CONCLUSION ON PESTICIDE PEER REVIEW

Conclusion on the peer review of the pesticide risk assessment of the active substance plant oils/clove oil[1]

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SUMMARY

Clove oil is one of the 295 substances of the fourth stage of the review programme covered by Commission Regulation (EC) No 2229/2004[3], as amended by Commission Regulation (EC) No 1095/2007[4].

Clove oil was included in Annex I to Directive 91/414/EEC on 1 September 2009 pursuant to Article 24b of the Regulation (EC) No 2229/2004 (hereinafter referred to as 'the Regulation'), and has subsequently been deemed to be approved under Regulation (EC) No 1107/2009[5], in accordance with Commission Implementing Regulation (EU) No 540/2011[6], as amended by Commission Implementing Regulation (EU) No 541/2011[7]. In accordance with Article 25a of the Regulation, as amended by Commission Regulation (EU) No 114/2010[8], the European Food Safety Authority (EFSA) is required to deliver by 31 December 2012 its view on the draft review report submitted by the European Commission in accordance with Article 25(1) of the Regulation. This review report was established as a result of the initial evaluation provided by the designated rapporteur Member State in the Draft Assessment Report (DAR). The EFSA therefore organised a peer review of the DAR. The conclusions of the peer review are set out in this report.

The United Kingdom being the designated rapporteur Member State submitted the DAR on clove oil in accordance with the provisions of Article 22(1) of the Regulation, which was received by the EFSA on 7 January 2008. The peer review was initiated on 11 July 2008 by dispatching the DAR to the notifier Xeda International SA and on 24 February 2011 to the Member States for consultation. Following consideration of the comments received on the DAR, it was concluded that EFSA should conduct a focused peer review in the area of mammalian toxicology and deliver its conclusions on clove oil.

The conclusions laid down in this report were reached on the basis of the evaluation of the representative uses of clove oil as a fungicide and bactericide by post-harvest indoor applications as a

[1] On request from the European Commission, Question No EFSA-Q-2009-00276, approved on 16 December 2011.
[2] Correspondence: pesticides.peerreview@efsa.europa.eu
[3] OJ L 379, 24.12.2004, p.13
[4] OJ L 246, 21.9.2007, p.19
[5] OJ L 309, 24.11.2009, p.1
[6] OJ L 153, 11.6.2011, p.1
[7] OJ L 153, 11.6.2011, p.187
[8] OJ L 37, 10.2.2010, p.12

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drench on apples, pears and peaches, as proposed by the notifier. Full details of the representative uses can be found in Appendix A to this report.

Data gaps were identified in the section for physical and chemical properties and analytical methods.

In the section mammalian toxicology, two data gaps were identified: the first one for an acute inhalation study with eugenol, the second one for an assessment of the toxicological profile of clove oil covering a representative technical specification. In this context two critical areas of concern were indicated: it could not be demonstrated that the material tested in the toxicological studies is representative of the technical specification and no reference values could be derived for clove oil. Consequently, a risk assessment for operators and workers could not be performed.

The consumer risk assessment could not be conducted based on the information available and the lack of toxicological reference values for clove oil.

Studies on the fate and behaviour of clove oil and/or its active component eugenol in the environment are not available. A waiver for the environmental data and risk assessment has been proposed by the notifier on basis of the representative uses. It was concluded during the peer review that the waiver is appropriate if the product is used in a closed installation and the treatment solutions are treated as waste residues.

A data gap was identified in the ecotoxicology section to address the risk from clove oil to the organisms involved in the biological methods for sewage treatment plants.

KEY WORDS

Plant oil, clove oil, peer review, risk assessment, pesticide, fungicide, bactericide

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BACKGROUND

Clove oil is one of the 295 substances of the fourth stage of the review programme covered by Commission Regulation (EC) No 2229/2004[9], as amended by Commission Regulation (EC) No 1095/2007[10].

Clove oil was included in Annex I to Directive 91/414/EEC on 1 September 2009 pursuant to Article 24b of the Regulation (EC) No 2229/2004 (hereinafter referred to as 'the Regulation'), and has subsequently been deemed to be approved under Regulation (EC) No 1107/2009[11], in accordance with Commission Implementing Regulation (EU) No 540/2011[12], as amended by Commission Implementing Regulation (EU) No 541/2011[13]. In accordance with Article 25a of the Regulation, as amended by Commission Regulation (EU) No 114/2010[14] the European Food Safety Authority (EFSA) is required to deliver by 31 December 2012 its view on the draft review report submitted by the European Commission in accordance with Article 25(1) of the Regulation (European Commission, 2008). This review report was established as a result of the initial evaluation provided by the designated rapporteur Member State in the Draft Assessment Report (DAR). The EFSA therefore organised a peer review of the DAR. The conclusions of the peer review are set out in this report.

The United Kingdom being the designated rapporteur Member State submitted the DAR on clove oil in accordance with the provisions of Article 22(1) of the Regulation, which was received by the EFSA on 7 January 2008 (The United Kingdom, 2007). The peer review was initiated on 11 July 2008 by dispatching the DAR to the notifier Xeda International SA and on 24 February 2011 to the Member States for consultation and comments. In addition, the EFSA conducted a public consultation on the DAR. The comments received were collated by the EFSA and forwarded to the RMS for compilation and evaluation in the format of a Reporting Table. The notifier was invited to respond to the comments in column 3 of the Reporting Table. The comments and the notifier's response were evaluated by the RMS in column 3 of the Reporting Table.

The scope of the peer review was considered in a telephone conference between the EFSA, the RMS, and the European Commission on 20 June 2011. On the basis of the comments received and the RMS' evaluation thereof it was concluded that the EFSA should organise a consultation with Member State experts in the area of mammalian toxicology.

The outcome of the telephone conference, together with EFSA's further consideration of the comments is reflected in the conclusions set out in column 4 of the Reporting Table. All points that were identified as unresolved at the end of the comment evaluation phase and which required further consideration, including those issues to be considered in consultation with Member State experts, and the additional information to be submitted by the notifier, were compiled by the EFSA in the format of an Evaluation Table.

The conclusions arising from the consideration by the EFSA, and as appropriate by the RMS, of the points identified in the Evaluation Table, together with the outcome of the expert discussions where these took place, were reported in the final column of the Evaluation Table.

A final consultation on the conclusions arising from the peer review of the risk assessment took place with Member States via a written procedure in November – December 2011.

This conclusion report summarises the outcome of the peer review of the risk assessment on the active substance and the representative formulation evaluated on the basis of the representative uses as a fungicide and bactericide by post-harvest indoor applications as a drench on apples, pears and peaches,

[9] OJ L 379, 24.12.2004, p.13
[10] OJ L 246, 21.9.2007, p.19
[11] OJ L 309, 24.11.2009, p.1
[12] OJ L 153, 11.6.2011, p.1
[13] OJ L 153, 11.6.2011, p.187
[14] OJ L 37, 10.2.2010, p.12

as proposed by the notifier. A list of the relevant end points for the active substance as well as the formulation is provided in Appendix A. In addition, a key supporting document to this conclusion is the Peer Review Report, which is a compilation of the documentation developed to evaluate and address all issues raised in the peer review, from the initial commenting phase to the conclusion. The Peer Review Report (EFSA, 2011) comprises the following documents, in which all views expressed during the course of the peer review, including minority views, can be found:

- the comments received on the DAR,
- the Reporting Table (21 June 2011),
- the Evaluation Table (6 December 2011),
- the report of the scientific consultation with Member State experts
- the comments received on the assessment of the points of clarification,
- the comments received on the draft EFSA conclusion.

Given the importance of the DAR including its addendum (compiled version of October 2011 containing all individually submitted addenda (The United Kingdom, 2011)) and the Peer Review Report, both documents are considered respectively as background documents A and B to this conclusion.

