Biocidal Products Committee (BPC)

Opinion on the application for approval of the active substance:

Margosa extract, cold-pressed oil of *Azadirachta indica* seeds without shells extracted with super-critical carbon dioxide

Product type: 19

ECHA/BPC/146/2017

Adopted

3 March 2017

Annankatu 18, P.O. Box 400, FI-00121 Helsinki, Finland | Tel. +358 9 686180 | Fax +358 9 68618210 | echa.europa.eu

Opinion of the Biocidal Products Committee

on the application for approval of the active substance margosa extract, cold-pressed oil of *Azadirachta indica* seeds without shells extracted with super-critical carbon dioxide for product type 19

In accordance with Article 89(1) of Regulation (EU) No 528/2012 of the European Parliament and of the Council 22 May 2012 concerning the making available on the market and use of biocidal products (BPR), the Biocidal Products Committee (BPC) has adopted this opinion on the approval in product type 19 of the following active substance:

Common name:	**margosa extract**
	Description: margosa extract, cold-pressed oil of *Azadirachta indica* seeds without shells extracted with super-critical carbon dioxide
Chemical name:	**Not applicable[1]**
EC No.:	**283-644-7**
CAS No.:	**84696-25-3**
Existing active substance	

This document presents the opinion adopted by the BPC, having regard to the conclusions of the evaluating Competent Authority. The assessment report, as a supporting document to the opinion, contains the detailed grounds for the opinion.

Process for the adoption of BPC opinions

Following the submission of an application by Terra Nostra GmbH on 26 April 2006, the evaluating Competent Authority Germany submitted an assessment report and the conclusions of its evaluation to the ECHA on 3 December 2015. In order to review the assessment report and the conclusions of the evaluating Competent Authority, the Agency organised consultations via the BPC (BPC-19) and its Working Groups (WG III 2016). Revisions agreed upon were presented and the assessment report and the conclusions were amended accordingly.

[1] Since margosa extract is a UVCB substance.

Adoption of the BPC opinion

Rapporteur: Germany

The BPC opinion on the approval of the active substance margosa extract, cold-pressed oil of *Azadirachta indica* seeds without shells extracted with super-critical carbon dioxide in product type 19 was adopted on 3 March 2017.

The BPC opinion was adopted by consensus. The opinion is published on the ECHA webpage at:

http://echa.europa.eu/regulations/biocidal-products-regulation/approval-of-active-substances/bpc-opinions-on-active-substance-approval.

Detailed BPC opinion and background

1. Overall conclusion

The overall conclusion of the BPC is that the margosa extract, cold-pressed oil of *Azadirachta indica* seeds without shells extracted with super-critical carbon dioxide in product type 19 may be approved. The detailed grounds for the overall conclusion are described in the assessment report.

2. BPC Opinion

2.1. BPC Conclusions of the evaluation

a) Presentation of the active substance including the classification and labelling of the active substance

This evaluation covers the use of margosa extract, cold-pressed oil of *Azadirachta indica* seeds without shells extracted with super-critical carbon dioxide (hereafter presented as margosa extract) in product type 19.

Specifications for the reference source are established. Margosa extract is an UVCB substance containing limonoids (represented by azadirachtin A and B, nimbin and salannin present in <2%).

Margosa extract has already been included in the Union list of approved active substances for PT 18 with the name margosa extract from the kernels of *Azadirachta indica* extracted with water and further processed with organic solvents[2], differing in composition and extraction method from the margosa extract being subject to the present opinion.

The physico-chemical properties of the active substance and biocidal product have been evaluated and are deemed acceptable for the appropriate use, storage and transportation of the active substance and biocidal product.

Validated analytical methods are available for the active substance as manufactured. Validated analytical methods are required and available for the relevant matrices soil, air, drinking and surface water, body fluids and body tissues.

A validated residue analytical method is available for detecting the analytical lead compound salannin in air. Sufficiently validated primary and confirmatory methods for detecting residues of the analytical lead compound salannin in soil, drinking water and surface water are missing and should be provided. Other analytical methods are not required, because no relevant residues are expected in food and feeding stuffs. Because the active substance is not classified as toxic or very toxic, residue analytical methods in body fluids and tissues are also not required.

