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CONCLUSION ON PESTICIDES PEER REVIEW

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Peer review of the pesticide risk assessment of the active substance clove oil

European Food Safety Authority (EFSA) | Fernando Álvarez | Maria Arena | Domenica Auteri | Sofia Batista Leite | Marco Binaglia | Anna Federica Castoldi | Arianna Chiusolo | Angelo Colagiorgi | Mathilde Colas | Federica Crivellente | Chloe De Lentdecker | Isabella De Magistris | Mark Egsmose | Gabriella Fait | Franco Ferilli | Varvara Gouliarmou | Katrin Halling | Laia Herrero Nogareda | Alessio Ippolito | Frederique Istace | Samira Jarrah | Dimitra Kardassi | Aude Kienzler | Anna Lanzoni | Roberto Lava | Renata Leuschner | Alberto Linguadoca | Jochem Louisse | Christopher Lythgo | Oriol Magrans | Iris Mangas | Andrea Mioč | Ileana Miron | Tunde Molnar | Laura Padovani | Vincenzo Padricello | Martina Panzarea | Juan Manuel Parra Morte | Simone Rizzuto | Anamarija Romac | Agnès Rortais | Miguel Santos | Rositsa Serafimova | Rachel Sharp | Csaba Szentes | Andrea Terron | Anne Theobald | Manuela Tiramani | Giorgia Vianello | Laura Villamar-Bouza

Correspondence:
pesticides.peerreview@efsa.europa.eu

Abstract

The conclusions of the EFSA following the peer review of the initial risk assessments carried out by the competent authority of the rapporteur Member State, Malta, for the pesticide active substance clove oil are reported. The context of the peer review was that required by Regulation (EC) No 1107/2009 of the European Parliament and of the Council. The conclusions for the amendment of approval were reached on the basis of the evaluation of the representative use of clove oil as a preharvest nematicide on tomatoes and cucumbers (permanent greenhouse use). The representative use evaluated for the renewal of approval of clove oil was as post-harvest fungicide and bactericide on apples, pears and peaches (indoor uses). The reliable endpoints appropriate for use in regulatory risk assessment are presented. Endpoints not relevant to the scope of the proposed amendment of approval conditions will be addressed in the context of the renewal of approval procedure of clove oil running in parallel (AIR IV, EFSA Q-2016-00809). Missing information identified as being required by the regulatory framework is listed. Concerns are reported where identified.

KEYWORDS

clove oil, nematicide, peer review, pesticide, risk assessment

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SUMMARY

Regulation (EC) No 1107/2009 of the European Parliament and of the Council lays down, inter alia, the detailed rules as regards the procedure for the assessment of applications for amendment to the conditions of approval of active substances.

Clove oil was renewed on 13 February 2014 by Commission Implementing Regulation (EU) No 141/2014 amending Implementing Regulation (EU) No 540/2011, following a peer review of the risk assessment as set out in the EFSA Conclusion on clove oil, published on 17 January 2012. It was a specific provision of the renewal of approval that only indoor uses as post-harvest fungicide and bactericide may be authorised. EFSA was asked by the European Commission to provide scientific assistance with respect to the risk assessment for clove oil in light of confirmatory data related to specific provision of the approval on (a) the technical specification, and (b) data comparing natural background exposure situations of plant oils/clove oil, eugenol and methyl eugenol in relation to exposure from the use of plant oils/clove oil as a plant protection product. The EFSA outcome of the consultation with Member States, the applicant and EFSA on the pesticide risk assessment for clove oil in light of confirmatory data was issued on 5 September 2017.

In accordance with Article 7 of the Regulation, the rapporteur Member State (RMS), Malta, received an application from Xeda International S.A. on 22 May 2019 for amendment to the conditions of approval of the active substance clove oil to lift the restriction and to allow uses as nematicide to be authorised.

The assessment of the amendment dossier was carried out against any new scientific data that may impact the risk assessment of the previous evaluation (EFSA, 2012a, 2017a) based on the current scientific and technical knowledge from the updated search of the scientific peer-reviewed open literature.

Endpoints not relevant to the scope of the proposed amendment of approval conditions will be addressed in the context of the renewal of approval procedure of clove oil running in parallel (AIR IV, EFSA Q-2016-00809).

An initial evaluation of the dossier on clove oil for the present application was provided by the RMS in a revised DAR and subsequently, a peer review of the pesticide risk assessment on the RMS evaluation was conducted by EFSA in accordance with Article 12 of Regulation (EC) No 1107/2009. The following conclusions are derived.

The representative use of clove oil applied via drip irrigation as a nematicide on permanent greenhouse tomato and cucumber crops, as proposed at EU level, results in a sufficient nematocidal efficacy against the target root knot nematodes.

The assessment of the data package revealed no issues that could not be finalised or that needed to be included as critical areas of concern with respect to **identity, physical–chemical and technical properties** of the active substance and the formulation for representative uses, and analytical methods.

With respect to **mammalian toxicology**, the non-dietary exposure estimates for eugenol during the use on fruiting vegetables in permanent greenhouses do not allow to conclude the risk assessment of clove oil for operators and workers since it could not be demonstrated that the toxicological reference values derived for eugenol will also apply to clove oil (critical area of concern).

With respect to **residues** in food and feed, several data gaps were identified to characterise the residues and to assess the magnitude of residues in cucumbers and tomatoes and in drinking water that may result from the proposed use as soil nematicide. With available information, consumer risk assessment cannot be finalised (critical area of concern). Additional information is also needed to assess the use of clove oil against the criteria for Annex IV of Commission Regulation (EC) No 839/2008.

The data available on **environmental fate and behaviour** were sufficient to carry out the required environmental exposure assessments at EU level for the representative use assessed. However, the presence of methyl eugenol in soil inside the greenhouse (and potentially in groundwater) after clove oil application cannot be excluded based on the available data.

In the area of **ecotoxicology**, low risk was concluded for all non-target organisms for the representative use in permanent greenhouse.

Critical areas of concerns identified in the previous conclusion (EFSA, 2012a) which remain unaddressed and are not relevant to the scope of the amendment of approval conditions, are still applicable.

During the peer review, the applicant proposed changes to the GAP table. However, due to the substantial nature of the proposed amendments, these changes were deemed unfeasible, and the request was rejected. Nonetheless, these changes to the GAP table would not have impacted on the outcome of the conclusions given that no toxicological reference values were established, and the consumer risk assessment could not therefore be performed.

BACKGROUND

Regulation (EC) No 1107/2009 of the European Parliament and of the Council[1] (hereinafter referred to as 'the Regulation') lays down, inter alia, the detailed rules as regards the procedure for the assessment for an amendment to the conditions of an approval of active substances. This regulates for the European Food Safety Authority (EFSA) the procedure for organising the consultation of Member States and the applicant(s) for comments on the initial evaluation in the draft assessment report (DAR), provided by the rapporteur Member State (RMS), and the organisation of an expert consultation, where appropriate.

In accordance with Article 12 of the Regulation, EFSA is required to adopt a conclusion on whether an active substance can be expected to meet the approval criteria provided for in Article 4 of the Regulation (also taking into consideration recital (10) of the Regulation) within 120 days from the end of the period provided for the submission of written comments, subject to an extension of 30 days where an expert consultation is necessary, and a further extension of up to 150 days where additional information is required to be submitted by the applicant(s) in accordance with Article 12(3).

Clove oil was renewed on 13 February 2014 by Commission Implementing Regulation (EU) No 141/2014 amending Implementing Regulation (EU) No 540/2011,[2] following a peer review of the risk assessment as set out in the EFSA Conclusion on clove oil, published on 17 January 2012 (EFSA, 2012a). It was a specific provision of the approval that only indoor uses as post-harvest fungicide and bactericide may be authorised. The EFSA outcome of the consultation with Member States, the applicant and EFSA on the pesticide risk assessment for clove oil in light of confirmatory data were issued on 5 September 2017 (EFSA, 2017a, 2017b). EFSA was asked by the European Commission to provide scientific assistance with respect to the risk assessment for clove oil in light of confirmatory data related to specific provision of the approval on (a) the technical specification and (b) data comparing natural background exposure situations of plant oils/clove oil, eugenol and methyl eugenol in relation to exposure from the use of plant oils/clove oil as a plant protection product. This data shall cover human exposure. Open points will be addressed under the renewal of approval procedure of clove oil (AIR IV; EFSA-Q-2016-00809).

