is available and the one-year report has not previously been evaluated at EU level.

It is important to note that in this storage stability study considers the stability of total residues in grapes. Whole grapes were fortified and homogenised prior to extraction and hence the stability of total residues was studied. This is different to the study which was fully evaluated at EU level by Brown (2007), where only the surface residues were extracted. Surface extractable residues are not relevant to this submission, since total fruit residues are determined in the residue trials. Total residues were found to be stable to storage, unlike surface extracted residues.

Comments of zRMS:	Stability of thymol, eugenol and geraniol residues in grapes (whole grapes) has been demonstrated for storage intervals of up to twelve months under frozen conditions. The study is acceptable.
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Reference: KCP 8.1/01

Report To determine the stability of thymol, eugenol and geraniol residues in grape specimens following storage at ca. -18° for 0, 1, 3, 7, 14 and 28 days, 3, 6 and 12 months after treatment with 3AEY (6.4% w/w geraniol, 3.2% w/w eugenol and 6.4% w/w thymol), Brown, D. 2012 Report No. AF/12351/ED

Guideline(s): Yes
Conducted in accordance with Commission Directive 96/68/EC (amending Council Directive 91/414/EC)

Deviations: No

GLP: Yes

Acceptability: Yes

Materials and methods

500 g samples of destalked, non-treated grapes were fortified with 3AEY CS formulation (3.2 % w/w eugenol, 6.4 % w/w geraniol, and 6.4 % w/w thymol nominal), such that samples were fortified at 1 mg/kg for geraniol and thymol, and 0.5 mg/kg for eugenol. At intervals of 0, 1, 3, 7, 14 and 27 days, 3, 6 and 12 months, stored samples were analysed for residues of eugenol, geraniol and thymol. Additional samples of unfortified grapes were stored frozen to be used as quality control samples on the day of each analysis. On Day 0, samples were not placed into freezer storage, but analysed immediately following fortification.

Residues of eugenol, geraniol and thymol were extracted from whole grapes by homogenising the whole sample with acetone followed by centrifugation to separate the phases. A known volume of the supernatant was then passed through a 0.45 µm PTFE filter. Final determination of the surface residue extract was performed by GC MS. Samples were analysed simultaneously for eugenol, geraniol and thymol using Agrisearch Method 'Thymol, Eugenol, Geraniol/Crops/DB/06/2'. At each time point, stored samples were analysed in triplicate in addition to two procedural recovery samples fortified on the day of analysis (at 1 mg/kg for geraniol and thymol, and 0.5 mg/kg for eugenol) and a single unfortified sample to act as a control.

Results and discussions

Samples were analysed simultaneously for eugenol, geraniol and thymol using Agrisearch Method ‘Thymol, Eugenol, Geraniol/Crops/DB/06/2’. The GC MS analytical method for the determination of eugenol, geraniol and thymol in grapes was validated with regards to specificity, linearity, accuracy and precision in the separate study AF/10728/ED by Bailey, 2007 (please refer to dRR Part B5 for further details).

Within this study the analytical calibration was performed over the range of 0.05 to 1.0 µg/mL for eugenol, geraniol and thymol. The response was shown to be linear with correlation coefficients >0.998. Procedural recoveries for this study are reported in the table below.

Table A 1: Summary of concurrent recoveries of eugenol, geraniol and thymol from whole grapes

Matrix	Spike level (mg/kg)	Storage Interval (days)	Sample size (n)	Individual procedural recoveries (%) *	Mean ± std dev
Eugenol					
Whole grapes	0.5	0	2	92	92
				91	
		1	2	73	81
				89	
		3	2	92	88
				84	
		7	2	84	82
				80	
		14	2	87	86
				85	
		27	2	100	104
				107	
		3 months	2	94	90
				85	
6 months	2	109	107		
		104			
12 months	2	71	70		
		69			
Overall		18	-	89 ± 13	
Geraniol					
Whole grapes	1.0	0	2	107	103
				99	
		1	2	103	90
				76	
		3	2	105	104
				102	
		7	2	99	100
				101	
		14	2	96	101
				105	

Matrix	Spike level (mg/kg)	Storage Interval (days)	Sample size (n)	Individual procedural recoveries (%) *	Mean ± std dev
		27	2	103	108
				113	
		3 months	2	85	90
				94	
		6 months	2	98	102
				105	
		12 months	2	96	99
				102	
		Overall	18	-	99 ± 8
		Thymol			
Whole grapes	1.0	0	2	84	80
				76	
		1	2	81	85
				88	
		3	2	80	82
				83	
		7	2	74	75
				76	
		14	2	95	86
				77	
		27	2	91	90
				89	
		3 months	2	80	86
				91	
6 months	2	101	96		
		90			
12 months	2	77	76		
		74			
Overall	18	-	84 ± 9		

*Corrected for recovery in untreated specimen

Table A 2: Stability of eugenol, geraniol and thymol residues in whole grapes following storage at -18°C

Matrix	Spike level (mg/kg)	Storage interval (days)	Individual recovered residues (mg/kg)	Individual recoveries (%) *
Eugenol				
Whole grapes	0.5	0	0.378, 0.452, 0.428	70, 84, 80
		1	0.409, 0.430, 0.379	81, 85, 75
		3	0.394, 0.375, 0.412	79, 75, 82
		7	0.456, 0.424, 0.410	91, 85, 82
		14	0.424, 0.503, 0.413	85, 101, 83

Matrix	Spike level (mg/kg)	Storage interval (days)	Individual recovered residues (mg/kg)	Individual recoveries (%) [*]
		27	0.443, 0.425, 0.431	89, 85, 86
		3 months	0.511, 0.473, 0.483	102, 95, 97
		6 months	0.437, 0.506, 0.469	87, 101, 94
		12 months	0.346, 0.362, 0.355	69, 72, 71
Geraniol				
Whole grapes	1.0	0	0.993, 1.074, 0.988	99, 107, 99
		1	0.930, 0.675, 0.857	93, 68, 86
		3	0.977, 1.047, 1.022	98, 105, 100
		7	0.987, 0.997, 0.913	99, 100, 91
		14	1.062, 1.098, 0.823	106, 110, 82
		27	1.087, 0.940, 1.080	109, 94, 108
		3 months	0.887, 0.819, 0.877	89, 82, 88
		6 months	1.005, 0.944, 0.993	100, 94, 99
		12 months	0.953, 0.949, 0.996	95, 95, 100
Thymol				
Whole grapes	1.0	0	0.786, 0.843, 0.761	79, 84, 76
		1	0.702, 0.711, 0.824	70, 71, 82
		3	0.947, 1.042, 0.936	79, 88, 77
		7	0.942, 0.894, 0.922	84, 80, 82
		14	0.850, 0.915, 0.797	85, 91, 80
		27	0.765, 0.791, 0.772	77, 79, 77
		3 months	0.996, 0.903, 0.966	100, 90, 97
		6 months	0.947, 0.869, 0.930	95, 87, 93
		12 months	0.813, 0.783, 0.784	81, 78, 78

^{*}Corrected for recovery in untreated specimen

Conclusion

Under these conditions, residues of eugenol, geraniol and thymol on whole grapes were stable for at least 12 months, with overall means 71, 97 and 79 % of fortified eugenol, geraniol and thymol, respectively recovered at 1 year.

This study is considered acceptable and satisfies the guideline requirements for residue storage stability (OECD test guideline 506, 2007).

A 2.1.1.1.1.2 Study 2

This study has also been submitted within the AIR dossier submitted 28th February 2021 (RMS: Spain) and updated December 2021.

Comments of zRMS:	Stability of thymol residues in grapes (homogenised grapes) has been demonstrated for storage intervals of up to 280 days under frozen conditions, stability of geraniol and methyleugenol residues in grapes (homogenised grapes) has been demonstrated for storage intervals of up to 278 days under frozen conditions, stability of eugenol residues in grapes has been demonstrated for storage intervals of up to 154 days under frozen conditions. The study is acceptable.
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	<p>Remark: At each time point, stored samples were analysed in duplicate (triplicate on day 0). Procedural recoveries for this study in the tables below are reported for one sample only at each time point (except 0 days). The mean recovery at each time point cannot be derived from this data (except 0 days).</p>
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Reference:	KCP 8.1/02
Report	Storage Stability of Eugenol, Geraniol, Thymol and Methyl Eugenol in Grape under Deep Freeze Conditions, Driss, F. 2021a Report No. S20-06526
Guideline(s):	Yes OECD 506 SANTE/2020/12830, rev.1
Deviations:	No
GLP:	Yes
Acceptability:	Yes

Materials and methods

10 g samples of destalked, non-treated homogenised grapes were fortified with eugenol, geraniol, thymol and methyleugenol at a rate of 0.1 mg/kg. Samples were placed directly into frozen storage at $\leq -18^{\circ}\text{C}$ immediately after fortification. At intervals of 0, 43, 111, 154 and 278 days stored samples were analysed for residues of eugenol, geraniol, thymol and methyleugenol.

Residues of eugenol, geraniol, thymol and methyleugenol were extracted from homogenised grapes with acetonitrile. A salt mixture containing magnesium sulphate, sodium chloride and sodium citrate was added and the extract was shaken. After centrifugation, the acetonitrile phase was cleaned by adding primary secondary amine and aliquots were then evaporated after the addition of toluene. The extract was reconstituted with acetonitrile prior to injection on the GC-MS. The method was fully validated in the separate study S20-06528 by Driss, 2021 (please refer to dRR Part B5 for further details). At each time point, stored samples were analysed in duplicate (triplicate on Day 0) in addition to a procedural recovery sample fortified on the day of analysis at 0.1 mg/kg and a single unfortified sample to act as a control.

Results and discussions

Samples were analysed for eugenol, geraniol, thymol and methyleugenol. The GC-MS analytical method for the determination of eugenol, geraniol and thymol in grapes was validated with regards to specificity, linearity, accuracy and precision in the separate study S20-06528 by Driss, 2021 (please refer to dRR Part B5 for further details).

Within this study the analytical calibration was performed over the range of 0.0025 to 0.5 mg/kg for eugenol, geraniol, thymol and methyleugenol. The response was shown to be linear with correlation coefficients >0.995 and the coefficients of determination were >0.99 . Procedural recoveries for this study are reported in the table below.

The maximum storage interval of final sample extracts at typically 1°C to 10°C from extraction until injection to GC-MS was 6 days. The stability of the analytes in the final extracts of grapes upon storage at typically 1°C to 10°C for 7 days was demonstrated in S20-06528 by Driss, 2021 (please refer to dRR Part B5 for further details).