Currently, a harmonised classification according to Regulation (EU) No 1272/2008 (CLP Regulation) is not available for margosa extract.

It is proposed that no classification and labelling for the active substance according to Regulation (EC) No 1272/2008 (CLP Regulation) is required. The eCA submitted a CLH dossier in December 2015.

b) Intended use, target species and effectiveness

Margosa extract is intended to be used as a repellent to deter ants (e.g. *Lasius niger*) from entering buildings. It is aimed at non-professional users to be used in private houses. The intended use is the application of a biocidal product containing margosa extract on doorsteps and windowsills in a 2 cm wide line, serving as a barrier for ants trying to enter the house from the outside.

[2] Commission Directive 2012/15/EU

The mode of action responsible for the repellent activity of margosa extract is not known. As the extract contains a mixture of limonoids, it is probably a combined effect of these that leads to a repellent effect.

The data on margosa extract and the representative biocidal product have demonstrated sufficient repellent efficacy against the target species. The application rate was 4 g margosa extract per linear meter on open-pored beech plywood, and 1.6 g margosa extract per linear meter on acacia terrace board. More specific testing should be assessed during product authorization, as the substance used in the efficacy trials was 100% margosa extract.

Since margosa extract is used as a repellent, it does not exert a selective pressure for developing resistance. Margosa extract is a plant extract from seed kernels of the Neem tree. Due to the complex composition of this plant extract and the complex mode of action which is not restricted to a single target site, the possibility of the development of resistance against this active ingredient is estimated as very low. Ants that are repelled from entering a premise are free to feed in different, unprotected areas. Development of resistance is not expected.

c) Overall conclusion of the evaluation including need for risk management measures

Human health

Margosa extract is of low overall toxicity. It is not acutely toxic when administered orally, dermally or by inhalation. It is not irritating to the skin or eyes of rabbits following single-application and did not sensitise the skin of guinea pigs. After repeated exposure skin irritation occurred in rats and rabbits whereas liver weight increases were observed as systemic effects. However, no classification for these effects is considered necessary. Overall, margosa extract is not genotoxic and does not show a potential for reproductive toxicity. Waiving arguments were submitted and accepted for carcinogenicity, immunotoxicity and endocrine disrupting properties.

The table below summarises the exposure scenarios assessed.

Summary table: human health scenarios			
Scenario	**Primary or secondary exposure and description of scenario**	**Exposed group**	**Conclusion**
Brushing	Primary medium-term exposure – application of margosa extract by brushing (incl. brush cleaning)	Non-professional users	Acceptable
Adult contact with bare feet	Adults Secondary acute exposure – contact to treated surfaces (acacia wood) with bare feet	General public, adults	Acceptable
Toddler crawling on treated surface	Toddlers Secondary acute exposure – contact to treated surfaces (acacia wood) with hand when crawling and subsequent licking of hand	General public, toddlers	Acceptable

No unacceptable risks have been identified for the application of the biocidal products by non-professional user. The same applies for secondary exposure of the general public (including adults and toddlers).

Environment

Biodegradation

Constituents significantly contributing to the environmental risk and hazard assessment are considered as relevant constituents and subject to a detailed evaluation. For margosa extract this applies to the limonoids salannin, nimbin and azadirachtin.

The table below summarises the exposure scenarios assessed.

Summary table: environment scenarios		
Scenario	**Description of scenario including environmental compartments**	**Conclusion**
Consumption based scenario		
Non-professional use: application phase and emission due to wet cleaning and brush residues	Barrier repellent indoor treatment against garden ants by non-professional users: Targeted barrier surface application of a product in gel form with a brush. Wet cleaning of treated area and brush residues. Emissions of STP and subsequently to surface water, sediment, soil and groundwater	Not acceptable for surface water, sediment and soil. Neither refinements nor degradation in STP were considered. Based on the identified risk, risk mitigation measures regarding application method, and/or amount of treated surface and/or cleaning of the barrier and brush would be required
Tonnage-based scenario		
Non-professional use	STP is considered as primary receiving compartment with subsequent emissions to surface water, sediment, soil and groundwater. Modelling is based on extrapolated total European production tonnage of the active substance considering a potentially increased use.	Acceptable for all environmental compartments considering 100% emission to wastewater, no degradation and uneven spatial and temporal distribution of product(s) used in the EU.