THE ACTIVE SUBSTANCE AND THE FORMULATED PRODUCT

Clove oil is a common name for an extract from the flower buds of *Syzygium aromaticum*. There is no ISO common name for this substance. Clove oil is a complex mixture of chemical substances, the main component being eugenol, 4-allyl-2-methoxyphenol (IUPAC).

The representative formulated product for the evaluation was 'Bioxeda', an emulsifiable concentrate (EC), containing 18 % eugenol.

The representative uses evaluated comprise post-harvest indoor applications in water as a drench, as a fungicide and bactericide for the control of various post-harvest diseases on apples, pears and peaches. The applications on citrus and as a hot fog to machines, bins, storage rooms and silos were not supported by appropriate data and no evaluation was performed, therefore these uses were not considered in the current assessment. Full details of the representative uses can be found in the list of end points in Appendix A.

CONCLUSIONS OF THE EVALUATION

1. Identity, physical/chemical/technical properties and methods of analysis

The following guidance documents were followed in the production of this conclusion: SANCO/3030/99 rev.4 (European Commission, 2000) and SANCO/825/00 rev. 7 (European Commission, 2004a).

Clove oil was approved with a minimum content of 800 g/kg eugenol. It should be noted however, that eugenol is also considered under Council Directive 91/414/EEC as a new active substance. If clove oil is considered the active substance, then all the components identified in the five batch analysis should be specified. As a consequence, a data gap has been indicated for the specification of the identified components of clove oil. No FAO specification exists.

A data gap was also identified for 5-batch data to confirm the absence of methyl eugenol, obtained with validated analytical methods.

The assessment of the data package revealed no issues that need to be included as critical areas of concern with respect to the identity, physical, chemical and technical properties of clove oil or the representative formulation, however data gaps were identified for the determination of the spectral data for the main component eugenol including determination of absorbance maxima, and for the determination of photochemical degradation, dissociation constant and stability in the air. A data gap was also identified for the determination of the low temperature stability of the EC formulation. It is noted that no information was given on the level of microbial contamination and the mechanism for the control of such contamination or its possible increase on storage. The main data regarding the identity of clove oil and its physical and chemical properties are given in Appendix A.

Adequate analytical methods are available for the determination of eugenol in clove oil technical material. A method is available for the determination of eugenol in the representative formulation.

The need for methods of analysis for monitoring of eugenol in food of plant and animal origin is currently open; pending on the final residue definition analytical methods might be required. The need for methods of analysis for monitoring eugenol in the environment has been waived due to the use pattern of the compound. A method for residues in body fluids and tissues is not required as the active substance is not classified as toxic or very toxic.

2. Mammalian toxicity

The following guidance document was followed in the production of this conclusion: SANCO/222/2000 rev. 7 (European Commission, 2004b).

Clove oil was discussed at the Pesticides Peer Review Experts' Meeting 88 in September 2011.

In the DAR, a detailed evaluation has been provided for the main component of clove oil, eugenol, representing minimum 80 % of the technical specification. However, the material tested in the toxicological studies is not considered to cover the technical specification for clove oil (including up to 20 % of other components) and it cannot be concluded whether the reference values derived for eugenol will also apply to clove oil (critical areas of concern). Consequently, an assessment of the toxicological profile of clove oil, compliant with the representative technical specification, has been identified as a data gap.

If confirmed to be present in the technical specification (see data gap in section 1), the impurity methyl eugenol will have to be considered as toxicologically relevant.

Rapidly and extensively absorbed, eugenol is excreted almost exclusively in urine. The available acute toxicity data indicate that eugenol is harmful if swallowed (R22 proposed), irritant for the skin and the eyes (R36/38 proposed), and a skin sensitiser (R43 proposed). Considering the high volatility of eugenol, a data gap has been identified for an acute inhalation study. In a 13-week oral study with rats, a NOAEL of 600 mg/kg bw/day was triggered by decreased body weight gain (≥ 10 %) in males. Based on the available data, eugenol is unlikely to be genotoxic at exposures that do not result in cytotoxicity and saturation of conjugation pathways. In the 2-year studies with rats and mice there was no evidence of a carcinogenic potential relevant to humans, and the systemic NOAEL is 300 mg/kg bw/day for rats and 450 mg/kg bw/day for mice. In rats and rabbits, the maternal and developmental NOAELs were 100 and 250 mg/kg bw/day respectively, for both species, with no teratogenic effect. No indication of a neurotoxic potential was observed in the available studies.

Based on the available data, reference values were derived for eugenol. The Acceptable Daily Intake (ADI) and Acceptable Operator Exposure Level (AOEL) are 1.0 mg/kg bw/day, based on the maternal NOAEL in the developmental studies and applying a safety factor of 100. No Acute Reference Dose (ARfD) was considered necessary. Based on the available data no reference values could be established for clove oil.

Exposure estimates for eugenol during post-harvest treatment of apples by drenching were made available. For the operators, the dermal exposure was estimated based on the UK POEM and German model for the mixing and loading phase, and with the "timber treatment model" for biocides for the application phase (ECB, 2002). In addition, considering the high volatility of eugenol, the inhalation exposure during application was estimated based on the saturated vapour concentration, with a correction for the molar fraction of eugenol in the dilution. For the workers ensuring the levelling of fruits during the treatment, the hand exposure estimates from the timber treatment model were provided. However, since it could not be demonstrated that the AOEL derived for eugenol will also apply to clove oil, the risk assessment for operators and workers could not be performed (critical area of concern). Taking into account the indoor uses, the exposure of bystanders is considered unlikely.

3. Residues

The assessment in the residue section below is based on the guidance documents listed in the document 1607/VI/97 rev.2 (European Commission, 1999), and the JMPR recommendations on livestock burden calculations stated in the 2004 and 2007 JMPR reports (JMPR, 2004 and 2007).

Clove oil is intended to be used on apples, pears and peaches as a post-harvest treatment after drenching of the fruits with a treatment solution at the critical dose rate of 450 g clove oil/hL. The RMS considered that given the post-harvest drench use, the metabolism of clove oil and its main component eugenol would be very limited and that eugenol should be used as the marker compound of the total residues on fruits. EFSA is of the opinion that the nature of the residues in fruits not only after treatment but also over a sufficiently long period of storage representative of the usual commercial storage period has to be addressed, as it is not excluded that the metabolic profile of clove oil might give a different picture over the storage time period. Therefore a data gap was identified to provide a

metabolism study on fruits representative of the normal commercial storage periods. The residue definitions for monitoring and risk assessment in fruits should be proposed once the nature of the residues in fruits after treatment and after a realistic period of storage has been clearly elucidated.

Two supervised residue trials were conducted on peaches and apples, respectively, as a dipping at dose rates of 400 and 120 g clove oil/hL. These trials determined the eugenol residue levels in apples and peaches just after treatment. EFSA considered that these trials did not comply with the representative uses and therefore a data gap was identified to provide 4 residue trials respectively on apples/pears and peaches as a drenching post-harvest application, where samples are analysed in accordance with the agreed residue definitions for monitoring and risk assessment once the metabolism data will have been submitted at the different time points covering the commercial storage periods. Furthermore, a data gap was identified for appropriate storage stability data to cover the length of time the residue samples were stored frozen. The nature of the residues in processed fruits under the standard hydrolytic conditions representative of pasteurisation, baking/cooking and sterilisation should also be addressed (data gap). A data gap has also been identified to address the transfer of the residues in processed fruit commodities.

The RMS considered that a livestock exposure assessment is not triggered, since apples treated with clove oil are intended for direct human consumption only and not for consumption by animals. However, a question remains over the fate of treated apples that could not be marketed and whether or not these leftover apples can be destined for industrial processing into apple juice. In that specific case, it is not excluded that apple pomace may contain clove oil residues. It is noted that any restriction with respect to the use of treated apples in animal feeding is not in the remit of the risk assessor. Therefore EFSA is of the opinion that a 'worst-case' assessment should be carried out, assuming that livestock may be exposed to clove oil residues from treated apples. Based on the outcome of the outstanding data on the nature and the magnitude of the residues in apple wet pomace, a data gap is identified to calculate the ruminant's dietary burden. It is therefore not excluded that a ruminant metabolism study might be triggered.