Table A 3: Summary of procedural recoveries from grapes

Matrix	Time point (days)	Fortification level (mg/kg)	Recovery (%)	Mean recoveries (%)
Eugenol				
Homogenised grapes	0	0.1	85	82
			81	

Matrix	Time point (days)	Fortification level (mg/kg)	Recovery (%)	Mean recoveries (%)
			79	
	43		91	91
	111		105	105
	154		110	110
	278		99	99
Geraniol				
Homogenised grapes	0	0.1	100	99
			97	
			101	
	43		96	96
	111		100	100
	154		110	110
278	109	109		
Thymol				
Homogenised grapes	0	0.1	87	90
			98	
			84	
	43		92	92
	111		107	107
	154		107	107
	278		109	109
280	105	105		
Methyleugenol				
Homogenised grapes	0	0.1	73	75
			73	
			79	
	43		90	90
	111		103	103
	154		108	108
278	103	103		

Table A 4: Stability of eugenol, geraniol and thymol residues in grapes following storage at -18°C

Storage Period (days)	Percentage of analyte found relative to the nominal fortification level (%)		Percentage recovered corrected for the (mean) procedural recovery of the individual date of extraction ^a	Percentage recovered relative to the mean percentage recovered at Day 0 ^a
	Single Values (%) ^b	Mean (%) ^a ± RSD (%)		
Eugenol at nominal fortification level of 0.1 mg/kg (10x LOQ)				
0	85, 81, 79	82 ± 3.7	-	-
43	86, 72	79	86	97
111	64, 70	67	64	82
154	79, 68	74	67	90
278	60, 58	59	60	73
Geraniol at nominal fortification level of 0.1 mg/kg (10x LOQ)				
0	100, 97, 101	99 ± 2.1	-	-
43	117, 84	101	105	101
111	62, 73	67	67	68
154	111, 108	109	100	110
278	76, 75	76	69	76
Thymol at nominal fortification level of 0.1 mg/kg (10x LOQ)				
0	87, 98, 84	90 ± 7.8	-	-
43	82, 104	93	101	104
111	69, 77	73	68	81
154	90, 75	83	77	92
278	20 ^c , 78	78	72	87
280	92, 88	90	86	100
Methyleugenol at nominal fortification level of 0.1 mg/kg (10x LOQ)				
0	73, 73, 79	75 ± 4.6	-	-
43	98, 70	84	93	112
111	86, 80	83	81	111
154	80, 106	93	86	124
278	90, 74	82	80	110

^a calculated from unrounded values

- ^b not corrected for procedural recoveries
- ^c the 20% result is excluded, which is clearly an erroneous result

Conclusion

Under these conditions, residues of geraniol, thymol and methyleugenol on homogenised grapes were stable for at least 278 days, with 76, 78 and 82 % of the nominal fortified amount of geraniol, thymol and methyleugenol respectively recovered at 278 days. Residues of eugenol on homogenised grapes were stable for at least 154 days, with 74 % of the nominal fortified amount recovered.

This study is considered acceptable and satisfies the guideline requirements for residue storage stability (OECD test guideline 506, 2007).

A 2.1.1.1.1.3 Study 3

This study has also been submitted within the AIR dossier submitted 28th February 2021 (RMS: Spain) and updated December 2021.

Comments of zRMS:	<p>For eugenol the average amount of analyte recovered relative to the nominal value was \leq 70% at 161 days and subsequent testing intervals, which can't be seen as criterion for sufficient storage stability. Stability was demonstrated for eugenol in homogenates of apples upon storage at \leq -18 °C for 112 days.</p> <p>For geraniol and thymol the average amount of analyte recovered relative to the nominal value was \leq 70% at 285 and 287 days, which can't be seen as criterion for sufficient storage stability. Stability was demonstrated for geraniol and thymol in homogenates of apples upon storage at \leq -18 °C for 161 days.</p> <p>For methyl-eugenol the average amount of analyte recovered relative to the nominal value was \geq 70% at all testing intervals, which can be seen as criterion for sufficient storage stability. Stability was demonstrated for methyl-eugenol in homogenates of apples upon storage at \leq -18 °C for 285 days.</p> <p>Conclusion Stability was demonstrated for eugenol in homogenates of apples upon storage at \leq -18 °C for 112 days. Stability was demonstrated for geraniol and thymol in homogenates of apples upon storage at \leq -18 °C for 161 days. Stability was demonstrated for methyl-eugenol in homogenates of apples upon storage at \leq -18 °C for 285 days.</p> <p>In the residue study (Chadwick, G. 2021b, Report No. S20-06361) in NEU trials, residues of eugenol, methyl-eugenol, geraniol and thymol in apples were analysed within the demonstrated stability period. The study is acceptable.</p> <p>Remark: Storage samples allow assessment of storage stability, while procedural recoveries demonstrate the performance of the analytical method. At each time point, stored samples were analysed in duplicate (triplicate on day 0). Procedural recoveries for this study in the tables below are reported for one sample only at each time point (except 0 days). The mean recovery at each time point cannot be derived from this data (except 0 days).</p>
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Reference:	KCP 8.1/03
Report	Storage Stability of Eugenol, Methyl Eugenol, Geraniol and Thymol in Apple under Deep Freeze Conditions, Driss, F. 2021b Report No. S20-06527
Guideline(s):	Yes OECD 506

SANTE/2020/12830, rev.1

Deviations: No
GLP: Yes
Acceptability: Yes

Materials and methods

10 g samples of destemmed, non-treated homogenised apples were fortified with eugenol, geraniol, thymol and methyleugenol at a rate of 0.1 mg/kg. Samples were placed directly into frozen storage at $\leq -18^{\circ}\text{C}$ immediately after fortification. At intervals of 0, 30, 112, 161, 202 (eugenol only), 285 and 287 (except methyleugenol) days stored samples were analysed for residues of eugenol, geraniol, thymol and methyleugenol.

Residues of eugenol, geraniol, thymol and methyleugenol were extracted from homogenised apples with acetonitrile. A salt mixture containing magnesium sulphate, sodium chloride and sodium citrate was added and the extract was shaken. After centrifugation, the acetonitrile phase was cleaned by adding primary secondary amine and aliquots were then evaporated after the addition of toluene. The extract was reconstituted with acetonitrile prior to injection on the GC-MS. The method was fully validated in the separate study S20-06529 by Driss, 2021 (please refer to dRR Part B5 for further details). At each time point, stored samples were analysed in duplicate (triplicate on Day 0) in addition to a procedural recovery sample fortified on the day of analysis at 0.1 mg/kg and a single unfortified sample to act as a control.

Results and discussions

Samples were analysed for eugenol, geraniol, thymol and methyleugenol. The GC-MS analytical method for the determination of eugenol, geraniol and thymol in apples was validated with regards to specificity, linearity, accuracy and precision in the separate study S20-06529 by Driss, 2021 (please refer to dRR Part B5 for further details).

Within this study the analytical calibration was performed over the range of 0.0025 to 0.5 mg/kg for eugenol, geraniol, thymol and methyleugenol. The response was shown to be linear with correlation coefficients ≥ 0.995 and the coefficients of determination were ≥ 0.99 . Procedural recoveries for this study are reported in the table below.

The maximum storage interval of final sample extracts at typically 1°C to 10°C from extraction until injection to GC-MS was 7 days. The stability of the analytes in the final extracts of apples upon storage at typically 1°C to 10°C for 15 days was demonstrated in S20-06529 by Driss, 2021 (please refer to dRR Part B5 for further details).

Table A 5: Summary of procedural recoveries from apples

Matrix	Time point (days)	Fortification level (mg/kg)	Recovery (%)	Mean recoveries (%)
Eugenol				
Homogenised apples	0	0.1	79	85
			91	
	30		83	
	112		109	109
	161		91	91
	202		96	96
	285		114*	114
287	101	101		
			114*	114
Geraniol				
Homogenised apples	0	0.1	87	80
			67	
	30		87	
	112		117*	117
	161		102	102
	285		99	99
	287		106 105	106
		118 121*	118	
Thymol				
Homogenised apples	0	0.1	90	89
			91	
	30		87	
	112		118*	118
	161		81	81
	285		109	109
	287		110 108	110
		124 123*	124	
Methyleugenol				
Homogenised apples	0	0.1	76	83
			91	
	30		82	
	112		116*	116
	161		91	91
	285		95	95
				105

*Result for fresh recoveries is out of criteria therefore accepted as the trend of the stability in samples is evaluated.

Table A 6: Stability of eugenol, geraniol and thymol residues in apples following storage at -18°C

Storage Period (days)	Percentage of analyte found relative to the nominal fortification level (%)		Percentage recovered corrected for the (mean) procedural recovery of the individual date of extraction ^a	Percentage recovered relative to the mean percentage recovered at Day 0 ^a
	Single Values (%) ^b	Mean (%) ^a ± RSD (%)		
Eugenol at nominal fortification level of 0.1 mg/kg (10x LOQ)				
0	79, 91, 83	85 ± 7.3	-	-
30	90, 70	80	73	94
112	92, 87	89	98	106
161	49, 62	55	57	65
202	56, 52	54	47	64
285	15, 36	26	23 26	30
287	29, 60	45	39	53
Geraniol at nominal fortification level of 0.1 mg/kg (10x LOQ)				
0	87, 67, 87	80 ± 14.6	-	-
30	95, 106	100	86	125
112	117, 125	121**	119	151
161	84, 100	92	93	115
285	13 10 12, 9	11	11 10	11 13
287	33, 26	29 30	24	36 37
Thymol at nominal fortification level of 0.1 mg/kg (10x LOQ)				
0	90, 91, 87	89 ± 2.3	-	-
30	103, 88	95	81	107

112	71, 63	67	82	75
161	78, 83	81	74	90
285	44, 49 42, 48	47 45	42	52 50
287	62, 48 61, 47	55 54	44	61 60
Methyleugenol at nominal fortification level of 0.1 mg/kg (10x LOQ)				
0	76, 91, 82	83 ± 9.3	-	-
30	93, 113	103	89	124
112	101, 101	101	111	122
161	86, 104	95	100	114
285	86, 72	79	75	95

^a calculated from unrounded values

^b not corrected for procedural recoveries

** Result for storage sample of geraniol at 112 days is accepted at 121% as the trend of the stability in samples is evaluated, results at 30 and 161 days are accepted and within the range 70-110%.