Unacceptable risks for the consumption approach are indicated for the environmental compartments surface water, sediment and soil. However, this outcome is based on pure margosa extract without any refinements with regard to its application phase (including wet cleaning and brush residues) and without considering available degradation data for the whole extract. For a formulated product, also risk mitigation measures could be considered. Multiple emissions in one catchment area were assessed with the method of the simultaneity factor (Fsimultaneity) for insecticides from the ESD PT 18 (2008), which results in an overestimation of occurring emissions for a PT 19 product. Therefore, an additional tonnage-based risk assessment considering uneven spatial and temporal distribution was performed.

The tonnage-based approach shows acceptable risks for all environmental compartments and was considered as appropriate for demonstrating a safe use for active substance approval. During product authorisation it is required that also the consumption-based approach indicates a safe use.

Overall conclusion

A safe use for human health and environment is identified for non-professional use of the product.

A safe use for the environment has been identified for the indoor barrier application by the non-professional user on the basis of a tonnage-based scenario. This was considered as appropriate for demonstrating a safe use at active substance approval stage, in this specific case. During product authorisation it is required that also the consumption-based approach indicates a safe use.

2.2. Exclusion, substitution and POP criteria

2.2.1. Exclusion and substitution criteria

At the time of the submission of the active substance dossier, a detailed assessment of the components was not subject of the relevant guidance[3,4]. Therefore, the assessment has been performed on the data already available.

The table below summarises the relevant information with respect to the assessment of exclusion and substitution criteria:

Property		Conclusions	
CMR properties	Carcinogenicity (C)	No classification required	Margosa extract does not fulfil criterion (a), (b) and (c) of Article 5(1)
	Mutagenicity (M)	No classification required	
	Toxic for reproduction (R)	No classification required	
PBT and vPvB properties	Persistent (P) or very Persistent (vP)	potentially P/vP, based on salannin, nimbin, azadirachtin A + B and stigmasterol	Margosa extract does not fulfil criterion (e) of Article 5(1) and does not fulfil criterion (d) of Article 10(1)]
	Bioaccumulative (B) or very Bioaccumulative (vB)	not B / not vB, based on stigmasterol, salannin, nimbin, azadirachtin A+B. B/vB assessment scientifically unjustified for lipids	
	Toxic (T)	potentially T, based on salannin, nimbin, azadirachtin A+B	
Endocrine disrupting properties	Margosa extract is not considered to have endocrine disrupting properties. Margosa extract does not fulfil criterion (d) of Article 5(1).		
Respiratory sensitisation properties	No classification required. Margosa extract does not fulfil criterion (b) of Article 10 (1).		
Concerns linked to critical effects	Margosa extract does not fulfil criterion (e) of Article 10 (1)		

[3] "How to deal with extracts and oils of plant or animal origin?" endorsed at the 23rd CA-Meeting.

[4] "Guidance to Member States and industry on the data requirements for naturally occurring substances used as attractants/repellents", endorsed at the 18th CA-Meeting.

Proportion of non-active isomers or impurities	Margosa extract does not fulfil criterion (f) of Article 10 (1)

Consequently, the following is concluded:

Margosa extract does not meet the exclusion criteria laid down in Article 5 of Regulation (EU) No 528/2012.

Margosa extract does not meet the conditions laid down in Article 10 of Regulation (EU) No 528/2012, and is therefore not considered as a candidate for substitution. The PBT assessment should be revised during the renewal procedure with regard to potential P/vP and potential T properties of the constituents. The exclusion and substitution criteria were assessed in line with the "Note on the principles for taking decisions on the approval of active substances under the BPR"[5] and in line with "Further guidance on the application of the substitution criteria set out under article 10(1) of the BPR"[6] agreed at the 54th and 58th meeting respectively, of the representatives of Member States Competent Authorities for the implementation of Regulation 528/2012 concerning the making available on the market and use of biocidal products. This implies that the assessment of the exclusion criteria is based on Article 5(1) and the assessment of substitution criteria is based on Article 10(1)(a, b, d, e and f).