The consumer dietary intake risk assessment could not be concluded and resulted in a critical area of concern based on the following outstanding issues:

- No residue definition for monitoring or risk assessment in fruits could be proposed.
- Data gaps were identified for complete residue database for apples or pears and peaches complying with the agreed residue definitions in fruit crops.
- The nature and magnitude of the residues in processed commodities and potentially in livestock matrices could not be finalised.
- Reference values for clove oil could not be established (see section 2).

4. Environmental fate and behaviour

The main active component of clove oil is the active substance eugenol (80 %). Other active components of clove oil may need to be considered once the data gap identified in the identity section is fulfilled.

Eugenol is stable to hydrolysis. No ready biodegradation study is available, either for eugenol or for clove oil, and therefore they have been considered as not readily biodegradable.

Studies on the degradation / dissipation of clove oil and/or its active component eugenol in soil and water / sediment are not available in the dossier.

A waiver for the environmental data and risk assessment has been proposed by the notifier on basis of the representative uses. It has been agreed during the peer review that the waiver is appropriate and negligible exposure is expected if the product is used for post-harvest treatment of fruits by drenching in a closed installation and the treatment solutions are treated as waste residues. However, depending on the kind of waste treatment used, exposure of sewage treatment plants cannot be excluded.

5. Ecotoxicology

Eugenol is the main active component of clove oil. No ecotoxicological toxicity studies were submitted, with the exception of the aquatic toxicity studies. Based on the available toxicity data clove oil (eugenol) is toxic to aquatic organisms.

Due to the negligible levels of exposure arising from the representative uses of clove oil as an indoor post-harvest drench to fruits (see section 4), the risk to birds and mammals, aquatic organisms, bees, non-target arthropods, earthworms, soil macro- and micro-organisms and terrestrial non-target plants is considered to be low.

The exposure of biological methods for sewage treatment plants from the representative uses of clove oil cannot be excluded. No activated sludge respiration inhibition test was presented, and only an unreliable ready biodegradation test was submitted with the plant protection product. Therefore, the risk from clove oil to the organisms involved in the biological methods for sewage treatment plants needs to be addressed and a data gap was identified.

6. Overview of the risk assessment of compounds listed in residue definitions triggering assessment of effects data for the environmental compartments

6.1. Soil

Compound (name and/or code)	Persistence	Ecotoxicology
Eugenol[a] Considering the representative uses it has been assessed that waivers for further environmental data and risk assessment are acceptable provided the product is used in closed installations and the drenching treatment solutions are treated as waste residues.	No data available.	The risk to soil organisms was considered as low.

(a): Other active components of clove oil may need to be considered once the data gap identified for the identity is fulfilled.

6.2. Ground water

Compound (name and/or code)	Mobility in soil	>0.1 µg/L 1m depth for the representative uses (at least one FOCUS scenario or relevant lysimeter)	Pesticidal activity	Toxicological relevance	Ecotoxicological activity
Eugenol[a] Considering the representative uses it has been assessed that waivers for further environmental data and risk assessment are acceptable provided the product is used in closed installations and the drenching treatment solutions are treated as waste residues.	No data available.	No data available.	Yes	Yes	Eugenol is toxic to aquatic organisms. The risk to aquatic organisms was considered as low.

(a): Other active components of clove oil may need to be considered once the data gap identified for the identity is fulfilled.

6.3. Surface water and sediment

Compound (name and/or code)	Ecotoxicology
Eugenol[a] Considering the representative uses it has been assessed that waivers for further environmental data and risk assessment are acceptable provided the product is used in closed installations and the drenching treatment solutions are treated as waste residues.	Eugenol is toxic to aquatic organisms. The risk to aquatic organisms was considered as low.

(a): Other active components of clove oil may need to be considered once the data gap identified for the identity is fulfilled.

6.4. Air

Compound (name and/or code)	Toxicology
Eugenol[a] Considering the representative uses it has been assessed that waivers for further environmental data and risk assessment are acceptable provided the product in used is closed installations and the drenching treatment solutions are treated as waste residues.	No data available. Data gap for acute inhalation study with eugenol.

(a): Other active components of clove oil may need to be considered once the data gap identified for the identity is fulfilled.

7. List of studies to be generated, still ongoing or available but not peer reviewed

This is a complete list of the data gaps identified during the peer review process, including those areas where a study may have been made available during the peer review process but not considered for procedural reasons (without prejudice to the provisions of Article 7 of Directive 91/414/EEC concerning information on potentially harmful effects).

- Specification of the identified components of the clove oil considered as active substance (relevant for all representative uses evaluated; submission date proposed by the notifier: unknown; see section 1)
- 5-batch data to confirm the absence of methyl eugenol, obtained with validated analytical methods (relevant for all representative uses evaluated; submission date proposed by the notifier: unknown; see section 1)
- UV, IR, NMR and MS spectra for the main component eugenol, including determination of absorbance maxima (relevant for all representative uses evaluated; submission date proposed by the notifier: unknown; see section 1)
- Photochemical degradation (relevant for all representative uses evaluated; submission date proposed by the notifier: unknown; see section 1)
- Dissociation constant (relevant for all representative uses evaluated; submission date proposed by the notifier: unknown; see section 1)
- Stability in the air (relevant for all representative uses evaluated; submission date proposed by the notifier: unknown; see section 1)
- Low temperature stability of the EC formulation (relevant for all representative uses evaluated; submission date proposed by the notifier: unknown; see section 1)
- Assessment of the toxicological profile of clove oil compliant with the technical specification, including risk assessment for operators and workers (relevant for all representative uses evaluated; submission date proposed by the notifier: unknown; see section 2)
- Acute inhalation study with eugenol (relevant for all representative uses evaluated; submission date proposed by the notifier: unknown; see section 2)
- A new metabolism study on fruit crops representative of normal commercial storage periods (relevant for all representative uses evaluated; data gap identified by EFSA in September 2011, submission date proposed by the notifier: unknown; see section 3)
- Four supervised residue trials respectively on apples/pears and peaches - drenching post-harvest treatment where samples are analysed in accordance with the agreed residue definitions for monitoring and risk assessment (relevant for all representative uses evaluated; data gap identified by EFSA in September 2011, submission date proposed by the notifier: unknown; see section 3)
- Storage stability data to cover the maximum storage time interval of the samples from the supervised residue trials in apples/pears and peaches (relevant for all representative uses evaluated; data gap identified by EFSA in September 2011, submission date proposed by the notifier: unknown; see section 3)
- A standard hydrolysis study representative of pasteurisation, baking/cooking and sterilisation investigating the nature of the residues in processed fruit commodities (relevant for all representative uses evaluated; data gap identified by EFSA in September 2011, submission date proposed by the notifier: unknown; see section 3)

- The magnitude of the residues in processed fruit commodities needs to be addressed (relevant for all representative uses evaluated; data gap identified by EFSA in September 2011, submission date proposed by the notifier: unknown; see section 3)

- The ruminant's dietary burden needs to be calculated (relevant for the representative use on apples; data gap identified by EFSA in September 2011, submission date proposed by the notifier: unknown; see section 3)

- The overall consumer risk assessment to be performed once the identified outstanding data are submitted (relevant for all representative uses evaluated; data gap identified by EFSA in September 2011, submission date proposed by the notifier: unknown; see sections 2 and 3)

- The risk from the exposure of clove oil to the organisms involved in the biological methods for sewage treatment plants needs to be addressed (relevant for all representative uses evaluated; submission date proposed by the notifier: unknown; see section 5)

8. Particular conditions proposed to be taken into account to manage the risk(s) identified

- No fate and behaviour data and no environmental risk assessment are available assuming the product will be only used in a closed installation as a post-harvest treatment of fruits by drenching and the treatment solutions are treated as waste residues. Therefore management measures tailored to local practice and legislation need to be put in place to control the waste disposal of spent application solution and prevent accidental spillage entering sewers or surface water drains. Only the use with drench application has been considered in the peer review.