In accordance with Article 7 of Regulation (EC) No 1107/2009, Malta (hereinafter referred to as the rapporteur Member State, 'RMS') subsequently received an application from Xeda International S.A. on 22 May 2019 for amendment to the conditions of approval of the active substance clove oil to lift the restriction and allow nematicide to be authorised.

The assessment of the amendment dossier was carried out against any new scientific data that may impact the risk assessment of the previous evaluation (EFSA, 2012a, 2017a) based on the current scientific and technical knowledge from the updated search of the scientific peer-reviewed open literature.

Endpoints not relevant to the scope of the proposed amendment of approval conditions will be addressed in the context of the renewal of approval procedure of clove oil running in parallel (AIR IV, EFSA Q-2016-00809).

The RMS provided its initial evaluation of the dossier on clove oil in the form of a revised DAR, which was received by EFSA on 5 October 2021 (Malta, 2021). The peer review was initiated on 21 July 2022 by dispatching the revised DAR to Member States and the applicant, Xeda International S.A., for consultation and comments. EFSA also provided comments. In addition, EFSA conducted a public consultation on the revised DAR. The comments received were collated by EFSA and forwarded to the RMS for compilation and evaluation in the format of a reporting table. The applicant was invited to respond to the comments in column 3 of the reporting table. The comments and the applicant response were evaluated by the RMS in column 3.

The need for expert consultation and the necessity for additional information to be submitted by the applicant in accordance with Article 12(3) of the Regulation were considered in a telephone conference between EFSA and the RMS, on 19 December 2022. On the basis of the comments received, the applicant's response to the comments and the RMS's evaluation thereof, it was concluded that additional information should be requested from the applicant, and that EFSA should conduct an expert consultation in the areas of mammalian toxicology, residues and environmental fate and behaviour.

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 an expert consultation, were compiled by EFSA in the format of an evaluation table.

The conclusions arising from the consideration by EFSA, and as appropriate by the RMS, of the points identified in the evaluation table, together with the outcome of the expert consultation and the written consultation on the assessment of additional information, where these took place, were reported in the final column of the evaluation table.

In accordance with Article 12 of the Regulation, EFSA should adopt a conclusion on whether clove oil can be expected to meet the approval criteria provided for in Article 4 of the Regulation, taking into consideration recital (10) of the Regulation.

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 February 2024.

This conclusion report summarises the outcome of the peer review of the risk assessment on the active substance and the formulation for representative uses evaluated on the basis of the representative use of clove oil as a preharvest nematicide on tomatoes and cucumbers (permanent indoor use) as proposed by the applicant. In accordance with Article 12(2) of

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

[2]Commission Implementing Regulation (EU) No 141/2014 of 13 February 2014 amending Implementing Regulation (EU) No 540/2011 as regards the conditions of approval of the active substance plant oils/clove oil. OJ L 44, 14.2.2014, p. 40–42.

Regulation (EC) No 1107/2009, risk mitigation options identified in the DAR and considered during the peer review, if any, are presented in the conclusion.

A list of the relevant end points for the active substance and the formulation is provided in Appendix B. In addition, the considerations as regards the cut-off criteria affected by the scope of amendment of the approval conditions for clove oil according to Annex II of Regulation (EC) No 1107/2009 are summarised in Appendix A.

A key supporting document to this conclusion is the peer review report (EFSA, 2024), 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 comprises the following documents, in which all views expressed during the course of the peer review, including minority views, where applicable, can be found:

- the comments received on the DAR;
- the reporting table (20 December 2022);
- the evaluation table (20 February 2024);
- the report(s) of the scientific consultation with Member State experts (where relevant);
- the comments received on the assessment of the additional information (where relevant);
- the comments received on the draft EFSA conclusion.

Given the importance of the DAR, including its revisions (Malta, 2023), and the peer review report, both documents are considered as background documents to this conclusion and thus are made publicly available.

It is recommended that this conclusion and its background documents would not be accepted to support any registration outside the EU for which the applicant has not demonstrated that it has regulatory access to the information on which this conclusion report is based.

THE ACTIVE SUBSTANCE AND THE FORMULATION(S) FOR REPRESENTATIVE USES

Clove oil is a common name for an extract from the flower buds of *Syzygium aromaticum*. Clove oil is a multi-constituent extract containing several components such as eugenol, methyl eugenol, β-caryophyllene (or caryophyllene), α-caryophyllene (or humulene), caryophyllene oxide, eugenol acetate, meta eugenol, δ-cadinene and calamenene. Its main constituent is eugenol with a minimum content of 800 g eugenol per kg of clove oil. There is no ISO common name for clove oil.

The formulated product for the representative use for this evaluation was 'Bioxeda', an emulsifiable concentrate (EC) containing 203.8 g clove oil/kg equivalent to 180 g of eugenol per kg. Methyl eugenol is considered as a relevant impurity in the technical clove oil at a maximum level of 0.1% according to the Commission Implementing Regulation (EU) No 141/2014,[3] and the applicant declared that 'Bioxeda' contains 20 mg methyl eugenol per L as a relevant impurity. However, it is noted that the previous peer review concluded that for methyl eugenol, no acceptable limit could be agreed in the technical specification on the basis of the available data and no toxicological reference values could be derived (see Section 2).

The representative use evaluated comprise soil drip-irrigation application in permanent greenhouse, as a nematicide for the control of root knot nematodes on tomato and cucumber. Full details of the GAP (good agricultural practice) can be found in the list of end points in Appendix B.

Data were submitted to conclude that the use of clove oil according to the representative use proposed at EU level as nematicide results in a sufficient nematocidal efficacy against the target pests following the guidance document SANCO/10054/2013-rev. 3 (European Commission, 2013).

The information on the formulation for representative uses 'Bioxeda' and related co-formulants will be addressed in the context of the renewal of approval procedure of clove oil (AIR IV, EFSA Q-2016-00809).

A data gap has been identified for an updated search of the scientific peer-reviewed open literature on the active substance and its relevant metabolites (including potentially methyl eugenol), dealing with side effects on health, and published within the 10 years before the date of submission of the dossier, to be conducted and reported in accordance with EFSA guidance on the submission of scientific peer-reviewed open literature for the approval of pesticide active substances under Regulation (EC) No 1107/2009 (EFSA, 2011).

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: European Commission (2000, 2010, 2013).

[3]Commission Implementing Regulation (EU) No 141/2014 of 13 February 2014 amending Implementing Regulation (EU) No 540/2011 as regards the conditions of approval of the active substance plant oils/clove oil. OJ L 44, 14.2.2014, p. 40–42.

The data submitted for amendment of approval conditions do not change the previous conclusions (EFSA, 2012a) relevant to the identity; the physical and chemical properties; the analytical methods used for the generation of risk assessment data and the analytical methods for the determination of eugenol in clove oil technical material and in the formulation for representative uses.

The main data regarding the identity of clove oil and its physical and chemical properties are given in the previous conclusion and technical report (EFSA, 2012a, 2017a). For the targeted assessment, as a nematicide, a data gap was identified on persistent foaming data at the highest recommended concentration of 2.47 L formulation/hL (data gap, see Section 10).

Adequate analytical methods were available for the generation of the pre-approval data required in the targeted assessment, except for the analytical method used in activated sludge – respiration inhibition test with clove oil for which no validation data were provided (data gap, see Section 10). A data gap was identified for a method for monitoring methyl eugenol in the formulation 'Bioxeda' (data gap, see Section 10).