Conclusion

Under these conditions, residues of geraniol and thymol on homogenised apples were stable for at least 161 days, with 92 and 81 % of nominal fortified amount of geraniol and thymol, respectively recovered at 161 days. For eugenol, stability was demonstrated for 112 days, with 89 % of the nominal fortified amount of eugenol recovered at 112 days. For methyleugenol, stability was demonstrated for 285 days, with 79 % of the nominal fortified amount of eugenol recovered at 285 days.

This study is considered acceptable and satisfies the guideline requirements for residue storage stability (OECD test guideline 506, 2007).

Discussion

The storage stability study on apples demonstrates that eugenol is stable for a period of at least 112 days (percent recovery compared to nominal spike = 89% after 112 days). However, at 161 days the recovery of eugenol is below the 70% trigger, at 55% relative to the nominal fortification level.

The storage duration prior to analysis for eugenol in apples in study S20-06361 is generally less than 112 days. However, in some cases the duration is longer than 112 days. The exceedances are detailed in the table below.

Trial	Sample	Storage duration (days)
S20-06361-04 (Spain)	005A	114
S20-06361-05 (France)	001A	118
	002A	119
	003A	118
	004A	117
	005A	116
S20-06361-06 (Italy)	001A	113

For Spain and Italy, the duration of storage was two and one days, respectively longer than the demonstrated stability period. This exceedance was only in 2 samples, representing 3DAA in the Spanish trial and the untreated control sample in the Italian trial.

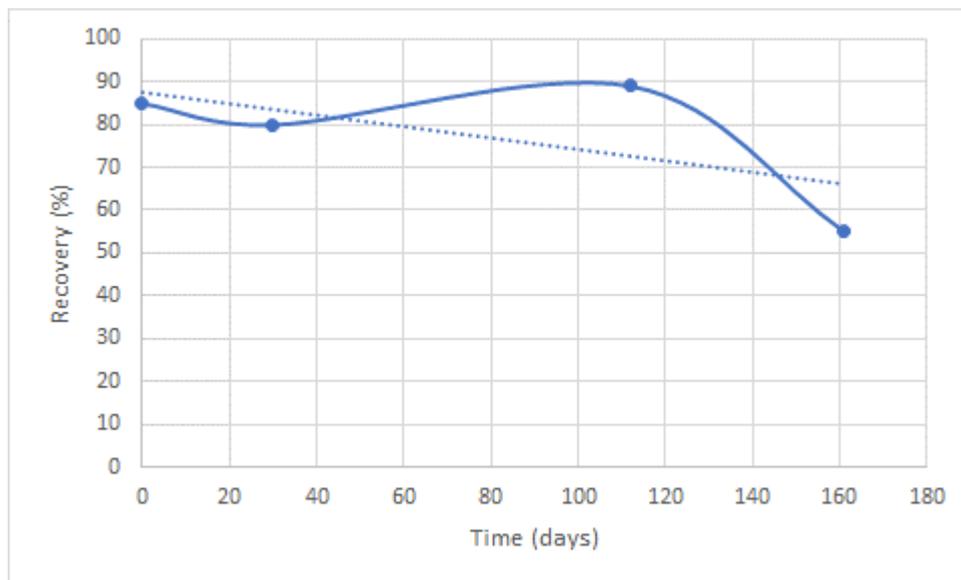
In the Spanish residue trial, residues of eugenol in apples were not detectable in samples taken 2DAA and 7DAA, which were analysed within the demonstrated stability period. This is in agreement with the results of the samples taken 3DAA, which were also not detectable. It can therefore be concluded that the 2 days exceedance of the demonstrated storage stability period has not had an impact on the validity of the trial. It is clear that the not detectable residue result at 3DAA is valid. Furthermore, a slight exceedance of two days over the demonstrated storage stability duration would not be expected to significantly affect the results, when such a long stability period is demonstrated.

In the Italian residue trial, residues of eugenol in apples were not detectable in the 0DAA untreated control. This is as expected and in agreement with the 7DAA untreated control sample that was analysed within the demonstrated stability period. Furthermore, a one-day exceedance over the demonstrated storage stability duration would not be expected to significantly affect the results, when such a long stability period is demonstrated. The results of the trial are therefore considered to be valid.

In the Southern France residue trial, exceedance of the 112 days storage stability period was by up to 7 days (6% exceedance), with the maximum duration of storage prior to analysis being 119 days. This was in the 0DAA untreated control and also treated samples taken at 0, 1, 2 and 3DAA. Residues of eugenol

in apples were not detectable in the 0DAA untreated control. This is as expected and in agreement with the 7DAA untreated control sample, which was analysed within the demonstrated storage stability period. The result is therefore considered to be reliable. Residues in the treated samples were also all not detectable and in agreement with the sample taken 7DAA, which was analysed within the demonstrated storage stability period. After 161 days of storage, recovery relative to the nominal fortification was still 55% and so even if there was a very sudden drop in stability of residues after 112 days, more than half would be expected to remain at the time of analysis and therefore it is clear that residues were all definitely <LOQ at the time of harvest, since the LOD represents 20% LOQ. Indeed n.d. residues are entirely in agreement with the results of the other residue trials for eugenol residues in apples and it is considered that the not detectable result is representative and reliable.

A review of the storage stability date trend line indicates that recovery above the 70% trigger would be predicted at 119 days, thus adding reassurance that the results are reliable.



A 2.1.1.1.2 Storage stability of residues in animal products

No new or additional studies have been submitted.

A 2.1.2 Nature of residues in plants, livestock and processed commodities

A 2.1.2.1 Nature of residue in plants

A 2.1.2.1.1 Nature of residue in primary crops

No new or additional studies have been submitted.

A 2.1.2.1.2 Nature of residue in rotational crops

No new or additional studies have been submitted.

A 2.1.2.1.3 Nature of residues in processed commodities

No new or additional studies have been submitted.

A 2.1.2.2 Nature of residues in livestock

No new or additional studies have been submitted.

A 2.1.3 Magnitude of residues in plants

A 2.1.3.1 Grapes

Table A 7: Comparison of intended and critical EU GAPs

Type of GAP	Number of applications	Application rate per treatment (g a.s./ha)	Interval between application	Growth stage at last application	PHI (days)
cGAP EU (DAR, UK, 2012)	4	132 (E) 264 (G) 264 (T)	7	BBCH 89	7
Intended cGAP (1)	4	132 (E) 264 (G) 264 (T)	7	BBCH 89	7

Comments of zRMS:	<p>Six residue trials were conducted on grape during 2020, one in France (S20-06337-01), one in Germany (S20- 06337-02), one in Austria (S20-06337-03), one in Spain (S20-06337-04), one in Portugal (S20-06337-05) and one in Italy (S20 06337-06).</p> <p>Four applications of Mevalone (3AEY / EDN-004) (66 g a.i./L, thymol, 66 g a.i./L geraniol and 33 g a.i./L eugenol) were applied at nominal rates of 264 g ai/ha thymol; 264 g ai/ha geraniol and 132 g ai/ha eugenol, diluted with water immediately prior to application to a spray volume of 1000 L/ha.</p> <p>Samples of grape bunches from the treated plots were taken by hand 0 (NCH), 1, 2, 3 and 7 days after the final application.</p> <p>Grape bunches samples were analysed for residues of eugenol, methyl-eugenol, thymol and geraniol according to the analytical method that was previously validated according to SANCO/3029/99, rev.4 for grapes matrix in the EAS Study S20-06528.</p> <p>The limit of quantitation for eugenol, methyl-eugenol, thymol and geraniol in grapes is set at 0.01 mg/kg.</p> <p>No residues above 30% of the LOQ were detected in the control (untreated) test portions used for recovery determinations, except for geraniol and thymol where the blank value was around 50%.</p> <p>The accuracy and precision of the method during sample analysis were considered to be acceptable since single recoveries were in the range of 60 - 120% and the mean recoveries at each fortification level were in the range of 70 – 110% with relative standard deviation below 20%.</p> <p>Results:</p> <p>There were no detectable residues of eugenol or methyleugenol in grapes (LOD = 0.003 mg/kg) at 1, 2, 3 and 7 days after last application.</p> <p>Residues of geraniol in grapes samples taken 7 days after last application were <0.01 mg/kg, 0.03 mg/kg, 0.04 mg/kg. The residue is the same as the natural background concentration. There is no increase over natural background concentrations.</p> <p>Residues of thymol in grapes samples taken 7 days after last application were below LOQ (0.01 mg/kg). The trials demonstrated no increase over natural background concentrations.</p> <p>These residue data are supported by the storage stability studies.</p> <p>The study is acceptable.</p>
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This study has also been submitted within the AIR dossier submitted 28th February 2021 (RMS: Spain).

Reference: KCP 8.3/01

Report Determination of residues of eugenol, methyl eugenol, geraniol and thymol after 4 foliar applications of Mevalone (3AEY / EDN-004) to grapevine, 3 trials in N EU (3 x DEC) and 3 trials in S EU (3 x DEC), 2020. Chadwick,

G. 2021a Report No. S20-06337

Guideline(s):	Yes OECD (2009) Guidance Document on Overview of Residue Chemistry Studies (Series on Testing and Assessment No. 64 and Series on Pesticides No. 32) OECD Test Guideline 509: Crop field trials OECD (2016) Guidance Document ENV/JM/MONO(2011)50/REV1 , Second Edition, on Crop Field Trials (Series on Testing and Assessment No. 164 and Series on Pesticides No. 66) EC (1997) Guidance Document 7029/VI/95 rev. 5 general recommendations for the design, preparation and realization of residue trials European Community Guideline SANCO 7525/VI/95, Rev. 10.3, 13/06/17: Comparability, extrapolation, group tolerances and data requirements for setting MRLs EU Guidance Document SANCO/3029/99 rev. 4 for generating and reporting methods of analysis in support of pre-registration data requirements
Deviations:	No
GLP:	Yes
Acceptability:	Yes