9. Concerns

9.1. Issues that could not be finalised

An issue is listed as an issue that could not be finalised where there is not enough information available to perform an assessment, even at the lowest tier level, for the representative uses in line with the Uniform Principles of Annex VI to Directive 91/414/EEC and where the issue is of such importance that it could, when finalised, become a concern (which would also be listed as a critical area of concern if it is of relevance to all representative uses).

None.

9.2. Critical areas of concern

An issue is listed as a critical area of concern where there is enough information available to perform an assessment for the representative uses in line with the Uniform Principles of Annex VI to Directive 91/414/EEC, and where this assessment does not permit to conclude that for at least one of the representative uses it may be expected that a plant protection product containing the active substance will not have any harmful effect on human or animal health or on groundwater or any unacceptable influence on the environment.

An issue is also listed as a critical area of concern where the assessment at a higher tier level could not be finalised due to a lack of information, and where the assessment performed at the lower tier level does not permit to conclude that for at least one of the representative uses it may be expected that a plant protection product containing the active substance will not have any harmful effect on human or animal health or on groundwater or any unacceptable influence on the environment.

1. The material tested in the toxicological studies (eugenol) has not been demonstrated to be representative of the technical specification (unknown contribution of other components).

2. Reference values are not available for clove oil, therefore the risk assessment for operators and workers could not be performed.

3. The consumer risk assessment could not be conducted based on the information available and the lack of toxicological reference values for clove oil.

9.3. Overview of the concerns identified for each representative use considered

(If a particular condition proposed to be taken into account to manage an identified risk, as listed in section 8, has been evaluated as being effective, then 'risk identified' is not indicated in this table.)

All columns are grey as the material tested in the toxicological studies has not been demonstrated to be representative of the technical specification.

Representative use		Post-harvest indoor applications by drenching as a fungicide and bactericide on **apples/pears**	Post-harvest indoor applications by drenching as a fungicide and bactericide on **peaches**
Operator risk	Risk identified	X[2]	X[2]
	Assessment not finalised		
Worker risk	Risk identified	X[2]	X[2]
	Assessment not finalised		
Bystander risk	Risk identified		
	Assessment not finalised		
Consumer risk	Risk identified	X[3]	X[3]
	Assessment not finalised		
Risk to wild non target terrestrial vertebrates	Risk identified		
	Assessment not finalised		
Risk to wild non target terrestrial organisms other than vertebrates	Risk identified		
	Assessment not finalised		
Risk to aquatic organisms	Risk identified		
	Assessment not finalised		
Groundwater exposure active substance	Legal parametric value breached		
	Assessment not finalised		
Groundwater exposure metabolites	Legal parametric value breached		
	Parametric value of 10µg/L[(a)] breached		
	Assessment not finalised		
Comments/Remarks			

The superscript numbers in this table relate to the numbered points indicated within section 9.1 and 9.2. Where there is no superscript number, see sections 2 to 6 for more explanation.

(a): Value for non relevant metabolites prescribed in SANCO/221/2000-rev 10-final, European Commission, 2003

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APPENDICES

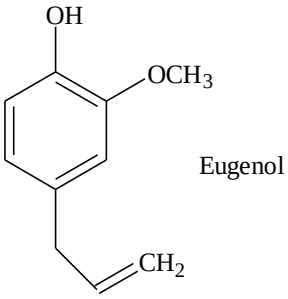
APPENDIX A – LIST OF END POINTS FOR THE ACTIVE SUBSTANCE AND THE REPRESENTATIVE FORMULATION

Identity, Physical and Chemical Properties, Details of Uses, Further Information

Active substance (ISO Common Name) ‡	Clove Oil, Essential Clove Oil An ISO common name is not available.
Function (*e.g.* fungicide)	Fungicide and bactericide
Rapporteur Member State	UK
Co-rapporteur Member State	None

Identity (Annex IIA, point 1)

Chemical name (IUPAC) ‡	4-allyl-2-methoxyphenol (for eugenol, the main component).
Chemical name (CA) ‡	2-methoxy-4-(2-propen-1-yl)phenol (for eugenol, the main component).
CIPAC No ‡	906
CAS No ‡	8000-34-8 (US) & 84961-50-2 (EU) (clove oil) 97-53-0 (eugenol – main component)
EC No (EINECS or ELINCS) ‡	284-638-7 (clove oil), 202-589-1 (eugenol)
FAO Specification (including year of publication) ‡	Not available
Minimum purity of the active substance as manufactured ‡	Clove oil contains minimum 80 % eugenol Open for the other components.
Identity of relevant impurities (of toxicological, ecotoxicological and/or environmental concern) in the active substance as manufactured	Open
Molecular formula ‡	Not applicable to the substance clove oil Molecular formula of the major component eugenol is $C_{10}H_{12}O_2$
Molecular mass ‡	Not applicable to the substance clove oil Molecular mass of the major component eugenol is 164
Structural formula ‡	Not applicable to the substance clove oil Structure for the major component eugenol is given below:



Eugenol

Physical and chemical properties (Annex IIA, point 2)

Melting point (state purity) ‡	-21.15 °C (99 % eugenol)
Boiling point (state purity) ‡	232.85 °C (99 % eugenol)
Temperature of decomposition (state purity)	No information
Appearance (state purity) ‡	99 % eugenol is pale yellow liquid 98 % eugenol is an amber liquid
Vapour pressure (state temperature, state purity) ‡	12.2 Pa at 25 °C (99% eugenol)
Henry's law constant ‡	0.2 Pa m^3 mol^{-1}
Solubility in water (state temperature, state purity and pH) ‡	2.17 g/L at 20 °C (pH) (99 % eugenol)
Solubility in organic solvents ‡ (state temperature, state purity)	eugenol is stated to be miscible in alcohol, ether, chloroform; soluble in acetic acid, alkali hydroxide solutions
Surface tension ‡ (state concentration and temperature, state purity)	49.4 mN/m at 22 °C (1.01 g/l solution) (eugenol of unknown purity)
Partition co-efficient ‡ (state temperature, pH and purity)	log P_{ow} at pH 4 = 2.25 log P_{ow} at pH 7 = 2.04 log P_{ow} at pH 10 = 2.01 (99 % eugenol)
Dissociation constant (state purity) ‡	Data gap
UV/VIS absorption (max.) incl. ε ‡ (state purity, pH)	Data gap. Eugenol has a chromaphore and therefore UV spectral information must be provided.
Flammability ‡ (state purity)	121°C
Explosive properties ‡ (state purity)	Predicted negative based on functional groups present.
Oxidising properties ‡ (state purity)	Not an oxidiser

Summary of representative uses evaluated clove oil (main component eugenol)

Crop and/ or situation (a)	Member State or Country	Product name	F G or I (b)	Pests or Group of pests controlled (c)	Preparation		Application				Application rate per treatment (for explanation see the text in front of this section)			PHI (days) (m)	Remarks
					Type (d-f)	Conc. of a.s. (i)	method kind (f-h)	growth stage & season (j)	number min/ max (k)	interval between applications (min)	g a.s./hL min – max (l)	water L/ha min – max	g a.s./ha min – max (l)		
Apples and Pears	Northern and Southern Europe	BIOXEDA	I	*Gloeosporium* spp and *Penicillium* spp	EC	225 g/kg clove oil [180 g/kg eugenol]	Drencher	Post-harvest	1	N.C	90 - 450 g clove oil/hL [72 – 360 g eugenol/hL]	N.C	N.C	N.C	N.C.
Peaches	Northern and Southern Europe	BIOXEDA	I	*Gloeosporium* spp and *Penicillium* spp	EC	225 g/kg clove oil [180 g/kg eugenol]	Drencher	Post-harvest	1	N.C	90 - 450 g clove oil/hL [72 – 360 g eugenol/hL]	N.C	N.C	N.C	N.C.