Analytical methods for monitoring of clove oil residues in food and feed of plant origin and food of animal origin are not required since a residue definition for monitoring was not proposed. A validated GC–MS analytical method for the determination of eugenol in soil matrices, with a limit of quantification (LOQ) of 0.01 mg/kg was provided. Eugenol residues in water can be monitored by a HPLC–MS/MS with LOQ of 0.1 µg/L. A data gap was identified for a method for monitoring eugenol residues in air (see Section 10). As no residue definition was set for body fluids and tissues, analytical methods for monitoring clove oil residues in body fluids and tissues are not required.

2 | MAMMALIAN TOXICITY

The toxicological profile of the active substance clove oil and its metabolites was discussed at the Pesticides Peer Review Experts' Teleconference 114 (6–8 September 2023). The assessment is based on the following guidance documents: (EFSA, 2014a, 2017b).

The data submitted for amendment of approval conditions do not change the previous conclusions for clove oil (EFSA, 2012a, 2017a).

For **methyl eugenol** (genotoxic and carcinogenic), identified during the previous EFSA conclusion (2012a) as a toxicologically relevant impurity in technical clove oil, and confirmed during the current peer review as minor component of the active substance clove oil, and potential metabolite of the main component eugenol, no acceptable limit could be agreed in the reference specification on the basis of the available data and no toxicological reference value could be derived (data gap, see Section 9.1.2; EFSA, 2017a).

Additionally, the toxicological reference values derived for **eugenol** ADI and acceptable operator exposure level (AOEL) of 1.0 mg/kg body weight (bw) per day, based on the maternal no observed adverse effect level (NOAEL) in the developmental studies and applying an uncertainty factor of 100, main component of clove oil, could not be concluded as applicable to clove oil due to the unknown toxicological properties and contribution of all the minor components present in total up to 20% (critical area of concern, see Section 9.1.2; EFSA, 2012a).

For the amendment of the approval conditions, the supported use of the product 'Bioxeda' is as a preharvest treatment nematicide in fruiting vegetables (tomato, cucumber) in permanent greenhouses, with application via drip irrigation system. The provisory non-dietary exposure estimates for this use have been discussed during the Pesticides Peer Review Teleconference 114 in September 2023.[4]

The **operator** exposure estimates were obtained with the EFSA calculator 2015 (EFSA, 2014a). It is noted that they are expressed as clove oil and compared to the AOEL for eugenol, the main component for which toxicological values could be derived and can only be considered as provisory. The resulting values are below the AOEL for this preharvest use of clove oil when considering that exposure to vapour will only occur during mixing/loading (considering the automatic drip irrigation in greenhouse) and that operators will wear respiratory protective equipment (with penetration factor 10%) and gloves. The **worker** dermal exposure estimates are below the AOEL for the exposure to soil residue while for the inhalation exposure, a re-entry period of 24 h after application should be applied. For **bystanders and residents**, both dermal and inhalation exposure are not expected to occur since no volatile eugenol has been detected in soil aerobic degradation study (see Section 4). 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 cannot be considered conclusive (critical area of concern, see Section 9.1.2).

3 | RESIDUES

The assessment in the residue section is based on the following guidance documents: OECD (2009, 2011), European Commission (2011) and JMPR (2004, 2007).

The residues of clove oil in food and feed for this application were discussed in Pesticides Peer Review Experts' Teleconference 116 (12 September 2023).

[4]Refer to experts' consultation 2.1 in the Report of Pesticides Peer Review Experts' TC 114 (EFSA, 2024).

Approved uses are for post-harvest stored fruits and only metabolism studies reflecting these uses were available in the dossier submitted for the approval. These metabolism studies are not directly applicable to assess the use as soil nematicide supported in the current application. A relevant minor component of the active substance clove oil, and also a potential metabolite of eugenol, is methyl eugenol that is a genotoxic carcinogenic substance for which a safe exposure could not be established due to its genotoxic properties (see Section 2; EFSA, 2017a). Further information is needed to fully characterise the residues of clove oil resulting from the proposed use. Evidence on the fate and the potential uptake and metabolic pathway of eugenol (main component) and methyl eugenol (relevant minor component and potential metabolite) should be provided considering all information and data available (data gap, see Section 9.1.2). Furthermore, as the toxicological reference values derived for eugenol could not be concluded as applicable to clove oil due to the unknown contribution to the residues and toxicological properties of all the minor components in total up to 20% and due to the fact that methyl eugenol is a minor component of clove oil with different toxicological properties than eugenol, efforts should be made to evaluate the potential availability for uptake by plants (data gap, see Section 9.1.2); see Section 2, critical area of concern in EFSA (2012a), and the outcome of the confirmatory data in EFSA (2017a). Considering the presented information, the residue definition for plants could not be finalised. The provisional risk assessment residue definition should include eugenol and methyl eugenol based on occurrence and toxicological concern, respectively.

The need of a residue definition for enforcement depends on outcome of the requested residue field trials and the decision of inclusion in Annex IV of Commission Regulation (EC) No 839/2008.[5]

Metabolism and feeding studies in livestock and fish are not needed for representative use on cucumber and tomato as they do not lead to dietary exposure of animals.[6] No residue definition for animal commodities is needed or proposed for these uses.

With available information, the assessment with respect to the magnitude of residues in treated crops, resulting from the proposed use and considering the provisional residue definition, could not be finalised. Four residue field trials for the representative use with tomato and cucumber according to the critical good agricultural practice (cGAP) and analysing for eugenol and methyl eugenol are needed (data gap, see Section 9.1.2). The number of four trials is only applicable in case the residues are below LOQ, otherwise a full data set of eight residue field trials will be needed.

In addition, as methyl eugenol toxicological properties do not allow to establish a lower safe limit of exposure (see Section 2), the LOQ of 0.01 mg/kg is not deemed sufficiently low to guarantee adequate protection of consumers. Therefore, the requested residue field trials should employ an analytical method with a sufficiently low LOQ for methyl eugenol to exclude any unacceptable risk to consumers from possible residues of methyl eugenol. In addition, storage stability data for eugenol and methyl eugenol in high water commodities covering the storage periods in the existing and requested residue field trials are needed (data gap, see Section 9.1.2).

With regard to the five assessment criteria according to the Commission guidance SANCO/11188/2013 Rev. 2 (European Commission, 2015) for potential inclusion in Annex IV of Regulation (EC) No 396/2005, i.e. approval as basic substance (criterion I), listed in Annex I of Regulation (EC) No 396/2005 (criterion II), having no identified hazardous properties (criterion III), natural exposure is higher than the one linked to the use as plant protection product (criterion IV) and consumer exposure is not expected considering the representative uses (criterion V); criteria I, II, III and V were considered not met. With respect to criteria IV in relation to natural exposure via diet cannot be evaluated as data available are not sufficient. In order to assess the residues in food resulting for the proposed use as nematicide against the criterion IV for inclusion in Annex IV of Commission Regulation (EC) No 839/2008, the dietary exposure to eugenol and/or clove oil from its natural presence in the diet should be estimated and compared with the exposure resulting from the intended uses (data gap, see Section 9.1.2; see also data gap already identified in EFSA (2012a) and the outcome of the confirmatory data in EFSA, 2017a).

With available information, consumer risk assessment cannot be finalised.

4 | ENVIRONMENTAL FATE AND BEHAVIOUR

Clove oil was discussed at the Pesticides Peer Review Meeting Teleconference (TC) 117 on 19 September 2023.

New studies performed on eugenol, the main component (80%) of clove oil, were submitted for the amendment of approval conditions of clove oil. The peer review accepted that the environmental fate and behaviour properties of eugenol could be used to read across the properties of other components in clove oil. Although it is acknowledged that this approach comes with an uncertainty, this uncertainty is accepted considering the use of clove oil in permanent greenhouse.