Table A 8: Summary of the trials

Trial No./ Location/ EU zone/ Year	Commodity/ Variety	Date of 1.Sowing or planting 2.Flowering 3. Harvest	Application rate per treatment			Dates of treatment or no. of treatments and last date	Growth stage at last treatment or date	Portion analysed	Residues (mg/kg)				PHI (days)	Details on trial
			g a.s./ ha	Water (l/ha)	g a.s./hL				E	ME	G	T		
S20-06337-01/ 45370 Cléry-Saint- André, Loiret, France / NEU / 2020	Grape / Cabernet	1.15/02/12	138.6, 130.8,	1050	13.2, 13.2,	24/08/20	81-83	Grapes	ND	ND	<LOQ	ND	0	E, ME, T controls all ND. G controls <LOQ. Validated Eurofins Method AGR-MOA- EUG-5 LOQ = 0.01 mg/kg Storage = 119 days
		2. 30/05/20- 10/06/20	136.7, 142.1 (E)	991 1036	13.2, 13.2 (E)	31/08/20 07/09/20	81-83 83	Grapes Grapes	ND ND	ND ND	<LOQ <LOQ	ND ND	1 2	
		3. 14/09/20 15/09/20	277.1, 261.5, 273.4, 284.2	1077	26.4, 26.4, 26.4, 26.4	14/09/20	85-89*	Grapes Grapes	ND ND	ND ND	0.01	ND ND	3 7	
		16/09/20	(G)		(G)				ND	ND	<LOQ	ND		
		17/09/20	277.1, 261.5,		26.4, 26.4,									
		21/09/20	273.4, 284.2 (T)		26.4, 26.4 (T)									
S20-06337-02/ 65234 Dielheim, Baden-Württemberg, Germany / NEU /2020	Grape / Riesling	1.1983	129.4, 133.9,	980	13.2, 13.2,	25/08/20	85	Grapes	<LOQ	ND	0.06	ND	0	E, ME, T controls all ND. G control 0.03 mg/kg at Day 0 and 0.04 mg/kg at Day 7 Validated Eurofins Method AGR-MOA- EUG-5 LOQ = 0.01 mg/kg Storage = 118 days
		2. 25/05/20- 06/06/20	138.1, 138.3 (E)	1014 1046	13.2, 13.2 (E)	01/09/20 08/09/20	87 87	Grapes Grapes	ND ND	ND ND	0.07 0.05	ND ND	1 2	
		3. 15/09/20 16/09/20	258.7, 267.7, 276.1, 276.7	1048	26.4, 26.4, 26.4, 26.4	15/09/20	89	Grapes Grapes	ND ND	ND ND	0.05 0.05	ND ND	3 7	
		17/09/20	(G)		(G)				ND	ND	0.04[†]	ND		
		18/09/20	258.7, 267.7,		26.4, 26.4,									
		22/09/20	276.1, 276.7 (T)		26.4, 26.4 (T)									
S20-06337-03/ 8182 Klettendorf, Styria, Austria / NEU / 2020	Grape / Sauvignon blanc	1.17/04/11	133.6, 130.5,	1012	13.2, 13.2,	25/08/20	81	Grapes	ND	ND	0.04	0.06	0	E, ME controls all ND. G control 0.04 mg/kg at Day 0 and 0.03 mg/kg at Day 7. T control ND at Day 0 and <LOQ at Day 7. Validated Eurofins Method AGR-MOA- EUG-5 LOQ = 0.01 mg/kg Storage = 119 days
		2.N/D	134.9, 133.0 (E)	989 1022	13.2, 13.2 (E)	01/09/20 08/09/20	83 85-87	Grapes Grapes	ND ND	ND ND	0.03 0.04	0.03 0.02	1 2	
		3. 15/09/20 16/09/20	267.1, 261.1, 269.8, 266.1	1008	26.4, 26.4, 26.4, 26.4	15/09/20	89	Grapes Grapes	ND ND	ND ND	0.03 0.03	0.02 0.02	3 7	
		17/09/20	(G)		(G)				ND	ND	0.03[†]	<LOQ		
		18/09/20	267.1, 261.1,		26.4, 26.4,									
		22/09/20	269.8, 266.1 (T)		26.4, 26.4 (T)									

* Sampled commodity = BBCH 89

[†] Exactly the same value as the corresponding control sample i.e. equal to natural background concentration

A 2.1.3.2 Pome fruit

Table A 9: Comparison of intended and critical EU GAPs

Type of GAP	Number of applications	Application rate per treatment (g a.s./ha)	Interval between application	Growth stage at last application	PHI (days)
cGAP EU (DAR, UK, 2012)	Pome fruit was not supported in the EU Review				
Intended cGAP (1)	4	132 (E) 264 (G) 264 (T)	7	BBCH 87	1

The following study was conducted on apples as the representative crop group for pome fruit. According to SANTE/2019/12752 trials on apples can be extrapolated to the whole of the pome fruit group. This study has also been submitted within the AIR dossier submitted 28th February 2021 (RMS: Spain).

Comments of zRMS:	<p>Six residue trials were conducted on apples during 2020, two in France (S20-06361-01 and S20-06361-05), one in Germany (S20-06361-02), one in Austria (S20-06361-03), one in Spain (S20-06361-04) and one in Italy (S20-06361-06).</p> <p>Four applications of Mevalone (3AEY / EDN-004) (66 g a.i./L, thymol, 66 g a.i./L geraniol and 33 g a.i./L eugenol) were applied at nominal rates of 264 g ai/ha thymol; 264 g ai/ha geraniol and 132 g ai/ha eugenol, diluted with water immediately prior to application to a spray volume of 1000 L/ha.</p> <p>Samples of apple fruit from the treated plots were taken by hand 0 (NCH), 1, 2, 3 and 7 days after the final application.</p> <p>Apple fruit samples were analysed for residues of eugenol, methyl-eugenol, thymol and geraniol according to the analytical method that was previously validated according to SANCO/3029/99, rev.4 for apple matrix in the EAS Study S20-06529.</p> <p>The limit of quantitation for eugenol, methyl-eugenol, thymol and geraniol in apple is set at 0.01 mg/kg.</p> <p>The accuracy and precision of the method during sample analysis were considered to be acceptable since single recoveries were in the range of 60 - 120% and the mean recoveries at each fortification level were in the range of 70 – 110% with relative standard deviation below 20%.</p> <p>Results: There were no detectable residues of eugenol, methyleugenol or geraniol in apples samples (LOD = 0.003 mg/kg) at 1 day after last application. Residues of thymol in apples samples were below LOQ (0.01 mg/kg) at 1 day after last application. The trials demonstrated no increase over natural background concentrations.</p> <p>These residue data are supported by the storage stability studies. The study is acceptable.</p>
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Reference: KCP 8.3/02

Report Determination of residues of eugenol, methyl eugenol, geraniol and thymol after 4 foliar applications of Mevalone (3AEY / EDN-004) to apple, 3 trials in N EU (3 x DEC) and 3 trials in S EU (3 x DEC), 2020. Chadwick, G. 2021b Report No. S20-06361

Guideline(s): Yes
OECD (2009) Guidance Document on Overview of Residue Chemistry Studies (Series on Testing and Assessment No. 64 and Series on Pesticides No. 32)
OECD Test Guideline 509: Crop field trials
OECD (2016) Guidance Document ENV/JM/MONO(2011)50/REV1 ,

Second Edition, on Crop Field Trials (Series on Testing and Assessment No. 164 and Series on Pesticides No. 66)

EC (1997) Guidance Document 7029/VI/95 rev. 5 general recommendations for the design, preparation and realization of residue trials

European Community Guideline SANCO 7525/VI/95, Rev. 10.3, 13/06/17: Comparability, extrapolation, group tolerances and data requirements for setting MRLs

EU Guidance Document SANCO/3029/99 rev. 4 for generating and reporting methods of analysis in support of pre-registration data requirements

Deviations:	No
GLP:	Yes
Acceptability:	Yes

A 2.1.4 Magnitude of residues in livestock

A 2.1.4.1 Livestock feeding studies

A 2.1.4.1.1 Livestock feeding study 1

No new or additional studies have been submitted.

A 2.1.5 Magnitude of residues in processed commodities (Industrial Processing and/or Household Preparation)

A 2.1.5.1 Distribution of the residue in peel/pulp

No new or additional studies have been submitted.

A 2.1.5.2 Processing studies on a core set of representative processes

No new or additional studies have been submitted.

A 2.1.6 Magnitude of residues in representative succeeding crops

No new or additional studies have been submitted.

A 2.1.7 Other/Special Studies

No new or additional studies have been submitted.

Appendix 3 Pesticide Residue Intake Model (PRIMo)

A 3.1 TMDI calculations Theoretical Maximum Daily Intake (TMDI) for eugenol calculated using EFSA PRIMo rev.3.1 (normal mode)



Eugenol	
LOQs (mg/kg) range from:	0.01 to: 0.01
Toxicological reference values	
ADI (mg/kg bw/day):	1 ARD (mg/kg bw): not necessary
Source of ADI:	Source of ARD:
Year of evaluation:	Year of evaluation:

Input values

Details - chronic risk assessment	Supplementary results - chronic risk assessment
Details - acute risk assessment/children	Details - acute risk assessment/adults

Comments:

Normal mode
 Chronic risk assessment: JMPR methodology (IEDI/TMDI)