(a) For crops, the EU and Codex classifications (both) should be taken into account; where relevant, the use situation should be described (e.g. fumigation of a structure)
(b) Outdoor or field use (F), greenhouse application (G) or indoor application (I)
(c) *e.g.* biting and suckling insects, soil born insects, foliar fungi, weeds
(d) *e.g.* wettable powder (WP), emulsifiable concentrate (EC), granule (GR)
(e) GCPF Codes - GIFAP Technical Monograph No 2, 1989
(f) All abbreviations used must be explained
(g) Method, e.g. high volume spraying, low volume spraying, spreading, dusting, drench
(h) Kind, *e.g.* overall, broadcast, aerial spraying, row, individual plant, between the plant- type of equipment used must be indicated
(i) g/kg or g/L. Normally the rate should be given for the active substance (according to ISO) and not for the variant in order to compare the rate for same active substances used in different variants (e.g. fluoroxypyr). **In certain cases, where only one variant is synthesised, it is more appropriate to give the rate for the variant (e.g. benthiavalicarb-isopropyl).**
(j) Growth stage at last treatment (BBCH Monograph, Growth Stages of Plants, 1997, Blackwell, ISBN 3-8263-3152-4), including where relevant, information on season at time of application
(k) Indicate the minimum and maximum number of application possible under practical conditions of use
(l) The values should be given in g or kg whatever gives the more manageable number (e.g. 200 kg/ha instead of 200 000 g/ha or 12.5 g/ha instead of 0.0125 kg/ha
(m) PHI - minimum pre-harvest interval

Methods of Analysis

Analytical methods for the active substance (Annex IIA, point 4.1)

Technical as (analytical technique)	Eugenol (main component) determined by GC-MS (scan mode m/z 29-300)
Impurities in technical as (analytical technique)	Open for potential relevant impurities.
Plant protection product (analytical technique)	Eugenol determined by GC-FID after dissolution in acetone.

Analytical methods for residues (Annex IIA, point 4.2)

Residue definitions for monitoring purposes

Food of plant origin		Open
Food of animal origin		Open (for ruminants only)
Soil		Not applicable
Water	surface	Not applicable
	drinking/ground	Not applicable
Air		Not applicable

Monitoring/Enforcement methods

Food/feed of plant origin (analytical technique and LOQ for methods for monitoring purposes)	Open
Food/feed of animal origin (analytical technique and LOQ for methods for monitoring purposes)	Open (for ruminants only)
Soil (analytical technique and LOQ)	Not required
Water (analytical technique and LOQ)	Not required
Air (analytical technique and LOQ)	Not required
Body fluids and tissues (analytical technique and LOQ)	Not required

Classification and proposed labelling with regard to physical and chemical data (Annex IIA, point 10)

	RMS/peer review proposal
Active substance	Not required

Impact on Human and Animal Health

Absorption, distribution, excretion and metabolism (toxicokinetics) (Annex IIA, point 5.1)

Rate and extent of oral absorption ‡	Clove oil: no data available Eugenol: rapid (>70 % excreted within 3h); extensive (>90 % in urine within 24h) – humans 2 mg/kg bw
Distribution ‡	No data available
Potential for accumulation ‡	Clove oil: no data available Eugenol: minimal
Rate and extent of excretion ‡	Clove oil: no data available Eugenol: extensive and rapid (> 90 % in urine in 24 hours)
Metabolism in animals ‡	Clove oil: no data available Eugenol: conjugation and hydroxylation
Toxicologically relevant compounds ‡ (animals and plants)	Eugenol Insufficient data available for the other components of clove oil
Toxicologically relevant compounds ‡ (environment)	Eugenol Insufficient data available for the other components of clove oil

Acute toxicity (Annex IIA, point 5.2)

Rat LD_{50} oral ‡	Clove oil: no data available Eugenol: 1930 mg/kg bw	 R22
Dog LD_{50} oral	Eugenol: < 2000 mg/kg bw	
Rat LD_{50} dermal ‡	No data available	
Rat LC_{50} inhalation ‡	No data available Eugenol: data gap	
Skin irritation ‡	Clove oil: no data available Eugenol: Irritating	 R38
Eye irritation ‡	Clove oil: no data available Eugenol: Irritating (no data, based on skin irritation)	 R36
Skin sensitisation ‡	Clove oil: no data available Eugenol: Sensitising (Maximisation test with guinea pigs, Local Lymph Node Assay with mice, human reports)	 R43

Short term toxicity (Annex IIA, point 5.3)

Target / critical effect ‡	Clove oil: no data available Eugenol: Reduced body weight gain (rat)	
Relevant oral NOAEL ‡	Dog: 100 mg eugenol/kg bw/d (highest dose tested, 10 administrations) Rat: 600 mg eugenol/kg bw/d (13-wk) Mouse: 900 mg eugenol/kg bw/d (13-wk)	
Relevant dermal NOAEL ‡	No data available	
Relevant inhalation NOAEL ‡	No data available	

Genotoxicity ‡ (Annex IIA, point 5.4)

Clove oil	No data available	
Eugenol	Positive at cytotoxic concentrations *in vitro* (gene mutation, DNA adducts and chromosomal aberrations in mammalian cells) and at very high doses *in vivo* (micronucleus). Unlikely to be genotoxic at exposures that do not result in cytotoxicity and saturation of conjugation pathways.	

Long term toxicity and carcinogenicity (Annex IIA, point 5.5)

Target/critical effect ‡	Clove oil: no data available Eugenol: spleen haemosiderosis, uterine cystic hyperplasia (rat); focal inflammation of the kidney, granulomatous inflammation of the lung (mouse)	
Relevant NOAEL ‡	300 mg eugenol/kg bw/d (2-yr rat) 450 mg eugenol/kg bw/d (2-yr mouse)	
Carcinogenicity ‡	No carcinogenic potential for humans	

Reproductive toxicity (Annex IIA, point 5.6)

Reproduction toxicity

Reproduction target / critical effect ‡	No data available	
Relevant parental NOAEL ‡	No data available	
Relevant reproductive NOAEL ‡	No data available	
Relevant offspring NOAEL ‡	No data available	

Developmental toxicity

Developmental target / critical effect ‡	Clove oil: no data available Eugenol: Developmental: decreased foetal weight and delayed ossification (rat), increased post-implantation loss (rabbit) Maternal: clinical signs (rat, rabbit) and reduced food consumption (rabbit)	
Relevant maternal NOAEL ‡	100 mg eugenol/kg bw/d (rat, rabbit)	
Relevant developmental NOAEL ‡	250 mg eugenol/kg bw/d (rat, rabbit)	

Neurotoxicity (Annex IIA, point 5.7)

Acute neurotoxicity ‡	Clove oil: no data available	
Repeated neurotoxicity ‡	Eugenol: no data available, no indication of a neurotoxic potential for eugenol in the available database.	
Delayed neurotoxicity ‡		

Other toxicological studies (Annex IIA, point 5.8)

Mechanism studies ‡	Clove oil: no data available Eugenol: glutathione pre-cursors provide protection against cytotoxicity *in vitro.*
Studies performed on metabolites or impurities ‡	Impurities have uses as food flavours. Insufficient data available.

Medical data ‡ (Annex IIA, point 5.9)

Reports of skin sensitisation in humans

Summary (Annex IIA, point 5.10)	Value	Study	Safety factor
	No reference values can be derived for clove oil (data gap)		
ADI for eugenol‡	1.0 mg/kg bw/d	rat & rabbit developmental	100
AOEL for eugenol‡	1.0 mg/kg bw/d	rat & rabbit developmental	100
ARfD for eugenol‡	Not necessary		

Dermal absorption ‡ (Annex IIIA, point 7.3)

Formulation Bioxeda	100 % (default)

Exposure scenarios (Annex IIIA, point 7.2)

Operators and workers	The operator and worker risk assessment could not be concluded in the absence of reference values for clove oil. Data gap.
Bystanders	Exposure expected to be unlikely (indoor use).