The rates of dissipation and degradation in the environmental matrices investigated were estimated using FOCUS (2006) kinetics guidance. In soil laboratory incubations under aerobic conditions in the dark, eugenol exhibited very low to low persistence. The presence of methyl eugenol (genotoxic and carcinogenic) in soil laboratory incubations and in greenhouse soil after clove oil application cannot be excluded based on the available data (**data gap**, see Section 9.1.2). Taking into consideration that a very low to low persistence of methyl eugenol in soil is expected, no soil exposure assessment is considered necessary for the representative use in greenhouse (EFSA, 2014c). No volatility of eugenol was detected and mineralisation of the phenyl ^{14}C radiolabel to carbon dioxide accounted for 17%–22% applied radioactivity (AR) after 120 days. The formation of unextractable residues (not extracted by acetonitrile and acidified acetonitrile) for this

[5]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 pesticides in or on certain products. OJ L 234, 30.8.2008, p. 1–216.

[6]Refer to experts' consultation 3.1 in the Report of Pesticides Peer Review Experts' TC 116 (EFSA, 2024).

radiolabel accounted for 66%–84% AR after 120 days. No volatility of eugenol was detected in these studies. Anaerobic conditions and soil photolysis are not considered relevant for the representative use. In the TC 117 meeting, the experts proposed not to conclude on the reliability of the new adsorption study from 2021 as its peer review is still ongoing in the context of the renewal process of eugenol.[7,8] However, for the low adsorbed percentage (< 20%) and the chemical instability of the test substance also in sterile soils, EFSA considers the adsorption study from 2021 not reliable to derive adsorption endpoints (**data gap**, see Section 10). In the TC 117 meeting, the experts also discussed the soil aerobic studies available in the dossier supporting the present amendment of approval of clove oil (with eugenol as lead component) and the renewal dossier for eugenol (EFSA-Q-2021-00014) and, in a weight of evidence approach, agreed that a DT50 in soil of 1 day is a good estimation for the degradation of clove oil in soil.[9]

The surface water, sediment and groundwater exposure assessments (predicted environmental concentrations (PEC) calculations) for the representative use in permanent greenhouses were calculated considering the intended application rate of clove oil and the substance properties of eugenol, the lead component. These PEC calculations can be found in Appendix B of this conclusion.

The necessary surface water and sediment exposure assessments were carried out using appropriate step 3 (FOCUS, 2001),[10] considering only drainage scenarios and no drift. Based on a DT50 in soil of 1 day and worst-case values for adsorption parameters, PEC_{SW} and PEC_{SED} for the representative use by clove oil components were minimal (10^{-6} µg/L and 10^{-6} µg/kg, respectively). Based on these results, experts in the TC 117 meeting concluded that the studies on fate and behaviour in water for clove oil were not triggered and the estimated concentrations in the aquatic compartment were at levels that a low risk for the aquatic organisms could be concluded (see Section 5).[11] Based on these concentrations, the aquatic risk assessment for any metabolite or minor component is not triggered.

The necessary groundwater exposure assessments were appropriately carried out considering an open-field approach using FOCUS (European Commission, 2014) scenarios and the models PEARL 5.5.5, PELMO 6.6.4 and MACRO 5.5.4.[12] The potential for groundwater exposure from the representative use by clove oil components above the parametric drinking water limit of 0.1 µg/L was concluded to be low in geoclimatic situations that are represented by five out of five FOCUS groundwater scenarios. However, no acceptable limit could be agreed for methyl eugenol due to its genotoxic properties on the basis of the available data (see Section 2), so its presence in groundwater could lead to a potential concern for consumer risk assessment even if below 0.1 µg/L if the potential presence of methyl eugenol in soil after clove oil application is confirmed (see Section 9.1.2).

Information to address the effect of water treatments processes on the nature of clove oil components that might be present in surface water and groundwater, when surface water or groundwater is abstracted for drinking water, is not considered necessary since concentrations in surface water and groundwater are far below 0.1 µg/L.

A key to the wording used to describe the persistence and mobility of the compounds assessed can be found in Appendix C of this conclusion.

5 | ECOTOXICOLOGY

The risk assessment was based on the following documents: European Commission (2002), SETAC (2001), EFSA (2009, 2013) and EFSA PPR Panel (2013).

Toxicity studies are available only for aquatic organisms and for effects on biological methods for sewage treatment. The available toxicity studies for aquatic organisms were carried out with eugenol which is the main component (80%) of clove oil. Additional ecotoxicology data from the EFSA conclusion on eugenol (EFSA, 2012b) have been taken into consideration in this conclusion on clove oil.

The intended use of clove oil is in permanent greenhouses via soil application using a drip irrigation system. Thus, in line with EFSA (2014b) and EFSA (2015), on based on minimal exposure, a low risk can be concluded for birds and mammals, bees, non-target arthropods other than bees and terrestrial non-target plants. A low risk can be concluded for biological methods for sewage treatment based on the available toxicity data, although validation data of the analytical method are missing (see Section 1).

Acute toxicity data were available for fish, aquatic invertebrates and algae. Chronic toxicity data were not available. The potential aquatic exposure and risk assessment for clove oil were discussed at the Peer Review Experts' Teleconference 117 (September 2023).[13] It was concluded that minimal exposure can be expected for aquatic organisms (see Section 4). Therefore, a low risk can be concluded for aquatic organisms.

No metabolites or other components of clove oil which would trigger a consideration in the aquatic and soil risk assessment were identified (see Section 4).

[7]See in Open EFSA: EFSA-Q-2021-00014.
[8]Refer to experts' consultation 5.1 in the Report of Pesticides Peer Review Experts' TC 117 (EFSA, 2024).
[9]Refer to experts' consultation 5.1 in the Report of Pesticides Peer Review Experts' TC 117 (EFSA, 2024).
[10]Simulations utilised the agreed Q10 of 2.58 (following EFSA, 2008) and Walker equation coefficient of 0.7.
[11]Refer to experts' consultation 5.1 in the Report of Pesticides Peer Review Experts' TC 117 (EFSA, 2024).
[12]Simulations utilised the agreed Q10 of 2.58 (following EFSA, 2008) and Walker equation coefficient of 0.7.
[13]Refer to experts' consultation 5.1 in the Report of Pesticides Peer Review Experts' TC 117 (EFSA, 2024).

6 | ENDOCRINE DISRUPTION PROPERTIES

The assessment of the endocrine disruption potential of clove **for humans and non-target organisms** according to points 3.6.5 and 3.8.2 of Annex II to Regulation (EC) No 1107/2009, as amended by Commission Regulation (EU) 2018/605 will be addressed in the context of the renewal of approval procedure of clove oil (AIR IV, EFSA Q-2016-00809).

7 | OVERVIEW OF THE RISK ASSESSMENT OF COMPOUNDS LISTED IN RESIDUE DEFINITIONS TRIGGERING ASSESSMENT OF EFFECTS DATA FOR THE ENVIRONMENTAL COMPARTMENTS (TABLES 1–4)

TABLE 1 Soil.

Compound (name and/or code)	Ecotoxicology
Clove oil (eugenol)	Low risk
Methyl eugenol[a]	Not required[b]

[a]Provisional, due to the data gap on the potential presence of methyl eugenol (genotoxic, carcinogenic) in soil following clove oil application.
[b]Not required, taking into consideration that a very low persistence of methyl eugenol in soil is expected, no soil exposure assessment is considered necessary for the representative use in greenhouse.

TABLE 2 Groundwater.[a]

Compound (name and/or code)	>0.1 μg/L at 1 m depth for the representative uses[c] step 2	Biological (pesticidal) activity/relevance step 3a	Hazard identified steps 3b. And 3c	Consumer RA triggered steps 4 and 5	Human health relevance
Clove oil (eugenol)	No	Yes	–	–	Yes
Methyl eugenol[b]	Open				

[a]Assessment according to European Commission guidance of the relevance of groundwater metabolites (2003).
[b]Provisional, the presence in groundwater has to be confirmed due to the data gap on the potential presence of methyl eugenol (genotoxic, carcinogenic) following clove oil application. No acceptable limit could be agreed for methyl eugenol on the basis of the available data.
[c]FOCUS scenarios or relevant lysimeter.