TMDI(NED)/IEDI calculation (based on average food consumption)	Calculated exposure (% of ADI)		Exposure (µg/kg bw per day)	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	Exposure resulting from	
	MS Diet									MRLs set at the LOQ (in % of ADI)	commodities not under assessment (in % of ADI)
TMDI(NED)/IEDI calculation (based on average food consumption)	0.1%	NL toddler	1.24	0.1%	Milk: Cattle	0.0%	Apples	0.0%	Maize/corn	0.1%	
	0.1%	NL child	0.65	0.0%	Milk: Cattle	0.0%	Sugar beet roots	0.0%	Apples	0.1%	
	0.1%	DE child	0.61	0.0%	Milk: Cattle	0.0%	Apples	0.0%	Wheat	0.1%	
	0.1%	UK infant	0.61	0.0%	Milk: Cattle	0.0%	Potatoes	0.0%	Wheat	0.1%	
	0.1%	FR toddler 2-3 yr	0.54	0.0%	Milk: Cattle	0.0%	Apples	0.0%	Wheat	0.1%	
	0.1%	FR child 3-15 yr	0.53	0.0%	Milk: Cattle	0.0%	Wheat	0.0%	Sugar beet roots	0.1%	
	0.0%	UK toddler	0.45	0.0%	Milk: Cattle	0.0%	Wheat	0.0%	Potatoes	0.0%	
	0.0%	DK child	0.41	0.0%	Milk: Cattle	0.0%	Rye	0.0%	Wheat	0.0%	
	0.0%	GEMSFood G11	0.39	0.0%	Milk: Cattle	0.0%	Potatoes	0.0%	Soyabeans	0.0%	
	0.0%	RO general	0.38	0.0%	Milk: Cattle	0.0%	Wheat	0.0%	Potatoes	0.0%	
	0.0%	GEMSFood G06	0.38	0.0%	Wheat	0.0%	Tomatoes	0.0%	Milk: Cattle	0.0%	
	0.0%	SE general	0.37	0.0%	Milk: Cattle	0.0%	Bovine: Muscle/meat	0.0%	Potatoes	0.0%	
	0.0%	GEMSFood G07	0.37	0.0%	Milk: Cattle	0.0%	Wheat	0.0%	Potatoes	0.0%	
	0.0%	GEMSFood G15	0.37	0.0%	Milk: Cattle	0.0%	Wheat	0.0%	Potatoes	0.0%	
	0.0%	GEMSFood G08	0.36	0.0%	Milk: Cattle	0.0%	Wheat	0.0%	Potatoes	0.0%	
	0.0%	GEMSFood G10	0.36	0.0%	Milk: Cattle	0.0%	Wheat	0.0%	Wheat	0.0%	
	0.0%	ES child	0.35	0.0%	Milk: Cattle	0.0%	Wheat	0.0%	Soyabeans	0.0%	
	0.0%	DE women 14-50 yr	0.34	0.0%	Milk: Cattle	0.0%	Wheat	0.0%	Oranges	0.0%	
	0.0%	DE general	0.34	0.0%	Milk: Cattle	0.0%	Sugar beet roots	0.0%	Apples	0.0%	
	0.0%	IE adult	0.32	0.0%	Milk: Cattle	0.0%	Sweet potatoes	0.0%	Wheat	0.0%	
	0.0%	FR infant	0.29	0.0%	Milk: Cattle	0.0%	Potatoes	0.0%	Apples	0.0%	
	0.0%	NL general	0.28	0.0%	Milk: Cattle	0.0%	Sugar beet roots	0.0%	Potatoes	0.0%	
	0.0%	PT general	0.21	0.0%	Potatoes	0.0%	Wheat	0.0%	Wine grapes	0.0%	
	0.0%	ES adult	0.20	0.0%	Milk: Cattle	0.0%	Wheat	0.0%	Oranges	0.0%	
	0.0%	FR adult	0.19	0.0%	Milk: Cattle	0.0%	Wine grapes	0.0%	Wheat	0.0%	
	0.0%	FI 3 yr	0.17	0.0%	Potatoes	0.0%	Bananas	0.0%	Wheat	0.0%	
	0.0%	IT toddler	0.16	0.0%	Wheat	0.0%	Other cereals	0.0%	Tomatoes	0.0%	
	0.0%	DK adult	0.16	0.0%	Milk: Cattle	0.0%	Potatoes	0.0%	Wheat	0.0%	
	0.0%	LT adult	0.16	0.0%	Milk: Cattle	0.0%	Potatoes	0.0%	Apples	0.0%	
	0.0%	UK vegetarian	0.14	0.0%	Milk: Cattle	0.0%	Wheat	0.0%	Potatoes	0.0%	
	0.0%	UK adult	0.13	0.0%	Milk: Cattle	0.0%	Wheat	0.0%	Potatoes	0.0%	
	0.0%	FI 6 yr	0.13	0.0%	Potatoes	0.0%	Wheat	0.0%	Bananas	0.0%	
	0.0%	FI adult	0.13	0.0%	Coffee beans	0.0%	Potatoes	0.0%	Rye	0.0%	
	0.0%	IT adult	0.12	0.0%	Wheat	0.0%	Tomatoes	0.0%	Apples	0.0%	
	0.0%	PL general	0.10	0.0%	Potatoes	0.0%	Apples	0.0%	Tomatoes	0.0%	
	0.0%	IE child	0.08	0.0%	Milk: Cattle	0.0%	Wheat	0.0%	Potatoes	0.0%	

Conclusion:
 The estimated long-term dietary intake (TMDI/NED)/IEDI) was below the ADI.
 The long-term intake of residues of Eugenol is unlikely to present a public health concern.

Theoretical Maximum Daily Intake (TMDI) for geraniol calculated using EFSA PRIMo rev.3.1 (normal mode)



Geraniol	
LOQs (mg/kg) range from:	0.01 to: 0.01
Toxicological reference values	
ADI (mg/kg bw/day):	0.5
ARID (mg/kg bw):	not necessary
Source of ADI:	Source of ARID:
Year of evaluation:	Year of evaluation:

Input values

Details - chronic risk assessment

Supplementary results - chronic risk assessment

Details - acute risk assessment/children

Details - acute risk assessment/adults

Comments:												
Normal mode												
Chronic risk assessment: JMPR methodology (IED/TMDI)												
No of diets exceeding the ADI : ---										Exposure resulting from		
	Calculated exposure (% of ADI)	MS Diet	Expsoure (µg/kg bw per day)	Highest contributor to MS diet (in % of ADI)		2nd contributor to MS diet (in % of ADI)		3rd contributor to MS diet (in % of ADI)		MRLs set at the LOQ (in % of ADI)	commodities not under assessment (in % of ADI)	
				Commodity / group of commodities	Commodity / group of commodities	Commodity / group of commodities	Commodity / group of commodities					
TMDI(NED)/IEDI calculation (based on average food consumption)	0.2%	NL toddler	1.24	0.1%	Milk: Cattle	0.0%	Apples	0.0%	Maize/corn	0.2%		
	0.1%	NL child	0.65	0.0%	Milk: Cattle	0.0%	Sugar beet roots	0.0%	Apples	0.1%		
	0.1%	DE child	0.61	0.0%	Milk: Cattle	0.0%	Apples	0.0%	Wheat	0.1%		
	0.1%	UK infant	0.61	0.1%	Milk: Cattle	0.0%	Potatoes	0.0%	Wheat	0.1%		
	0.1%	FR toddler 2 3 yr	0.54	0.1%	Milk: Cattle	0.0%	Apples	0.0%	Wheat	0.1%		
	0.1%	FR child 3 15 yr	0.53	0.0%	Milk: Cattle	0.0%	Wheat	0.0%	Sugar beet roots	0.1%		
	0.1%	UK toddler	0.45	0.0%	Milk: Cattle	0.0%	Wheat	0.0%	Potatoes	0.1%		
	0.1%	DK child	0.41	0.0%	Milk: Cattle	0.0%	Rye	0.0%	Wheat	0.1%		
	0.1%	GEMS/Food G11	0.39	0.0%	Milk: Cattle	0.0%	Potatoes	0.0%	Soyabeans	0.1%		
	0.1%	RO general	0.38	0.0%	Milk: Cattle	0.0%	Wheat	0.0%	Potatoes	0.1%		
	0.1%	GEMS/Food G06	0.38	0.0%	Wheat	0.0%	Tomatoes	0.0%	Milk: Cattle	0.1%		
	0.1%	SE general	0.37	0.0%	Milk: Cattle	0.0%	Bovine: Muscle/meat	0.0%	Potatoes	0.1%		
	0.1%	GEMS/Food G07	0.37	0.0%	Milk: Cattle	0.0%	Wheat	0.0%	Potatoes	0.1%		
	0.1%	GEMS/Food G15	0.37	0.0%	Milk: Cattle	0.0%	Wheat	0.0%	Potatoes	0.1%		
	0.1%	GEMS/Food G08	0.36	0.0%	Milk: Cattle	0.0%	Wheat	0.0%	Potatoes	0.1%		
	0.1%	GEMS/Food G10	0.36	0.0%	Milk: Cattle	0.0%	Wheat	0.0%	Soyabeans	0.1%		
	0.1%	ES child	0.35	0.0%	Milk: Cattle	0.0%	Wheat	0.0%	Oranges	0.1%		
	0.1%	DE women 14-50 yr	0.34	0.0%	Milk: Cattle	0.0%	Sugar beet roots	0.0%	Apples	0.1%		
	0.1%	DE general	0.34	0.0%	Milk: Cattle	0.0%	Sugar beet roots	0.0%	Apples	0.1%		
	0.1%	IE adult	0.32	0.0%	Milk: Cattle	0.0%	Sweet potatoes	0.0%	Wheat	0.1%		
	0.1%	FR infant	0.29	0.0%	Milk: Cattle	0.0%	Potatoes	0.0%	Apples	0.1%		
	0.1%	NL general	0.28	0.0%	Milk: Cattle	0.0%	Sugar beet roots	0.0%	Potatoes	0.1%		
	0.0%	PT general	0.21	0.0%	Potatoes	0.0%	Wheat	0.0%	Wine grapes	0.0%		
	0.0%	ES adult	0.20	0.0%	Milk: Cattle	0.0%	Wheat	0.0%	Oranges	0.0%		
	0.0%	FR adult	0.19	0.0%	Milk: Cattle	0.0%	Wine grapes	0.0%	Wheat	0.0%		
	0.0%	FI 3 yr	0.17	0.0%	Potatoes	0.0%	Bananas	0.0%	Wheat	0.0%		
	0.0%	IT toddler	0.16	0.0%	Wheat	0.0%	Other cereals	0.0%	Tomatoes	0.0%		
	0.0%	DK adult	0.16	0.0%	Milk: Cattle	0.0%	Potatoes	0.0%	Wheat	0.0%		
	0.0%	LT adult	0.16	0.0%	Milk: Cattle	0.0%	Potatoes	0.0%	Apples	0.0%		
	0.0%	UK vegetarian	0.14	0.0%	Milk: Cattle	0.0%	Wheat	0.0%	Potatoes	0.0%		
0.0%	UK adult	0.13	0.0%	Milk: Cattle	0.0%	Wheat	0.0%	Potatoes	0.0%			
0.0%	FI 6 yr	0.13	0.0%	Potatoes	0.0%	Wheat	0.0%	Bananas	0.0%			
0.0%	FI adult	0.13	0.0%	Coffee beans	0.0%	Potatoes	0.0%	Rye	0.0%			
0.0%	IT adult	0.12	0.0%	Wheat	0.0%	Tomatoes	0.0%	Apples	0.0%			
0.0%	PL general	0.10	0.0%	Potatoes	0.0%	Apples	0.0%	Tomatoes	0.0%			
0.0%	IE child	0.08	0.0%	Milk: Cattle	0.0%	Wheat	0.0%	Potatoes	0.0%			
Conclusion: The estimated long-term dietary intake (TMDI/NED/IEDI) was below the ADI. The long-term intake of residues of Geraniol is unlikely to present a public health concern.												