Classification and proposed labelling with regard to toxicological data (Annex IIA, point 10)

	RMS/peer review proposal
Clove oil	R22 Harmful if swallowed R36 Irritating to eyes R38 Irritating to skin R43 May cause sensitisation by skin contact

Residues

Metabolism in plants (Annex IIA, point 6.1 and 6.7, Annex IIIA, point 8.1 and 8.6)

Plant groups covered	Data gap identified for a metabolism study on fruit crops (drenching post-harvest treatment) representative of the normal commercial storage periods.
Rotational crops	Not applicable as post-harvest treatment
Metabolism in rotational crops similar to metabolism in primary crops?	Not applicable as post-harvest treatment
Processed commodities	Data gap is identified for a standard hydrolysis study representative of pasteurisation, baking/cooking and sterilisation.
Residue pattern in processed commodities similar to residue pattern in raw commodities?	Open
Plant residue definition for monitoring	Open
Plant residue definition for risk assessment	Open
Conversion factor (monitoring to risk assessment)	Open

Metabolism in livestock (Annex IIA, point 6.2 and 6.7, Annex IIIA, point 8.1 and 8.6)

Animals covered	Open for ruminants. The leftover treated apples can be destined for juice processing and apple pomace used as a ruminant feed item. Based on the outcome of the calculated ruminant's dietary burden (data gap), a ruminant metabolism study might be required.
Time needed to reach a plateau concentration in milk and eggs	Open for milk
Animal residue definition for monitoring	Open (for ruminants only)
Animal residue definition for risk assessment	Open (for ruminants only)
Conversion factor (monitoring to risk assessment)	Open (for ruminants only)
Metabolism in rat and ruminant similar (yes/no)	Open
Fat soluble residue: (yes/no)	No (based on the log P_{ow} value)

Residues in succeeding crops (Annex IIA, point 6.6, Annex IIIA, point 8.5)

Not applicable as post harvest treatment

Stability of residues (Annex IIA, point 6 introduction, Annex IIIA, point 8 Introduction)

Data gap. Storage stability data (-18 °C) are required to cover the storage time period of the residue samples (if storage period >30 days).

Residues from livestock feeding studies (Annex IIA, point 6.4, Annex IIIA, point 8.3)

	Ruminant:	Poultry:	Pig:
	Conditions of requirement of feeding studies		
Expected intakes by livestock ≥ 0.1 mg/kg diet (dry weight basis) (yes/no - If yes, specify the level)	Open	Not applicable	Open
Potential for accumulation (yes/no):	Open	Not applicable	Open
Metabolism studies indicate potential level of residues ≥ 0.01 mg/kg in edible tissues (yes/no)	Open	Not applicable	Open
	Feeding studies (Specify the feeding rate in cattle and poultry studies considered as relevant) Residue levels in matrices : Mean (max) mg/kg		
Muscle	Open	Not applicable	Open
Liver	Open	Not applicable	Open
Kidney	Open	Not applicable	Open
Fat	Open	Not applicable	Open
Milk	Open		
Eggs		Not applicable	

Summary of residues data according to the representative uses on raw agricultural commodities and feedingstuffs (Annex IIA, point 6.3, Annex IIIA, point 8.2)

Crop	Northern or Mediterranean Region, field or glasshouse, and any other useful information	Trials results relevant to the representative uses (a)	Recommendation/comments	MRL estimated from trials according to the representative use	HR (c)	STMR (b)
Peaches	Indoor	Data gap: 4 residue trials complying with the representative use (drenching) and the agreed residue definitions for monitoring and risk assessment.		Open	Open	Open
Apples/pears	Indoor	Data gap: 4 residue trials on apples or pears complying with the representative use (drenching) and the agreed residue definitions for monitoring and risk assessment.		Open	Open	Open

(a) Numbers of trials in which particular residue levels were reported *e.g.* 3 x <0.01, 1 x 0.01, 6 x 0.02, 1 x 0.04, 1 x 0.08, 2 x 0.1, 2 x 0.15, 1 x 0.17
(b) Supervised Trials Median Residue *i.e.* the median residue level estimated on the basis of supervised trials relating to the representative use
(c) Highest residue

Consumer risk assessment (Annex IIA, point 6.9, Annex IIIA, point 8.8)[1]

ADI Clove oil	No value could be derived (see section on mammalian toxicology)
ADI Eugenol	1 mg/kg bw/day
TMDI (% ADI) according to WHO European diet	Open
TMDI (% ADI) according to EFSA model rev.2A	Open
IEDI (WHO European Diet) (% ADI)	Open
Factors included in IEDI and NEDI	Open
ARfD Clove oil	No value could be derived (see section on mammalian toxicology).
ARfD Eugenol	Not required.
IESTI (% ARfD)	Open
Factors included in IESTI and NESTI	Open

[1]: The chronic and acute dietary intake risk assessment could not be conducted based on the information available and the lack of toxicological reference values for clove oil.

Processing factors (Annex IIA, point 6.5, Annex IIIA, point 8.4)[2]

Crop/ process/ processed product	Number of studies	Processing factors		Amount transferred (%) (Optional)
		Transfer factor	Yield factor	
[2]: The nature and the magnitude of the residues in processed fruit matrices need to be addressed.				

Proposed MRLs (Annex IIA, point 6.7, Annex IIIA, point 8.6)

Apples/pears.....	Open
Peaches.....	Open
Ruminant's matrices.....	Open

When the MRL is proposed at the LOQ, this should be annotated by an asterisk after the figure.

Environmental fate and behaviour

Route of degradation (aerobic) in soil (Annex IIA, point 7.1.1.1.1)

Mineralization after 100 days ‡	No data submitted
Non-extractable residues after 100 days ‡	No data submitted
Metabolites requiring further consideration ‡ - name and/or code, % of applied (range and maximum)	No data submitted

Route of degradation in soil - Supplemental studies (Annex IIA, point 7.1.1.1.2)

Anaerobic degradation ‡

Mineralization after 100 days	No data submitted
Non-extractable residues after 100 days	No data submitted
Metabolites that may require further consideration for risk assessment - name and/or code, % of applied (range and maximum)	No data submitted

Soil photolysis ‡

Metabolites that may require further consideration for risk assessment - name and/or code, % of applied (range and maximum)	No data submitted

Rate of degradation in soil (Annex IIA, point 7.1.1.2, Annex IIIA, point 9.1.1)

Laboratory studies ‡ No data submitted

Field studies ‡ No data submitted

pH dependence ‡ (yes / no) (if yes type of dependence)	No data submitted
Soil accumulation and plateau concentration ‡	No data submitted

Soil adsorption/desorption (Annex IIA, point 7.1.2)

Parent ‡ No data submitted

Mobility in soil (Annex IIA, point 7.1.3, Annex IIIA, point 9.1.2)

Column leaching ‡	No data submitted
Aged residues leaching ‡	No data submitted
Lysimeter/ field leaching studies ‡	No data submitted

PEC (soil) (Annex IIIA, point 9.1.3)

Parent Method of calculation	No calculation made due to no agreed method. Application method makes soil contamination unlikely.

Route and rate of degradation in water (Annex IIA, point 7.2.1)

Hydrolytic degradation of the active substance and metabolites > 10 % ‡	pH 4: stable at 50˚C (<10 % degradation in 5 days)
	pH 7: stable at 50˚C (<10 % degradation in 5 days)
	pH 9: 71.7 days at 25 °C (1st order)
Photolytic degradation of active substance and metabolites above 10 % ‡	No data submitted
Quantum yield of direct phototransformation in water at Σ > 290 nm	No data submitted
Readily biodegradable ‡ (yes/no)	No data submitted for eugenol or clove oil. In the absence of an adequate study eugenol and clove oil are considered as not readily biodegradable.