TABLE 3 Surface water and sediment.

Compound (name and/or code)	Ecotoxicology
Clove oil (eugenol)	Low risk
Methyl eugenol[a]	Not required[b]

[a]Provisional, due to the data gap on the potential presence of methyl eugenol (genotoxic, carcinogenic) following clove oil application.
[b]Not required. An aquatic risk assessment is not triggered for methyl eugenol.

TABLE 4 Air.

Compound (name and/or code)	Toxicology
Clove oil (eugenol)	Eugenol: rat LC_{50} > 2.58 mg/L

8 | PARTICULAR CONDITIONS PROPOSED TO BE TAKEN INTO ACCOUNT BY RISK MANAGERS

Risk mitigation measures (RMMs) identified following consideration of Member State (MS) and/or applicant's proposal(s) during the peer review, if any, are presented in this section. These measures applicable for human health and/or the environment leading to a reduction of exposure levels of operators, workers, bystanders/residents, environmental compartments and/or non-target organisms for the representative uses are listed below. The list may also cover any RMMs as appropriate, leading to an acceptable level of risks for the respective non-target organisms.

It is noted that final decisions on the need of RMMs to ensure the safe use of the plant protection product containing the concerned active substance will be taken by risk managers during the decision-making phase. Consideration of the validity and appropriateness of the RMMs remains the responsibility of MSs at product authorisation, taking into account their specific agricultural, plant health and environmental conditions at national level.

8.1 | Particular conditions refer only to the representative uses assessed

TABLE 5 Risk mitigation measures proposed for the representative uses assessed based on the provisory non-dietary exposure assessment.[a]

Representative use	Fruiting vegetables (soil application via drip irrigation in greenhouses)
Operator exposure[b]	Use of PPE is required[a]
Worker exposure[b]	No re-entry during 24 h after application
Bystander/resident exposure[b]	No RMM

[a]It could not be demonstrated that the AOEL derived for eugenol will also apply to clove oil, the risk assessment for operators and workers cannot be considered conclusive (critical area of concern, see Section 9.1.2).

[b]Indicative risk assessment for eugenol (main component of clove oil).

9 | CONCERNS AND RELATED DATA GAPS

9.1 | Concerns and related data gaps for the representative uses evaluated

9.1.1 | Issues that could not be finalised

An issue is listed as 'could not be finalised' if there is not enough information available to perform an assessment, even at the lowest tier level, for one or more of the representative uses in line with the uniform principles in accordance with Article 29(6) of Regulation (EC) No 1107/2009 and as set out in Commission Regulation (EU) No 546/2011[14] and if 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).

An issue is also listed as 'could not be finalised' if the available information is considered insufficient to conclude on whether the active substance can be expected to meet the approval criteria provided for in Article 4 of Regulation (EC) No 1107/2009.

The following issues or assessments that could not be finalised falling under the scope of the amendment of approval conditions have been identified, together with the reasons including the associated data gaps where relevant, which are reported directly under the specific issue to which they are related:

Issues not finalised were not identified.

9.1.2 | Critical areas of concern

An issue is listed as a critical area of concern if there is enough information available to perform an assessment for the representative uses in line with the uniform principles in accordance with Article 29(6) of Regulation (EC) No 1107/2009 and as set out in Commission Regulation (EU) No 546/2011, and if this assessment does not permit the conclusion 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 if the assessment at a higher tier level could not be finalised due to lack of information, and if the assessment performed at the lower tier level does not permit the conclusion 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 if, in the light of current scientific and technical knowledge using guidance documents available at the time of application, the active substance is not expected to meet the approval criteria provided for in Article 4 of Regulation (EC) No 1107/2009.

Critical areas of concern identified in the previous conclusion (EFSA, 2012a) which remain unaddressed and not impacted by the scope of the amendment are still applicable but have not been reproduced in this conclusion.

The following critical areas of concern falling under the scope of the amendment of approval conditions are identified, together with any associated data gaps, where relevant, which are reported directly under the specific critical area of concern to which they are related.

1. The **non-dietary risk assessment for operators and workers** for clove oil in the absence of toxicological reference values for the representative technical material, and the **consumer dietary risk assessment** for clove oil and its related metabolites (including methyl eugenol) could not be performed since the risk assessment residue

[14]Commission Regulation (EU) No 546/2011 of 10 June 2011 implementing Regulation (EC) No 1107/2009 of the European Parliament and of the Council as regards uniform principles for evaluation and authorisation of plant protection products. OJ L 155, 11.6.2011, p. 127–175.

definition for fruiting vegetables crops could not be finalised, and additional data are needed to assess the magnitude of residues in food and drinking water and to assess the criteria for inclusion in Annex IV of Commission Regulation (EC) No 839/2008 (see Sections 2, 3 and 4).

a. The technical material tested in the toxicological studies (eugenol) has not been demonstrated to be representative of the technical specification (unknown toxicological properties of all the other components present in total up to 20%) (relevant for the representative use evaluated, see Section 2).
b. No toxicological reference values could be derived for the genotoxic and carcinogenic metabolite and minor component methyl eugenol (relevant for the representative use evaluated, see Sections 2 and 3).
c. Evidence on the fate and the potential metabolic pathway of eugenol and methyl eugenol contained in clove oil (including potential presence of methyl eugenol in the metabolic pathway of eugenol) should be provided by retrieving and combining information/data from all available sources (e.g. environmental fate and behaviour studies, metabolism from post-harvest and other metabolism studies). In addition, the presence of methyl eugenol in soil inside the greenhouse (and potentially in groundwater) after clove oil application cannot be excluded based on the available data (relevant for the use evaluated, see Sections 3 and 4).
d. As regards the remaining up to 20% of minor components of clove oil, considering the representative use conditions and application rate, efforts should be made to evaluate the potential availability for uptake by plants, information on their toxicological profile might be needed (relevant for the use evaluated, see Sections 2 and 3).
e. Sufficient field residue trials compliant with the proposed uses on cucumbers and tomatoes are not available. At least four residue field trials tomato and cucumber according to the cGAP analysing for eugenol and methyl eugenol should be provided. Eight residue field trials will be needed in case residue are above the LOQ. The residue field trials should employ an analytical method with a sufficiently low LOQ for methyl eugenol to exclude any unacceptable risk to consumers considering the lack of toxicological reference values of methyl eugenol (relevant for the use proposed, see Section 3, see critical area of concern point 1 b).
f. Storage stability data for eugenol and methyl eugenol in high-water commodities covering the storage periods in the existing and requested residue field trials are needed (relevant for the use proposed, see Section 3).
g. In order to assess the residues in food resulting for the proposed use as nematicide against the criterion IV for inclusion in Annex IV of Commission Regulation (EC) No 839/2008, the dietary exposure to eugenol and/or clove oil from its natural presence in the diet should be estimated and compared with the exposure resulting from the intended uses (relevant for the proposed uses; see Section 3).

9.1.3 | Overview of the concerns identified for each representative use considered (Table 6)

(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 Table 6.)

TABLE 6 Overview of concerns reflecting the issues not finalised, critical areas of concerns and the risks identified that may be applicable for some but not for all uses or risk assessment scenarios.

Representative use		Tomatoes and cucumber Permanent greenhouse
Operator risk	Risk identified	X[1]
	Assessment not finalised	
Worker risk	Risk identified	X[1]
	Assessment not finalised	
Resident/bystander risk	Risk identified	
	Assessment not finalised	
Consumer risk	Risk identified	X[1]
	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 to active substance	Legal parametric value breached	
	Assessment not finalised	

(Continues)

TABLE 6 (Continued)

Representative use		Tomatoes and cucumber Permanent greenhouse
Groundwater exposure to metabolites	Legal parametric value breached	
	Parametric value of 10 µg/L[a] breached	
	Assessment not finalised	

Note: The superscript numbers relate to the numbered points indicated in Sections 9.1.1 and 9.1.2. Where there is no superscript number, see Sections 2–7 for further information.