Theoretical Maximum Daily Intake (TMDI) for thymol calculated using EFSA PRIMo rev.3.1 (normal mode)



Thymol			
LOQs (mg/kg) range from:	0.01	to:	0.01
Toxicological reference values			
ADI (mg/kg bw/day):	0.03	ARID (mg/kg bw):	0.08
Source of ADI:		Source of ARID:	
Year of evaluation:		Year of evaluation:	

Input values

Details - chronic risk assessment

Supplementary results - chronic risk assessment

Details - acute risk assessment/children

Details - acute risk assessment/adults

Comments:

Normal mode

Chronic risk assessment: JMPR methodology (IEDI/TMDI)

	Calculated exposure (% of ADI)	MS Diet	Exposure (µg/kg bw per day)	No of diets exceeding the ADI : ---			Exposure resulting from				
				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	MRLs set at the LOQ (in % of ADI)	commodities not under assessment (in % of ADI)
TMDI/NEDI/IEDI calculation (based on average food consumption)	4%	NL toddler	1.24	2%	Milk: Cattle	0.4%	Apples	0.2%	Maize/corn	4%	
	2%	NL child	0.65	0.8%	Milk: Cattle	0.3%	Sugar beet roots	0.2%	Apples	2%	
	2%	DE child	0.61	0.7%	Milk: Cattle	0.4%	Apples	0.1%	Wheat	2%	
	2%	UK infant	0.61	1%	Milk: Cattle	0.1%	Potatoes	0.1%	Wheat	2%	
	2%	FR toddler 2-3 yr	0.54	1.0%	Milk: Cattle	0.1%	Apples	0.1%	Wheat	2%	
	2%	FR child 3-15 yr	0.53	0.8%	Milk: Cattle	0.2%	Wheat	0.1%	Sugar beet roots	2%	
	1%	UK toddler	0.45	0.7%	Milk: Cattle	0.1%	Wheat	0.1%	Potatoes	1%	
	1%	DK child	0.41	0.4%	Milk: Cattle	0.2%	Rye	0.1%	Wheat	1%	
	1%	GEMS/Food G11	0.39	0.3%	Milk: Cattle	0.1%	Potatoes	0.1%	Soyabeans	1%	
	1%	RO general	0.38	0.4%	Milk: Cattle	0.2%	Wheat	0.1%	Potatoes	1%	
	1%	GEMS/Food G06	0.38	0.2%	Wheat	0.1%	Tomatoes	0.1%	Milk: Cattle	1%	
	1%	SE general	0.37	0.4%	Milk: Cattle	0.1%	Bovine: Muscle/meat	0.1%	Potatoes	1%	
	1%	GEMS/Food G07	0.37	0.2%	Milk: Cattle	0.1%	Wheat	0.1%	Potatoes	1%	
	1%	GEMS/Food G15	0.37	0.2%	Milk: Cattle	0.2%	Wheat	0.1%	Potatoes	1%	
	1%	GEMS/Food G08	0.36	0.2%	Milk: Cattle	0.1%	Wheat	0.1%	Potatoes	1%	
	1%	GEMS/Food G10	0.36	0.2%	Milk: Cattle	0.1%	Wheat	0.1%	Soyabeans	1%	
	1%	ES child	0.35	0.4%	Milk: Cattle	0.1%	Wheat	0.1%	Oranges	1%	
	1%	DE women 14-50 yr	0.34	0.4%	Milk: Cattle	0.2%	Sugar beet roots	0.1%	Apples	1%	
	1%	DE general	0.34	0.4%	Milk: Cattle	0.1%	Sugar beet roots	0.1%	Apples	1%	
	1%	IE adult	0.32	0.1%	Milk: Cattle	0.1%	Sweet potatoes	0.1%	Wheat	1%	
	1.0%	FR infant	0.29	0.6%	Milk: Cattle	0.1%	Potatoes	0.1%	Apples	1.0%	
	0.9%	NL general	0.28	0.3%	Milk: Cattle	0.1%	Sugar beet roots	0.1%	Potatoes	0.9%	
	0.7%	PT general	0.21	0.2%	Potatoes	0.1%	Wheat	0.1%	Wine grapes	0.7%	
	0.7%	ES adult	0.20	0.2%	Milk: Cattle	0.1%	Wheat	0.0%	Oranges	0.7%	
	0.6%	FR adult	0.19	0.1%	Milk: Cattle	0.1%	Wine grapes	0.1%	Wheat	0.6%	
	0.6%	FI 3 yr	0.17	0.2%	Potatoes	0.0%	Bananas	0.0%	Wheat	0.6%	
	0.5%	IT toddler	0.16	0.2%	Wheat	0.1%	Other cereals	0.0%	Tomatoes	0.5%	
	0.5%	DK adult	0.16	0.2%	Milk: Cattle	0.0%	Potatoes	0.0%	Wheat	0.5%	
	0.5%	LT adult	0.16	0.1%	Milk: Cattle	0.1%	Potatoes	0.1%	Apples	0.5%	
	0.5%	UK vegetarian	0.14	0.1%	Milk: Cattle	0.1%	Wheat	0.0%	Potatoes	0.5%	
0.4%	UK adult	0.13	0.1%	Milk: Cattle	0.1%	Wheat	0.0%	Potatoes	0.4%		
0.4%	FI 6 yr	0.13	0.1%	Potatoes	0.0%	Wheat	0.0%	Bananas	0.4%		
0.4%	FI adult	0.13	0.2%	Potatoes	0.0%	Coffee beans	0.0%	Rye	0.4%		
0.4%	IT adult	0.12	0.1%	Wheat	0.0%	Tomatoes	0.0%	Apples	0.4%		
0.3%	PL general	0.10	0.1%	Potatoes	0.1%	Apples	0.0%	Tomatoes	0.3%		
0.3%	IE child	0.08	0.1%	Milk: Cattle	0.0%	Wheat	0.0%	Potatoes	0.3%		

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

Theoretical Maximum Daily Intake (TMDI) for eugenol calculated using EFSA PRIMo rev.3.1 (refined mode)



Eugenol	
LOGs (mg/kg) range from:	0.01 to: 0.01
Toxicological reference values	
ADI (mg/kg bw/day):	1 ARfD (mg/kg bw): not necessary
Source of ADI:	Source of ARfD:
Year of evaluation:	Year of evaluation:

Input values

Details - chronic risk assessment

Supplementary results - chronic risk assessment

Details - acute risk assessment/children

Details - acute risk assessment/adults

Refined calculation mode											
Chronic risk assessment: JMPR methodology (IEDI/TMDI)											
No of diets exceeding the ADI : --										Exposure resulting from	
	Calculated exposure (% of ADI)	MS Diet	Exposure (µg/kg bw per day)	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	MRLs set at the LOQ (in % of ADI)	commodities not under assessment (in % of ADI)
TMDI/NEDI/IEDI calculation (based on average food consumption)	0.0%	NL toddler	0.17	0.0%	Apples	0.0%	Pears	0.0%	Table grapes	0.0%	0.0%
	0.0%	DE child	0.15	0.0%	Apples	0.0%	Table grapes	0.0%	Pears	0.0%	0.0%
	0.0%	NL child	0.08	0.0%	Apples	0.0%	Pears	0.0%	Table grapes	0.0%	0.0%
	0.0%	PT general	0.04	0.0%	Wine grapes	0.0%	Apples	0.0%	Pears	0.0%	0.0%
	0.0%	DE women 14-50 yr	0.04	0.0%	Apples	0.0%	Wine grapes	0.0%	Table grapes	0.0%	0.0%
	0.0%	FR toddler 2 3 yr	0.04	0.0%	Apples	0.0%	Pears	0.0%	Wine grapes	0.0%	0.0%
	0.0%	DE general	0.04	0.0%	Apples	0.0%	Wine grapes	0.0%	Table grapes	0.0%	0.0%
	0.0%	RO general	0.03	0.0%	Wine grapes	0.0%	Apples	0.0%	Table grapes	0.0%	0.0%
	0.0%	FR adult	0.03	0.0%	Wine grapes	0.0%	Apples	0.0%	Pears	0.0%	0.0%
	0.0%	DK child	0.03	0.0%	Apples	0.0%	Pears	0.0%	Table grapes	0.0%	0.0%
	0.0%	GEMS/Food G11	0.03	0.0%	Apples	0.0%	Wine grapes	0.0%	Table grapes	0.0%	0.0%
	0.0%	GEMS/Food G07	0.03	0.0%	Wine grapes	0.0%	Apples	0.0%	Table grapes	0.0%	0.0%
	0.0%	FR child 3 15 yr	0.03	0.0%	Apples	0.0%	Wine grapes	0.0%	Table grapes	0.0%	0.0%
	0.0%	IE adult	0.03	0.0%	Wine grapes	0.0%	Apples	0.0%	Pears	0.0%	0.0%
	0.0%	GEMS/Food G08	0.03	0.0%	Apples	0.0%	Wine grapes	0.0%	Table grapes	0.0%	0.0%
	0.0%	GEMS/Food G15	0.03	0.0%	Apples	0.0%	Wine grapes	0.0%	Table grapes	0.0%	0.0%
	0.0%	PL general	0.03	0.0%	Apples	0.0%	Table grapes	0.0%	Pears	0.0%	0.0%
	0.0%	NL general	0.03	0.0%	Apples	0.0%	Wine grapes	0.0%	Table grapes	0.0%	0.0%
	0.0%	DK adult	0.02	0.0%	Apples	0.0%	Wine grapes	0.0%	Pears	0.0%	0.0%
	0.0%	UK toddler	0.02	0.0%	Apples	0.0%	Table grapes	0.0%	Strawberries	0.0%	0.0%
	0.0%	GEMS/Food G06	0.02	0.0%	Table grapes	0.0%	Apples	0.0%	Pears	0.0%	0.0%
	0.0%	FR infant	0.02	0.0%	Apples	0.0%	Pears	0.0%	Strawberries	0.0%	0.0%
	0.0%	UK infant	0.02	0.0%	Apples	0.0%	Pears	0.0%	Strawberries	0.0%	0.0%
	0.0%	LT adult	0.02	0.0%	Apples	0.0%	Pears	0.0%	Strawberries	0.0%	0.0%
	0.0%	GEMS/Food G10	0.02	0.0%	Apples	0.0%	Wine grapes	0.0%	Table grapes	0.0%	0.0%
	0.0%	ES child	0.02	0.0%	Apples	0.0%	Pears	0.0%	Strawberries	0.0%	0.0%
	0.0%	FI 3 yr	0.02	0.0%	Apples	0.0%	Strawberries	0.0%	Table grapes	0.0%	0.0%
	0.0%	UK adult	0.02	0.0%	Wine grapes	0.0%	Apples	0.0%	Pears	0.0%	0.0%
	0.0%	UK vegetarian	0.02	0.0%	Wine grapes	0.0%	Apples	0.0%	Pears	0.0%	0.0%
	0.0%	ES adult	0.02	0.0%	Apples	0.0%	Wine grapes	0.0%	Pears	0.0%	0.0%
0.0%	SE general	0.02	0.0%	Apples	0.0%	Pears	0.0%	Strawberries	0.0%	0.0%	
0.0%	IT toddler	0.01	0.0%	Apples	0.0%	Pears	0.0%	Strawberries	0.0%	0.0%	
0.0%	FI 6 yr	0.01	0.0%	Apples	0.0%	Strawberries	0.0%	Pears	0.0%	0.0%	
0.0%	IT adult	0.01	0.0%	Apples	0.0%	Pears	0.0%	Table grapes	0.0%	0.0%	
0.0%	FI adult	0.01	0.0%	Apples	0.0%	Wine grapes	0.0%	Strawberries	0.0%	0.0%	
0.0%	IE child	0.00	0.0%	Apples	0.0%	Table grapes	0.0%	Pears	0.0%	0.0%	
Conclusion: The estimated long-term dietary intake (TMDI/NEDI/IEDI) was below the ADI. The long-term intake of residues of Eugenol is unlikely to present a public health concern.											