Degradation in water / sediment No data submitted

PEC (surface water) and PEC sediment (Annex IIIA, point 9.2.3)

Parent	No calculation made due to no agreed method. Application method makes soil contamination unlikely.

PEC (ground water) (Annex IIIA, point 9.2.1)

Method of calculation and type of study (*e.g.* modelling, field leaching, lysimeter)	No calculation made due to no agreed method. Application method makes soil contamination unlikely.

Fate and behaviour in air (Annex IIA, point 7.2.2, Annex III, point 9.3)

Direct photolysis in air ‡	Not studied - no data requested
Quantum yield of direct phototransformation	No data submitted

Photochemical oxidative degradation in air ‡	DT_{50} of 1.975 hours derived by the Atkinson model (version 1.91). OH (12h) concentration assumed = 1.5 x 10^6 OH/cm^3
Volatilisation ‡	No data submitted
Metabolites	No data submitted

PEC (air)

Method of calculation	Expert judgement, based on vapour pressure, dimensionless Henry's Law Constant and information on volatilisation from plants and soil.

$PEC_{(a)}$

Maximum concentration	Considered to be negligible

Residues requiring further assessment

Environmental occurring residues requiring further assessment by other disciplines (toxicology and ecotoxicology) and or requiring consideration for groundwater exposure.	Soil: eugenol Surface water: eugenol Sediment: eugenol Ground water: eugenol Air: eugenol Other active components of clove oil may need to be considered once the data gap identified for the identity is fulfilled.

Monitoring data, if available (Annex IIA, point 7.4)

Soil (indicate location and type of study)	No data submitted
Surface water (indicate location and type of study)	No data submitted
Ground water (indicate location and type of study)	No data submitted
Air (indicate location and type of study)	No data submitted

Points pertinent to the classification and proposed labelling with regard to fate and behaviour data

Candidate to R53.

Ecotoxicology

Effects on terrestrial vertebrates (Annex IIA, point 8.1, Annex IIIA, points 10.1 and 10.3)

Species	Test substance	Time scale	End point (mg/kg bw(/day))	End point (mg/kg feed)
Birds ‡				
	a.s.	Acute	No data submitted.	No data submitted.
	a.s.	Short-term	No data submitted.	No data submitted.
	a.s.	Long-term	No data submitted.	No data submitted.
Mammals ‡				
Rat	Eugenol.	Acute	1930 mg/kg bw	-
	a.s.	Long-term	No data submitted.	-
Additional higher tier studies ‡				
Not required.				

Toxicity/exposure ratios for terrestrial vertebrates (Annex IIIA, points 10.1 and 10.3)

Post-harvest drench treatment to apples, pears and peaches

Indicator species/Category	Time scale	ETE	TER	Annex VI Trigger
Tier 1 (Birds)				
	Acute	n/a[1]	n/a[1]	10
	Short-term	n/a[1]	n/a[1]	10
	Long-term	n/a[1]	n/a[1]	5
Tier 1 (Mammals)				
	Acute	n/a[1]	n/a[1]	10
	Long-term	n/a[1]	n/a[1]	5

[1] Representative use of clove oil as a post-harvest drench treatment to apples, pears and peaches therefore negligible exposure is expected to birds and mammals.

Toxicity data for aquatic species (most sensitive species of each group) (Annex IIA, point 8.2, Annex IIIA, point 10.2)

Group	Test substance	Time-scale (Test type)	End point	Toxicity[1] (mg/L)
Laboratory tests ‡				
Fish				
Oncorhynchus mykiss	eugenol	96 hr (flow-through)	Mortality, $_{nom}LC_{50}$	5.6 mg/L
Zebra danio	eugenol	96 hr (flow-through)	Mortality, $_{nom}LC_{50}$	13.0 mg/L
Aquatic invertebrate				
Daphnia magna	eugenol	48 h (static)	Mortality, $_{nom}EC_{50}$	1.9 mg/L
Sediment dwelling organisms				
	a.s.	28 d (static)	NOEC	No data submitted.
Algae				
Scenedesmus subcapicatus	eugenol	72 h (static)	Biomass: $_{mm}E_bC_{50}$	22 mg/L
			Growth rate: $_{mm}E_rC_{50}$	41 mg/L
Higher plant				
	a.s.	14 d (static)	Fronds, EC_{50}	No data submitted.
Microcosm or mesocosm tests				
Not required				

[1] Nominal ($_{nom}$) or mean measured concentrations ($_{mm}$).

Toxicity/exposure ratios for the most sensitive aquatic organisms (Annex IIIA, point 10.2)

FOCUS Step1

Post-harvest drench treatment to apples, pears and peaches.

Test substance	Organism	Toxicity end point (mg/L)	Time scale	PEC_i	PEC_{twa}	TER	Annex VI Trigger
a.s.	Fish		Acute	-	-	n/a[1]	100
a.s.	Aquatic invertebrates		Acute	-	-	n/a[1]	100
a.s.	Algae		-	-	-	n/a[1]	10
a.s.	Higher plants		Chronic	-	-	n/a[1]	10
a.s.	Sediment-dwelling organisms		Chronic	-	-	n/a[1]	10

[1] Representative use of clove oil as a post-harvest drench treatment to apples, pears and peaches therefore negligible exposure to aquatic organisms is expected.

Bioconcentration				
	Active substance	Metabolite 1	Metabolite 2	Metabolite 3
$logP_{O/W}$	2.04 at pH 7	-	-	-
Bioconcentration factor (BCF)[1] ‡	-	-	-	-
Annex VI Trigger for the bioconcentration factor	-	-	-	-
Clearance time (days) (CT_{50})	-	-	-	-
(CT_{90})	-	-	-	-
Level and nature of residues (%) in organisms after the 14 day depuration phase	-	-	-	-

[1] only required if log $P_{O/W}$ >3.

Effects on honeybees (Annex IIA, point 8.3.1, Annex IIIA, point 10.4)

Test substance	Acute oral toxicity (LD_{50} µg/bee)	Acute contact toxicity (LD_{50} µg/bee)
a.s. ‡	No data submitted. Not required.	No data submitted. Not required.
Preparation	No data submitted.	No data submitted.
Field or semi-field tests		
Not required		

Hazard quotients for honey bees (Annex IIIA, point 10.4)

Post-harvest drench treatment to apples, pears and peaches.

Test substance	Route	Hazard quotient	Annex VI Trigger
a.s.	Contact	n/a[1]	50
a.s.	oral	n/a[1]	50
Preparation	Contact	n/a[1]	50
Preparation	oral	n/a[1]	50

[1] Representative use of clove oil as a post-harvest drench treatment to apples, pears and peaches therefore negligible exposure is expected to bees.

Effects on other arthropod species (Annex IIA, point 8.3.2, Annex IIIA, point 10.5)

Laboratory tests with standard sensitive species

Species	Test Substance	End point	Effect (LR_{50} g/ha[1])

Species	Test Substance	End point	Effect (LR_{50} g/ha[1])
Typhlodromus pyri ‡	-	Mortality	No data submitted. Not required.
Aphidius rhopalosiphi ‡	-	Mortality	No data submitted. Not required.

Post-harvest drench treatment to apples, pears and peaches.

Test substance	Species	Effect (LR_{50} g/ha)	HQ in-field	HQ off-field	Trigger
	Typhlodromus pyri	-	n/a[1]	n/a[1]	2
	Aphidius rhopalosiphi	-	n/a[1]	n/a[1]	2

[1] Representative use of clove oil as a post-harvest drench treatment to apples, pears and peaches therefore negligible exposure is expected to non-target arthropods.

Field or semi-field tests
Not required

Effects on earthworms, other soil macro-organisms and soil micro-organisms (Annex IIA points 8.4 and 8.5. Annex IIIA, points, 10.6 and 10.7)

Test organism	Test substance	Time scale	End point
Earthworms			
	a.s. ‡	No data submitted.	No data submitted. Not required.
	a.s. ‡	No data submitted.	No data submitted. Not required.
Soil micro-organisms			
Nitrogen mineralisation	a.s. ‡	No data submitted.	No data submitted. Not required.
	Metabolite 1		
Carbon mineralisation	a.s. ‡	No data submitted.	No data submitted. Not required.
	Metabolite 1		
Field studies			
Not required			

Toxicity/exposure ratios for soil organisms

Post-harvest drench treatment to apples, pears and peaches.