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

10 | LIST OF OTHER OUTSTANDING ISSUES

Remaining data gaps not leading to critical areas of concern or issues not finalised but considered necessary to comply with the data requirements falling under the scope of the amendment of approval conditions, and which are relevant for some or all of the representative uses assessed at EU level. Although not critical, these data gaps may lead to uncertainties in the assessment and are considered relevant.

Data gaps identified in the previous conclusion (EFSA, 2012a) which remain unaddressed and are not impacted by the scope of the amendment, are still applicable but have been not reproduced in this conclusion.

- Specification of the identified components of the clove oil considered as active substance (relevant for the representative use evaluated; see Section 1; EFSA, 2012a).
- UV, IR, NMR and MS spectra for the main component eugenol, including determination of absorbance maxima (relevant for the representative use evaluated; see Section 1; EFSA, 2012a).
- Photochemical degradation (relevant for the representative use evaluated; see Section 1; EFSA, 2012a).
- Dissociation constant (relevant for the representative use evaluated; see Section 1; EFSA, 2012a).
- Stability in the air (relevant for the representative use evaluated; see Section 1; EFSA, 2012a).
- Persistent foaming data at the highest recommended concentration of 2.47 L formulation/hL were not provided (relevant for the representative use evaluated; see Section 1).
- Validation data for the analytical method used in activated sludge – respiration inhibition test with clove oil were not provided (relevant for the representative use evaluated; see Section 1).
- An analytical method for monitoring methyl eugenol in the formulation 'Bioxeda' (relevant for the representative use evaluated; see Section 1).
- A validated method for monitoring eugenol residues in air was not provided (relevant for the representative use evaluated; see Section 1).
- Acute inhalation study with eugenol (relevant for the representative use evaluated; see Section 2; EFSA, 2012a).
- An update review of the scientific literature including the search for data on clove oil component methyl eugenol and the search for data on non-dietary exposure need to be provided to support the assessment of the residues in food (relevant for the representative use evaluated; see Section 'the active substance and the formulation(s) for representative uses').
- Further information to determine the origin of the detection of eugenol dimer in the study Palau (2020) (already at time 0) is missing (relevant for the representative use evaluated; see Evaluation Table Section 4).
- A reliable adsorption study for clove oil is missing, according to data requirements in Regulation 283/2013. Reliable adsorption parameters are not considered essential to finalise the risk assessment of the representative use (drip irrigation in greenhouse), since PECsw and PECgw calculated with a DT50 in soil of 1 day and Koc of 10 mL/g (worst-case) indicate that exposure to surface water and groundwater can be considered very low (relevant for the representative use evaluated; see Evaluation Table Section 4, EFSA (2024)).
- A reliable hydrolysis degradation study for clove oil is missing (relevant for the representative use evaluated; see Evaluation Table Section 4, EFSA (2024).
- Applicant did not justify whether there is available monitoring data of clove oil components or not. If there is, such monitoring data should be provided in the dossier (relevant for the representative use evaluated; see Evaluation Table Section 4, EFSA (2024).

ABBREVIATIONS

1/*n*	slope of Freundlich isotherm
λ	wavelength
ε	decadic molar extinction coefficient
AMA	Amphibian Metamorphosis Assay
a.s.	active substance
ADE	actual dermal exposure
ADI	acceptable daily intake

AF	assessment factor
AhR	aryl hydrocarbon receptor
AOEL	acceptable operator exposure level
AP	alkaline phosphatase
AR	applied radioactivity
AR	androgen receptor
AST	aspartate aminotransferase (SGOT)
AUC	area under the blood concentration/time curve
AV	avoidance factor
BCF	bioconcentration factor
BUN	blood urea nitrogen
bw	body weight
CAS	Chemical Abstracts Service
CFU	colony-forming units
ChE	cholinesterase
CHO	Chinese hamster ovary cells
CI	confidence interval
CL	confidence limits
DAA	days after application
DAR	draft assessment report
DAT	days after treatment
DM	dry matter
DT_{50}	period required for 50% dissipation (define method of estimation)
dw	dry weight
EAS	oestrogen, androgen and steroidogenesis modalities
ECHA	European Chemicals Agency
EEC	European Economic Community
ERO	ecological recovery option
ETO	ecological threshold option
ETR	exposure toxicity ratio
FAO	Food and Agriculture Organization of the United Nations
FOCUS	Forum for the Co-ordination of Pesticide Fate Models and their Use
GAP	Good Agricultural Practice
GC	gas chromatography
HPLC	high-pressure liquid chromatography or high-performance liquid chromatography
HPLC-MS/MS	high-pressure liquid chromatography with tandem mass spectrometry
HQ	hazard quotient
HR	hazard rate
ISO	International Organization for Standardization
IUPAC	International Union of Pure and Applied Chemistry
iv	intravenous
JMPR	Joint Meeting of 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
K_{Foc}	Freundlich organic carbon adsorption coefficient
LC	liquid chromatography
LC_{50}	lethal concentration, median
LC-MS	liquid chromatography–mass spectrometry
LC-MS-MS	liquid chromatography with tandem mass spectrometry
LH	luteinizing hormone
LOQ	limit of quantification
MCV	mean corpuscular volume
mm	millimetre (also used for mean measured concentrations)
mN	milli-Newton
MRL	maximum residue level
MS	mass spectrometry
MTD	maximum tolerated dose
NESTI	national estimated short-term intake
NOAEL	no observed adverse effect level
NOEL	no observed effect level
OECD	Organisation for Economic Co-operation and Development
OM	organic matter content

Pa	pascal
PD	proportion of different food types
PEC	predicted environmental concentration
PEC_{gw}	predicted environmental concentration in groundwater
PEC_{sw}	predicted environmental concentration in surface water
PHI	preharvest interval
PIE	potential inhalation exposure
P_{ow}	partition coefficient between *n*-octanol and water
PPE	personal protective equipment
ppm	parts per million (10^{-6})
PT	proportion of diet obtained in the treated area
PTT	partial thromboplastin time
RAC	regulatory acceptable concentration
RBC	red blood cells
REACH	Registration, Evaluation, Authorisation of Chemicals Regulation
RUD	residue per unit dose
SC	suspension concentrate
SD	standard deviation
SFO	single first-order
SMILES	simplified molecular-input line-entry system
SSD	species sensitivity distribution
TER	toxicity exposure ratio
TER_A	toxicity exposure ratio for acute exposure
TER_{LT}	toxicity exposure ratio following chronic exposure
TK	technical concentrate
TLV	threshold limit value
TWA	time-weighted average
UV	ultraviolet
WHO	World Health Organization

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CONFLICT OF INTEREST
If you wish to access the declaration of interests of any expert contributing to an EFSA scientific assessment, please contact interestmanagement@efsa.europa.eu.