Theoretical Maximum Daily Intake (TMDI) for geraniol calculated using EFSA PRIMo rev.3.1 (refined mode)



Geraniol	
LOQs (mg/kg) range from:	0.01 to: 0.01
Toxicological reference values	
ADI (mg/kg bw/day):	0.5
ARID (mg/kg bw):	not necessary
Source of ADI:	Source of ARID:
Year of evaluation:	Year of evaluation:

Input values

Details - chronic risk assessment

Supplementary results - chronic risk assessment

Details - acute risk assessment/children

Details - acute risk assessment/adults

Comments:											
Refined calculation mode											
Chronic risk assessment: Jmpr methodology (IED/TMDI)											
No of diets exceeding the ADI : ---										Exposure resulting from	
	Calculated exposure (% of ADI)	MS Diet	Exposure (µg/kg bw per day)	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	MRLs set at the LOQ (in % of ADI)	
										MRLs set at the LOQ (in % of ADI)	commodities not under assessment (in % of ADI)
TMDI(NEDI/IED) calculation (based on average food consumption)	0.0%	NL toddler	0.17	0.0%	Apples	0.0%	Pears	0.0%	Table grapes	0.0%	0.0%
	0.0%	DE child	0.15	0.0%	Apples	0.0%	Table grapes	0.0%	Pears	0.0%	0.0%
	0.0%	NL child	0.08	0.0%	Apples	0.0%	Pears	0.0%	Table grapes	0.0%	0.0%
	0.0%	PT general	0.04	0.0%	Wine grapes	0.0%	Apples	0.0%	Pears	0.0%	0.0%
	0.0%	DE women 14-50 yr	0.04	0.0%	Apples	0.0%	Wine grapes	0.0%	Table grapes	0.0%	0.0%
	0.0%	FR toddler 2-3 yr	0.04	0.0%	Apples	0.0%	Pears	0.0%	Table grapes	0.0%	0.0%
	0.0%	DE general	0.04	0.0%	Apples	0.0%	Wine grapes	0.0%	Table grapes	0.0%	0.0%
	0.0%	RO general	0.03	0.0%	Wine grapes	0.0%	Apples	0.0%	Table grapes	0.0%	0.0%
	0.0%	FR adult	0.03	0.0%	Wine grapes	0.0%	Apples	0.0%	Pears	0.0%	0.0%
	0.0%	DK child	0.03	0.0%	Apples	0.0%	Pears	0.0%	Table grapes	0.0%	0.0%
	0.0%	GEMS/Food G11	0.03	0.0%	Apples	0.0%	Wine grapes	0.0%	Table grapes	0.0%	0.0%
	0.0%	GEMS/Food G07	0.03	0.0%	Wine grapes	0.0%	Apples	0.0%	Table grapes	0.0%	0.0%
	0.0%	FR child 3-15 yr	0.03	0.0%	Apples	0.0%	Wine grapes	0.0%	Table grapes	0.0%	0.0%
	0.0%	IE adult	0.03	0.0%	Wine grapes	0.0%	Apples	0.0%	Pears	0.0%	0.0%
	0.0%	GEMS/Food G08	0.03	0.0%	Apples	0.0%	Wine grapes	0.0%	Table grapes	0.0%	0.0%
	0.0%	GEMS/Food G15	0.03	0.0%	Apples	0.0%	Wine grapes	0.0%	Table grapes	0.0%	0.0%
	0.0%	PL general	0.03	0.0%	Apples	0.0%	Table grapes	0.0%	Pears	0.0%	0.0%
	0.0%	NL general	0.03	0.0%	Apples	0.0%	Wine grapes	0.0%	Table grapes	0.0%	0.0%
	0.0%	DK adult	0.02	0.0%	Apples	0.0%	Wine grapes	0.0%	Pears	0.0%	0.0%
	0.0%	UK toddler	0.02	0.0%	Apples	0.0%	Table grapes	0.0%	Strawberries	0.0%	0.0%
	0.0%	GEMS/Food G06	0.02	0.0%	Table grapes	0.0%	Apples	0.0%	Pears	0.0%	0.0%
	0.0%	FR infant	0.02	0.0%	Apples	0.0%	Pears	0.0%	Strawberries	0.0%	0.0%
	0.0%	UK infant	0.02	0.0%	Apples	0.0%	Pears	0.0%	Strawberries	0.0%	0.0%
	0.0%	LT adult	0.02	0.0%	Apples	0.0%	Pears	0.0%	Strawberries	0.0%	0.0%
	0.0%	GEMS/Food G10	0.02	0.0%	Apples	0.0%	Wine grapes	0.0%	Table grapes	0.0%	0.0%
	0.0%	ES child	0.02	0.0%	Apples	0.0%	Pears	0.0%	Strawberries	0.0%	0.0%
	0.0%	FI 3 yr	0.02	0.0%	Apples	0.0%	Strawberries	0.0%	Table grapes	0.0%	0.0%
	0.0%	UK adult	0.02	0.0%	Wine grapes	0.0%	Apples	0.0%	Pears	0.0%	0.0%
	0.0%	UK vegetarian	0.02	0.0%	Wine grapes	0.0%	Apples	0.0%	Pears	0.0%	0.0%
	0.0%	ES adult	0.02	0.0%	Apples	0.0%	Wine grapes	0.0%	Pears	0.0%	0.0%
0.0%	SE general	0.02	0.0%	Apples	0.0%	Pears	0.0%	Strawberries	0.0%	0.0%	
0.0%	IT toddler	0.01	0.0%	Apples	0.0%	Pears	0.0%	Strawberries	0.0%	0.0%	
0.0%	FI 6 yr	0.01	0.0%	Apples	0.0%	Strawberries	0.0%	Pears	0.0%	0.0%	
0.0%	IT adult	0.01	0.0%	Apples	0.0%	Pears	0.0%	Table grapes	0.0%	0.0%	
0.0%	FI adult	0.01	0.0%	Apples	0.0%	Wine grapes	0.0%	Strawberries	0.0%	0.0%	
0.0%	IE child	0.00	0.0%	Apples	0.0%	Table grapes	0.0%	Pears	0.0%	0.0%	
Conclusion: The estimated long-term dietary intake (TMDI/NEDI/IEDI) was below the ADI. The long-term intake of residues of Geraniol is unlikely to present a public health concern.											

Theoretical Maximum Daily Intake (TMDI) for thymol calculated using EFSA PRIMo rev.3.1 (refined mode)



Thymol	
LOQs (mg/kg) range from:	0.01 to: 0.01
Toxicological reference values	
ADI (mg/kg bw/day):	0.03
ARID (mg/kg bw):	0.08
Source of ADI:	Source of ARID:
Year of evaluation:	Year of evaluation:

Input values

Details - chronic risk assessment

Supplementary results - chronic risk assessment

Details - acute risk assessment/children

Details - acute risk assessment/adults

Refined calculation mode												
Chronic risk assessment: JMPR methodology (IEDI/TMDI)												
No of diets exceeding the ADI :										Exposure resulting from		
	Calculated exposure (% of ADI)	MS Diet	Exposure (µg/kg bw per day)	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	MRLs set at the LOQ (in % of ADI)		
										commodities not under assessment (in % of ADI)		
TMDI/NEDI/IEDI calculation (based on average food consumption)	0.6%	NL toddler	0.17	0.4%	Apples	0.1%	Pears	0.1%	Table grapes	0.6%	0.6%	
	0.5%	DE child	0.15	0.4%	Apples	0.0%	Table grapes	0.0%	Pears	0.5%	0.5%	
	0.3%	NL child	0.08	0.2%	Apples	0.0%	Pears	0.0%	Table grapes	0.3%	0.3%	
	0.1%	PT general	0.04	0.1%	Wine grapes	0.0%	Apples	0.0%	Pears	0.1%	0.1%	
	0.1%	DE women 14-50 yr	0.04	0.1%	Apples	0.0%	Wine grapes	0.0%	Table grapes	0.1%	0.1%	
	0.1%	FR toddler 2 3 yr	0.04	0.1%	Apples	0.0%	Pears	0.0%	Wine grapes	0.1%	0.1%	
	0.1%	DE general	0.04	0.1%	Apples	0.0%	Wine grapes	0.0%	Table grapes	0.1%	0.1%	
	0.1%	RO general	0.03	0.1%	Wine grapes	0.0%	Apples	0.0%	Table grapes	0.1%	0.1%	
	0.1%	FR adult	0.03	0.1%	Wine grapes	0.0%	Apples	0.0%	Pears	0.1%	0.1%	
	0.1%	DK child	0.03	0.1%	Apples	0.0%	Pears	0.0%	Table grapes	0.1%	0.1%	
	0.1%	GEMS/Food G11	0.03	0.1%	Apples	0.0%	Wine grapes	0.0%	Table grapes	0.1%	0.1%	
	0.1%	GEMS/Food G07	0.03	0.0%	Wine grapes	0.0%	Apples	0.0%	Table grapes	0.1%	0.1%	
	0.1%	FR child 3 15 yr	0.03	0.1%	Apples	0.0%	Wine grapes	0.0%	Table grapes	0.1%	0.1%	
	0.1%	IE adult	0.03	0.0%	Wine grapes	0.0%	Apples	0.0%	Pears	0.1%	0.1%	
	0.1%	GEMS/Food G08	0.03	0.0%	Apples	0.0%	Wine grapes	0.0%	Table grapes	0.1%	0.1%	
	0.1%	GEMS/Food G15	0.03	0.0%	Apples	0.0%	Wine grapes	0.0%	Table grapes	0.1%	0.1%	
	0.1%	PL general	0.03	0.1%	Apples	0.0%	Table grapes	0.0%	Pears	0.1%	0.1%	
	0.1%	NL general	0.03	0.0%	Apples	0.0%	Wine grapes	0.0%	Table grapes	0.1%	0.1%	
	0.1%	DK adult	0.02	0.0%	Apples	0.0%	Wine grapes	0.0%	Pears	0.1%	0.1%	
	0.1%	UK toddler	0.02	0.1%	Apples	0.0%	Table grapes	0.0%	Strawberries	0.1%	0.1%	
	0.1%	GEMS/Food G06	0.02	0.0%	Table grapes	0.0%	Apples	0.0%	Pears	0.1%	0.1%	
	0.1%	FR infant	0.02	0.1%	Apples	0.0%	Pears	0.0%	Strawberries	0.1%	0.1%	
	0.1%	UK infant	0.02	0.1%	Apples	0.0%	Pears	0.0%	Strawberries	0.1%	0.1%	
	0.1%	LT adult	0.02	0.1%	Apples	0.0%	Pears	0.0%	Strawberries	0.1%	0.1%	
	0.1%	GEMS/Food G10	0.02	0.0%	Apples	0.0%	Wine grapes	0.0%	Table grapes	0.1%	0.1%	
	0.1%	ES child	0.02	0.0%	Apples	0.0%	Pears	0.0%	Strawberries	0.1%	0.1%	
	0.1%	FI 3 yr	0.02	0.0%	Apples	0.0%	Strawberries	0.0%	Table grapes	0.1%	0.1%	
	0.1%	UK adult	0.02	0.0%	Wine grapes	0.0%	Apples	0.0%	Pears	0.1%	0.1%	
	0.1%	UK vegetarian	0.02	0.0%	Wine grapes	0.0%	Apples	0.0%	Pears	0.1%	0.1%	
	0.1%	ES adult	0.02	0.0%	Apples	0.0%	Wine grapes	0.0%	Pears	0.1%	0.1%	
	0.1%	SE general	0.02	0.0%	Apples	0.0%	Pears	0.0%	Strawberries	0.1%	0.1%	
	0.0%	IT toddler	0.01	0.0%	Apples	0.0%	Pears	0.0%	Strawberries	0.0%	0.0%	
	0.0%	FI 6 yr	0.01	0.0%	Apples	0.0%	Strawberries	0.0%	Pears	0.0%	0.0%	
	0.0%	IT adult	0.01	0.0%	Apples	0.0%	Pears	0.0%	Table grapes	0.0%	0.0%	
	0.0%	FI adult	0.01	0.0%	Apples	0.0%	Wine grapes	0.0%	Strawberries	0.0%	0.0%	
	0.0%	IE child	0.00	0.0%	Apples	0.0%	Table grapes	0.0%	Pears	0.0%	0.0%	
	Conclusion: The estimated long-term dietary intake (TMDI/NEDI/IEDI) was below the ADI. The long-term intake of residues of Thymol is unlikely to present a public health concern.											

A 3.2 IESTI calculations - Raw commodities

International Estimate of Short-Term Intake (IESTI) for thymol calculated using EFSA PRIMo rev.3.1 (normal mode)

Acute risk assessment /children		Acute risk assessment / adults / general population		Acute risk assessment /children		Acute risk assessment / adults / general population		
Details - acute risk assessment /children		Details - acute risk assessment/adults		Hide IESTI new calculations		Show IESTI new calculations		
The acute risk assessment is based on the ARID. The calculation is based on the large portion of the most critical consumer group.				IESTI new calculations: The calculation is performed with the MRL and the peeling/processing factor (PF), taking into account the residue in the edible portion and/or the conversion factor for the residue definition (CF). For case 2a, 2b and 3 calculations a variability factor of 3 is used. Since this methodology is not based on internationally agreed principles, the results are considered as indicative only. Since this methodology is not based on internationally agreed principles, the results are considered as indicative only.				
Show results for all crops								
Unprocessed commodities	Results for children No. of commodities for which ARID/ADI is exceeded (IESTI):		---		Results for adults No. of commodities for which ARID/ADI is exceeded (IESTI):		---	
	IESTI		IESTI		IESTI new		IESTI new	
	Highest % of ARID/ADI	Commodities	MRL / input for RA (mg/kg)	Exposure (µg/kg bw)	Highest % of ARID/ADI	Commodities	MRL / input for RA (mg/kg)	Exposure (µg/kg bw)
	2%	Potatoes	0.01 / 0.01	1.5	0.5%	Head cabbages	0.01 / 0.01	0.42
	2%	Melons	0.01 / 0.01	1.5	0.5%	Watermelons	0.01 / 0.01	0.41
	2%	Pears	0.01 / 0.01	1.4	0.5%	Melons	0.01 / 0.01	0.39
	2%	Oranges	0.01 / 0.01	1.3	0.5%	Milk: Cattle	0.01 / 0.01	0.39
	2%	Milk: Cattle	0.01 / 0.01	1.2	0.4%	Swedes/rutabagas	0.01 / 0.01	0.34
	2%	Watermelons	0.01 / 0.01	1.2	0.4%	Table grapes	0.01 / 0.01	0.34
	1%	Apples	0.01 / 0.01	1.1	0.4%	Oranges	0.01 / 0.01	0.31
1%	Pineapples	0.01 / 0.01	1.0	0.4%	Pears	0.01 / 0.01	0.31	
1%	Bananas	0.01 / 0.01	0.97	0.4%	Potatoes	0.01 / 0.01	0.30	
1%	Peaches	0.01 / 0.01	0.95	0.4%	Pineapples	0.01 / 0.01	0.30	
1.0%	Mangoes	0.01 / 0.01	0.79	0.4%	Yams	0.01 / 0.01	0.28	
1.0%	Grapefruits	0.01 / 0.01	0.79	0.4%	Apples	0.01 / 0.01	0.28	
0.9%	Table grapes	0.01 / 0.01	0.73	0.3%	Cucumbers	0.01 / 0.01	0.28	
0.8%	Cucumbers	0.01 / 0.01	0.66	0.3%	Aubergines/egg plants	0.01 / 0.01	0.27	
0.8%	Carrots	0.01 / 0.01	0.63	0.3%	Mangoes	0.01 / 0.01	0.26	
Expand/collapse list								
Total number of commodities exceeding the ARID/ADI in children and adult diets (IESTI calculation)								
				Total number of commodities found exceeding the ARID/ADI in children and adult diets (IESTI new calculation)				
Processed commodities	Results for children No. of processed commodities for which ARID/ADI is exceeded (IESTI):		---		Results for adults No. of processed commodities for which ARID/ADI is exceeded (IESTI):		---	
	IESTI		IESTI		IESTI new		IESTI new	
	Highest % of ARID/ADI	Processed commodities	MRL / input for RA (mg/kg)	Exposure (µg/kg bw)	Highest % of ARID/ADI	Processed commodities	MRL / input for RA (mg/kg)	Exposure (µg/kg bw)
	1%	Sugar beets (root) / sugar	0.01 / 0.12	1.1	0.7%	Pumpkins / boiled	0.01 / 0.01	0.55
	1%	Potatoes / fried	0.01 / 0.01	0.93	0.5%	Sugar beets (root) / sugar	0.01 / 0.12	0.44
	1%	Pumpkins / boiled	0.01 / 0.01	0.89	0.5%	Cauliflowers / boiled	0.01 / 0.01	0.42
	1%	Witloofs / boiled	0.01 / 0.01	0.89	0.5%	Beetroots / boiled	0.01 / 0.01	0.39
	1.0%	Broccoli / boiled	0.01 / 0.01	0.79	0.4%	Celeries / boiled	0.01 / 0.01	0.34
	0.9%	Cauliflowers / boiled	0.01 / 0.01	0.70	0.4%	Apples / juice	0.01 / 0.01	0.33
	0.8%	Escaroles/broad-leaved endives / boiled	0.01 / 0.01	0.66	0.3%	Broccoli / boiled	0.01 / 0.01	0.24
0.7%	Potatoes / dried (flakes)	0.01 / 0.05	0.59	0.3%	Courgettes / boiled	0.01 / 0.01	0.23	
0.7%	Leeks / boiled	0.01 / 0.01	0.57	0.3%	Parsnips / boiled	0.01 / 0.01	0.21	
0.7%	Apples / juice	0.01 / 0.01	0.54	0.3%	Kohlrabies / boiled	0.01 / 0.01	0.21	
0.7%	Oranges / juice	0.01 / 0.01	0.53	0.3%	Wine grapes / juice	0.01 / 0.01	0.21	
0.6%	Turnips / boiled	0.01 / 0.01	0.51	0.3%	Escaroles/broad-leaved endives / boiled	0.01 / 0.01	0.20	
0.6%	Parsnips / boiled	0.01 / 0.01	0.51	0.2%	Florence fennels / boiled	0.01 / 0.01	0.19	
0.6%	Sweet potatoes / boiled	0.01 / 0.01	0.50	0.2%	Turnips / boiled	0.01 / 0.01	0.19	
0.6%	Florence fennels / boiled	0.01 / 0.01	0.45	0.2%	Cassava roots / boiled	0.01 / 0.01	0.19	
Expand/collapse list								
				Total number of commodities found exceeding the ARID/ADI in children and adult diets (IESTI new calculation)				
Conclusion: No exceedance of the toxicological reference value was identified for any unprocessed commodity. A short term intake of residues of Thymol is unlikely to present a public health risk. For processed commodities, no exceedance of the ARID/ADI was identified.								