Test organism	Test substance	Time scale	Soil PEC	TER	Trigger
Earthworms					
	a.s. ‡	Acute	-	n/a[1]	10
	a.s. ‡	Chronic	-	n/a[1]	5

[1] Representative use of clove oil as a post-harvest drench treatment to apples, pears and peaches therefore negligible exposure is expected to non-target soil organisms.

Effects on non target plants (Annex IIA, point 8.6, Annex IIIA, point 10.8)
Preliminary screening data

No data submitted.

Effects on biological methods for sewage treatment (Annex IIA 8.7)

Test type/organism	end point
Activated sludge	No data submitted. Data gap.
Pseudomonas sp	

Ecotoxicologically relevant compounds (consider parent and all relevant metabolites requiring further assessment from the fate section)

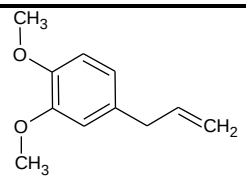
Compartment	
soil	-
water	-
sediment	-
groundwater	-

Classification and proposed labelling with regard to ecotoxicological data (Annex IIA, point 10 and Annex IIIA, point 12.3)

	RMS/peer review proposal
Active substance	R51/R53

	RMS/peer review proposal
Preparation	Not classified.

APPENDIX B – USED COMPOUND CODE(S)

Code/Trivial name	Chemical name*	Structural formula*
methyl eugenol	4-allyl-1,2-dimethoxybenzene	

* ACD/ChemSketch, Advanced Chemistry Development, Inc., ACD/Labs Release: 12.00 Product version: 12.00 (Build 29305, 25 Nov 2008)

ABBREVIATIONS

1/n	slope of Freundlich isotherm
λ	wavelength
ε	decadic molar extinction coefficient
°C	degree Celsius (centigrade)
µg	microgram
µm	micrometer (micron)
a.s.	active substance
AChE	acetylcholinesterase
ADE	actual dermal exposure
ADI	acceptable daily intake
AF	assessment factor
AOEL	acceptable operator exposure level
AP	alkaline phosphatase
AR	applied radioactivity
ARfD	acute reference dose
AST	aspartate aminotransferase (SGOT)
AV	avoidance factor
BCF	bioconcentration factor
BUN	blood urea nitrogen
bw	body weight
CAS	Chemical Abstracts Service
CFU	colony forming units
ChE	cholinesterase
CI	confidence interval
CIPAC	Collaborative International Pesticides Analytical Council Limited
CL	confidence limits
cm	centimetre
d	day
DAA	days after application
DAR	draft assessment report
DAT	days after treatment
DM	dry matter
DNA	deoxyribonucleic acid
DT_{50}	period required for 50 percent disappearance (define method of estimation)
DT_{90}	period required for 90 percent disappearance (define method of estimation)
dw	dry weight
EbC_{50}	effective concentration (biomass)
EC	emulsifiable concentrate
EC_{50}	effective concentration
ECHA	European Chemical Agency
EEC	European Economic Community
EINECS	European Inventory of Existing Commercial Chemical Substances
ELINCS	European List of New Chemical Substances
EMDI	estimated maximum daily intake
ER_{50}	emergence rate/effective rate, median
ErC_{50}	effective concentration (growth rate)
EU	European Union
EUROPOEM	European Predictive Operator Exposure Model
f(twa)	time weighted average factor
FAO	Food and Agriculture Organisation of the United Nations
FIR	Food intake rate
FOB	functional observation battery
FOCUS	Forum for the Co-ordination of Pesticide Fate Models and their Use

g	gram
GAP	good agricultural practice
GC	gas chromatography
GC-FID	gas chromatography with flame ionisation detector
GC-MS	gas chromatography-mass spectrometry
GCPF	Global Crop Protection Federation (formerly known as GIFAP)
GGT	gamma glutamyl transferase
GM	geometric mean
GS	growth stage
GSH	glutathion
h	hour(s)
ha	hectare
Hb	haemoglobin
Hct	haematocrit
hL	hectolitre
HN	hot fogging concentrate
HPLC	high pressure liquid chromatography or high performance liquid chromatography
HPLC-MS	high pressure liquid chromatography – mass spectrometry
HQ	hazard quotient
IEDI	international estimated daily intake
IESTI	international estimated short-term intake
IR	infrared
ISO	International Organisation for Standardisation
IUPAC	International Union of Pure and Applied Chemistry
JMPR	Joint Meeting on the FAO Panel of Experts on Pesticide Residues in Food and the Environment and the WHO Expert Group on Pesticide Residues (Joint Meeting on Pesticide Residues)
K_{doc}	organic carbon linear adsorption coefficient
kg	kilogram
K_{Foc}	Freundlich organic carbon adsorption coefficient
L	litre
LC	liquid chromatography
LC_{50}	lethal concentration, median
LC-MS	liquid chromatography-mass spectrometry
LC-MS-MS	liquid chromatography with tandem mass spectrometry
LD_{50}	lethal dose, median; dosis letalis media
LDH	lactate dehydrogenase
LOAEL	lowest observable adverse effect level
LOD	limit of detection
LOQ	limit of quantification (determination)
m	metre
M/L	mixing and loading
MAF	multiple application factor
MCH	mean corpuscular haemoglobin
MCHC	mean corpuscular haemoglobin concentration
MCV	mean corpuscular volume
mg	milligram
mL	millilitre
mm	millimetre
mN	milli-newton
MRL	maximum residue limit or level
MS	mass spectrometry
MSDS	material safety data sheet
MTD	maximum tolerated dose

MWHC	maximum water holding capacity
NESTI	national estimated short-term intake
ng	nanogram
NMR	nuclear magnetic resonance
NOAEC	no observed adverse effect concentration
NOAEL	no observed adverse effect level
NOEC	no observed effect concentration
NOEL	no observed effect level
OC	organic carbon content
OM	organic matter content
Pa	pascal
PD	proportion of different food types
PEC	predicted environmental concentration
PEC_{air}	predicted environmental concentration in air
PEC_{gw}	predicted environmental concentration in ground water
PEC_{sed}	predicted environmental concentration in sediment
PEC_{soil}	predicted environmental concentration in soil
PEC_{sw}	predicted environmental concentration in surface water
pH	pH-value
PHED	pesticide handler's exposure data
PHI	pre-harvest interval
PIE	potential inhalation exposure
pK_a	negative logarithm (to the base 10) of the dissociation constant
P_{ow}	partition coefficient between *n*-octanol and water
PPE	personal protective equipment
ppm	parts per million (10^{-6})
ppp	plant protection product
PT	proportion of diet obtained in the treated area
PTT	partial thromboplastin time
QSAR	quantitative structure-activity relationship
r^2	coefficient of determination
RPE	respiratory protective equipment
RUD	residue per unit dose
SC	suspension concentrate
SD	standard deviation
SFO	single first-order
SSD	species sensitivity distribution
STMR	supervised trials median residue
$t_{1/2}$	half-life (define method of estimation)
TER	toxicity exposure ratio
TER_A	toxicity exposure ratio for acute exposure
TER_{LT}	toxicity exposure ratio following chronic exposure
TER_{ST}	toxicity exposure ratio following repeated exposure
TK	technical concentrate
TLV	threshold limit value
TMDI	theoretical maximum daily intake
TRR	total radioactive residue
TSH	thyroid stimulating hormone (thyrotropin)
TWA	time weighted average
UDS	unscheduled DNA synthesis
UV	ultraviolet
W/S	water/sediment
w/v	weight per volume
w/w	weight per weight
WBC	white blood cell

WHO	World Health Organisation
wk	week
yr	year