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NOTE/UPDATE
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REFERENCES
EFSA (European Food Safety Authority). (2008). Opinion on a request from EFSA related to the default Q10 value used to describe the temperature effect on transformation rates of pesticides in soil. *EFSA Journal*, *6*(1), 622. https://doi.org/10.2903/j.efsa.2008.622

EFSA (European Food Safety Authority). (2009). Guidance on risk assessment for birds and mammals on request from EFSA. *EFSA Journal*, *7*(12), 1438. https://doi.org/10.2903/j.efsa.2009.1438

EFSA (European Food Safety Authority). (2011). Submission of scientific peer-reviewed open literature for the approval of pesticide active substances under regulation (EC) No 1107/2009. *EFSA Journal*, *9*(2), 2092. https://doi.org/10.2903/j.efsa.2011.2092

EFSA (European Food Safety Authority). (2012a). Conclusion on the peer review of the pesticide risk assessment of the active substance clove oil. *EFSA Journal*, *10*(1), 2506. https://doi.org/10.2903/j.efsa.2012.2506

EFSA (European Food Safety Authority). (2012b). Conclusion on the peer review of the pesticide risk assessment of the active substance eugenol. *EFSA Journal*, *10*(11), 2914. https://doi.org/10.2903/j.efsa.2012.2914

EFSA (European Food Safety Authority). (2013). EFSA guidance document on the risk assessment of plant protection products on bees (*Apis mellifera, Bombus* spp. and solitary bees). *EFSA Journal*, *11*(7), 3295. https://doi.org/10.2903/j.efsa.2013.3295

EFSA (European Food Safety Authority). (2014a). Guidance on the assessment of exposure of operators, workers, residents and bystanders in risk assessment for plant protection products. *EFSA Journal*, *12*(10), 3874. https://doi.org/10.2903/j.efsa.2014.3874

EFSA (European Food Safety Authority). (2014b). Guidance document on clustering and ranking of emissions of active substances of plant protection products and transformation products of these active substances from protected crops (greenhouses and crops grown under cover) to relevant environmental compartments. *EFSA Journal*, *12*(3), 3615. https://doi.org/10.2903/j.efsa.2014.3615

EFSA (European Food Safety Authority). (2015). Technical report on the outcome of the pesticides peer review meeting on general recurring issues in ecotoxicology. *EFSA Supporting Publication*, 2015:EN-924. 62 pp. https://doi.org/10.2903/j.efsa.2015.EN-924

EFSA (European Food Safety Authority). (2017a). Technical report on the outcome of the consultation with member states, the applicant and EFSA on the pesticide risk assessment for clove oil in light of confirmatory data. *EFSA Supporting Publication*, 2017:EN-1193. 24 pp. https://doi.org/10.2903/sp.efsa.2017.EN-1193

EFSA (European Food Safety Authority), Buist, H., Craig, P., Dewhurst, I., HougaardBennekou, S., Kneuer, C., Machera, K., Pieper, C., Court Marques, D., Guillot, G., Ruffo, F., & Chiusolo, A. (2017b). Guidance on dermal absorption. *EFSA Journal*, *15*(6), 4873. https://doi.org/10.2903/sp.efsa.2017.4873

EFSA (European Food Safety Authority). (2024). Peer review report to the conclusion regarding the peer review of the pesticide risk assessment of the active substance clove oil. www.efsa.europa.eu

EFSA PPR Panel (EFSA Panel on Plant Protection Products and their Residues). (2013). Guidance on tiered risk assessment for plant protection products for aquatic organisms in edge-of-field surface waters. *EFSA Journal*, *11*(7), 3290. https://doi.org/10.2903/j.efsa.2013.3290

European Commission. (2000). Residues: guidance for generating and reporting methods of analysis in support of pre-registration data requirements for Annex II (Part A, Section 4) and Annex III (Part A, Section 5) of Directive 91/414. SANCO/3029/99-rev. 4, 11 July 2000.

European Commission. (2002). Guidance Document on Terrestrial Ecotoxicology Under Council Directive 91/414/EEC. SANCO/10329/2002-rev. 2 final, 17 October 2002.

European Commission. (2003). Guidance Document on Assessment of the Relevance of Metabolites in Groundwater of Substances Regulated under Council Directive 91/414/EEC. SANCO/221/2000-rev. 10 final, 25 February 2003.

European Commission. (2010). Guidance document on residue analytical methods. SANCO/825/00-rev. 8.1, 16 November 2010.

European Commission. (2011). Guidelines on comparability, extrapolation, group tolerances and data requirements for setting MRLs. SANCO 7525/VI/95-rev. 9. March 2011. pp. 1–46.

European Commission. (2013). Guidance document on data requirements on efficacy for the dossier to be submitted for the approval of new active substances contained in plant protection products. SANCO/10054/2013-rev. 3, 11 July 2013.

European Commission. (2014). Assessing potential for movement of active substances and their metabolites to ground water in the EU. Report of the FOCUS Workgroup. EC Document Reference SANCO/13144/2010-v. 3, 613 pp., as outlined in Generic guidance for tier 1 FOCUS groundwater assessment, v. 2.2, May 2014.

European Commission. (2015). Guidance document on criteria for the inclusion of active substances into Annex IV of Regulation (EC) No. 396/2005. SANCO/11188/2013, rev. 2, 14 September 2015.

FOCUS (Forum for the Co-ordination of Pesticide Fate Models and their Use). (2001). FOCUS surface water scenarios in the EU evaluation process under 91/414/EEC. Report of the FOCUS Working Group on Surface Water Scenarios. EC Document Reference SANCO/4802/2001-rev. 2, 245 pp., as updated by Generic guidance for FOCUS surface water scenarios, v. 1.4, May 2015.

FOCUS (Forum for the Co-ordination of Pesticide Fate Models and their Use). (2006). Guidance document on estimating persistence and degradation kinetics from environmental fate studies on pesticides in EU Registration Report of the FOCUS Work Group on Degradation Kinetics. EC Document Reference SANCO/10058/2005-v. 2.0, 434 pp., as updated by the Generic guidance for Estimating Persistence and Degradation Kinetics from Environmental Fate Studies on Pesticides in EU Registration, v. 1.1.

JMPR (Joint Meeting on Pesticide Residues). (2004). Report of the Joint Meeting of the FAO Panel of Experts on Pesticide Residues in Food and the Environment and the WHO Core Assessment Group on Pesticide Residues, Rome, Italy, 20–29 September 2004, 383 pp.

JMPR (Joint Meeting on Pesticide Residues). (2007). Report of the Joint Meeting of the FAO Panel of Experts on Pesticide Residues in Food and the Environment and the WHO Core Assessment Group on Pesticide Residues, Geneva, Switzerland, 18–27 September 2007, 164 pp.

Malta. (2021). Draft Assessment Report (DAR) on the active substance clove oil prepared by the rapporteur Member State Malta, in the framework of Regulation (EC) No 1107/2009, October 2021. www.efsa.europa.eu

Malta. (2023). Revised draft assessment report (DAR) on clove oil prepared by the rapporteur member state Malta in the framework of regulation (EC) No 1107/2009, October 2023. www.efsa.europa.eu

McCall, P. J., Laskowski, D. A., Swann, R. L., & Dishburger, H. J. (1980). Measurements of sorption coefficients of organic chemicals and their use in environmental fate analysis. In: Test protocols for environmental fate and movement of toxicants. In: Proceedings of the 94th annual meeting of the American Association of Official Analytical Chemists (AOAC). October 21–22, Washington, DC. pp. 89–109.

OECD (Organisation for Economic Co-operation and Development). (2009). Guidance document on overview of residue chemistry studies. ENV/JM/MONO(2009)31, 28 July 2009.

OECD (Organisation for Economic Co-operation and Development). (2011). OECD MRL calculator: Spreadsheet for single data set and spreadsheet for multiple data set, 2 march 2011. In: Pesticide Publications/Publications on Pesticide Residues. www.oecd.org

SETAC (Society of Environmental Toxicology and Chemistry), Candolfi, M. P., Barrett, K. L., Campbell, P. J., Forster, R., Grandy, N., Huet, M. C., Lewis, G., Oomen, P. A., Schmuck, R., & Vogt, H. (Eds.). (2001). *Guidance document on regulatory testing and risk assessment procedures for plant protection products with non-target arthropods*. ESCORT 2 workshop.