2.2.2. POP criteria

Margosa extract does not fulfil the criteria for being a persistent organic pollutant.

2.3. BPC opinion on the application for approval of the active substance margosa extract, cold-pressed oil of *Azadirachta indica* seeds without shells extracted with super-critical carbon dioxide in product type 19

In view of the conclusions of the evaluation, it is proposed that margosa extract, cold-pressed oil of *Azadirachta indica* seeds without shells extracted with super-critical carbon dioxide shall be approved and be included in the Union list of approved active substances, subject to the following specific conditions:

1. Specification: minimum purity of the active substance evaluated: 1,000 g/kg.
2. The authorisations of biocidal products are subject to the following condition(s):
    a. The product assessment shall pay particular attention to the exposures, the risks and the efficacy linked to any uses covered by an application for authorisation, but not addressed in the Union level risk assessment of the active substance.
    b. In view of the risks identified for the uses assessed, the product assessment shall pay particular attention to:
        i. Surface water, sediment and soil.
    c. For products that may lead to residues in food or feed, the need to set new or to amend existing maximum residue levels (MRLs) in accordance with Regulation (EC) No 470/2009 or Regulation (EC) No 396/2005 shall be verified, and any appropriate risk mitigation measures shall be taken to ensure that the applicable MRLs are not exceeded.

[5] See document: Note on the principles for taking decisions on the approval of active substances under the BPR (available from https://circabc.europa.eu/d/a/workspace/SpacesStore/c41b4ad4-356c-4852-9512-62e72cc919df/CA-March14-Doc.4.1%20-%20Final%20-%20Principles%20for%20substance%20approval.doc)
[6] See document: Further guidance on the application of the substitution criteria set out under article 10(1) of the BPR (available from https://circabc.europa.eu/d/a/workspace/SpacesStore/dbac71e3-cd70-4ed7-bd40-fc1cb92cfe1c/CA-Nov14-Doc.4.4%20-%20Final%20-%20Further%20guidance%20on%20Art10(1).doc)

Formally, the active substance margosa extract cold-pressed oil of *Azadirachta indica* seeds without shells extracted with super-critical carbon dioxide gives no rise to concern according to Article 28 (2). Given that a definitive conclusion on the P and T criterion and consequently the fulfilment of criterion (d) of Article 10(1) is still outstanding, margosa extract is currently not proposed for Annex I of Regulation (EU) 528/2012.

2.4. Elements to be taken into account when authorising products

The following recommendations and risk mitigation measures have been identified for the uses assessed. Authorities should consider these risk mitigation measures when authorising products, together with possible other risk mitigation measures, and decide whether these measures are applicable for the concerned product:

a. Unacceptable risks for the environmental compartments surface water, sediment and soil have been identified based on a consumption-based approach. For product authorisation it is required that both the consumption and tonnage based environmental risk assessment show acceptable risks for the environment. During active substance approval a safe use has only been demonstrated for the tonnage based approach. This is mainly attributed to the lack of product specific refinement options for the assessed product and the non-inclusion of degradation processes in the environmental risk assessment. Therefore, it was agreed that for product authorisation both approaches should demonstrate acceptable risks. The tonnage based calculation should be performed on recent tonnage data. Furthermore, alternative approaches for the assessment of multiple emissions in a STP catchment area for PT 19 should be considered.

b. An assessment of the risk in food and feed areas may be required at product authorisation where use of the product may lead to contamination of food and feeding stuffs.

2.5. Requirement for further information

Sufficient data have been provided to verify the conclusions on the active substance, permitting the proposal for the approval of margosa extract, cold-pressed oil of azadirachta indica seeds without shells extracted with super-critical carbon dioxide. However, the following data must be provided as soon as possible but no later than 6 months before the date of approval to the evaluating Competent Authority (DE):

- Sufficiently validated primary and confirmatory methods for detecting the analytical lead compound salannin in soil, drinking and surface water should be provided.

For the renewal process, further information is required for the PBT assessment to conclude whether the limonoids meet the P and T criteria. The information is required at renewal and not 6 month before the date of approval because at the time of the submission of the active substance dossier, a detailed assessment of the components was not subject of the relevant guidance as explained in section 2.2.1.

o0o