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APPENDIX A

Consideration of cut-off criteria for clove oil according to Annex II of Regulation (EC) No 1107/2009 of the European Parliament and of the Council

Properties		Conclusion[a]
CMR	**Carcinogenicity (C)**	The carcinogenicity properties of clove oil according to point 3.6.3 of Annex II of Regulation (EC) No 1107/2009 were not discussed in this conclusion. This endpoint will be addressed in the context of the renewal of approval procedure of clove oil (AIR IV, EFSA Q-2016-00809)
	Mutagenicity (M)	The mutagenicity properties of clove oil according to point 3.6.2 of Annex II of Regulation (EC) No 1107/2009 were not discussed in this conclusion. This endpoint will be addressed in the context of the renewal of approval procedure of clove oil (AIR IV, EFSA Q-2016-00809)
	Toxic for Reproduction (R)	The toxic for reproduction properties of clove oil according to point 3.6.4 of Annex II of Regulation (EC) No 1107/2009 was not discussed in this conclusion. This endpoint will be addressed in the context of the renewal of approval procedure of clove oil (AIR IV, EFSA Q-2016-00809)
Endocrine-disrupting properties		The endocrine disruption properties of clove oil according to points 3.6.5 and 3.8.2 of Annex II of Regulation No 1107/2009, as amended by Commission Regulation (EU) 2018/605 were not discussed in this conclusion. This endpoint will be addressed in the context of the renewal of approval procedure of clove oil (AIR IV, EFSA Q-2016-00809)
POP	**Persistence** **Bioaccumulation** **Long-range transport**	The persistence, bioaccumulation and long-range transport (POP) properties of clove oil were not discussed in this conclusion. This endpoint will be addressed in the context of the renewal of approval procedure of clove oil (AIR IV, EFSA Q-2016-00809)
PBT	**Persistence** **Bioaccumulation** **Toxicity**	The persistence, bioaccumulation and toxicity (PBT) properties of clove oil were not discussed in this conclusion. This endpoint will be addressed in the context of the renewal of approval procedure of clove oil (AIR IV, EFSA Q-2016-00809)
vPvB	**Persistence** **Bioaccumulation**	The very persistent, very bioaccumulative (vPvB) properties of clove oil were not discussed in this conclusion. This endpoint will be addressed in the context of the renewal of approval procedure of clove oil (AIR IV, EFSA Q-2016-00809)

[a]Origin of data to be included where applicable (e.g. EFSA, EChA RAC, Regulation).

APPENDIX B

List of end points for the active substance and the formulation(s) for representative uses relevant for the amendment of approval conditions

Appendix B can be found in the online version of this output ('Supporting information' section): https://doi.org/10.2903/j.efsa.2024.8671

APPENDIX C

Wording EFSA used in Section 4 of this conclusion, in relation to DT and K_{oc} 'classes' exhibited by each compound assessed

Wording	DT_{50} normalised to 20°C for laboratory incubations[a] or not normalised DT_{50} for field studies (SFO equivalent, when biphasic, the DT_{90} was divided by 3.32 to estimate the DT50 when deciding on the wording to use)
Very low persistence	< 1 day
Low persistence	1 to < 10 days
Moderate persistence	10 to < 60 days
Medium persistence	60 to < 100 days
High persistence	100 days to < 1 year
Very high persistence	A year or more

Note: These classes and descriptions are unrelated to any persistence class associated with the active substance cut-off criteria in Annex II of Regulation (EC) No 1107/2009. For consideration made in relation to Annex II, see Appendix A.

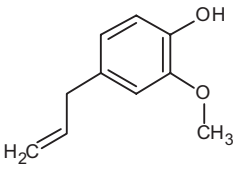
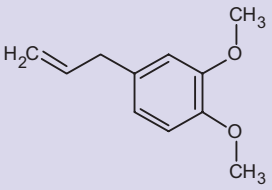
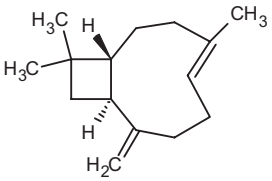
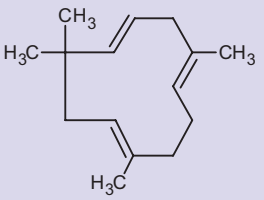
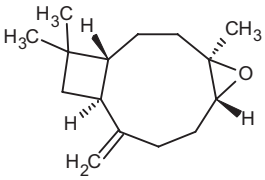
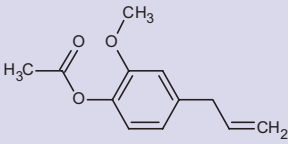
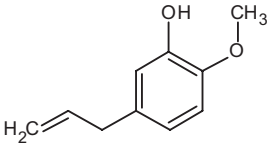
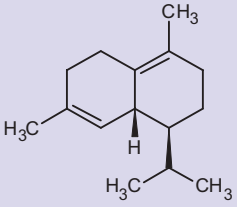
[a]For laboratory soil incubations, normalisation was also to field capacity soil moisture (pF2/10 kPa). For laboratory sediment water system incubations, the whole system DT values were used.

Wording	K_{oc} (either K_{Foc} or K_{doc}) mL/g
Very high mobility	0–50
High mobility	51–150
Medium mobility	151–500
Low mobility	501–2000
Slight mobility	2001–5000
Immobile	> 5000

Note: Based on McCall et al. (1980).

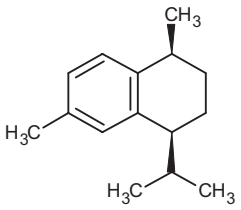
APPENDIX D

Used compound codes

Code/trivial name[a]	IUPAC name/SMILES notation/InChiKey[b]	Structural formula[c]
Eugenol	2-methoxy-4-(prop-2-en-1-yl)phenol Oc1ccc(cc1OC)CC=C RRAFCDWBNXTKKO-UHFFFAOYSA-N	
Methyl eugenol	1,2-dimethoxy-4-(prop-2-en-1-yl)benzene COc1cc(ccc1OC)CC=C ZYEMGPIYFIJGTP-UHFFFAOYSA-N	
β-caryophyllene, caryophyllene)	(1*R*,4*E*,9*S*)-4,11,11-trimethyl-8-methylidenebicyclo[7.2.0]undec-4-ene C=C1CCC=C©CC[C@@H]2[C@@H]1CC2©C NPNUFJAVOOONJE-GFUGXAQUSA-N	
α-caryophyllene, (or humulene)	(1*E*,4*E*,8*E*)-2,6,6,9-tetramethylcycloundeca-1,4,8-triene CC=1CC=CC(C)(C)CC=C(C)CCC=1 FAMPSKZZVDUYOS-HRGUGZIWSA-N	
Caryophyllene oxide	(1*R*,4*R*,6*R*,10*S*)-4,12,12-trimethyl-9-methylidene-5-oxatricyclo[8.2.0.0^{4,6}] dodecane C=C1CC[C@H]2O[C@]2©CC[C@@H]2[C@@H]1CC2©C NVEQFIOZRFFVFW-RGCMKSIDSA-N	
Eugenol acetate	2-methoxy-4-(prop-2-en-1-yl)phenyl acetate Coc1cc(ccc1OC©=O)CC=C SCCDQYPEOIRVGX-UHFFFAOYSA-N	
Meta eugenol	2-methoxy-5-(prop-2-en-1-yl)phenol Oc1cc(ccc1OC)CC=C NPBVQXIMTZKSBA-UHFFFAOYSA-N	
δ-cadinene	(1*S*,8a*R*)-4,7-dimethyl-1-(propan-2-yl)-1,2,3,5,6,8a-hexahydronaphthalene CC©[C@@H]1CCC©=C2CCC©=C[C@H]21 FUCYIEXQVQJBKY-ZFWWWQNUSA-N	

(Continues)

(Continued)

Code/trivial name[a]	IUPAC name/SMILES notation/InChiKey[b]	Structural formula[c]
Calamenene	(1*S*,4*S*)-1,6-dimethyl-4-(propan-2-yl)-1,2,3,4-tetrahydronaphthalene CC(C)[C@@H]1CC[C@H](C)c2ccc(C)cc21 PGTJIOWQJWHTJJ-STQMWFEESA-N	

[a]The name in bold is the name used in the conclusion.

[b]ACD/Name 2021.1.3 ACD/Labs 2021.1.3 (File Version N15E41, Build 123232, 7 July 2021).

[c]ACD/ChemSketch 2021.1.3 ACD/Labs 2021.1.3 (File Version C25H41, Build 123835, 28 August 2021).