CONCLUSION ON PESTICIDES PEER REVIEW

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Peer review of the pesticide risk assessment of the active substance hydrolysed proteins

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Abstract

The conclusions of EFSA following the peer review of the initial risk assessments carried out by the competent authorities of the rapporteur Member State Spain and co-rapporteur Member State Greece for the pesticide active substance hydrolysed proteins and the considerations as regards the inclusion of the substance in Annex IV of Regulation (EC) No 396/2005 are reported. The context of the peer review was that required by Commission Implementing Regulation (EU) No 844/2012, as amended by Commission Implementing Regulation (EU) No 2018/1659. The conclusions were reached on the basis of the evaluation of the representative uses of hydrolysed proteins as an insect attractant on olive tree, deciduous fruit tree, stone fruit tree, pome fruit tree, walnut tree, citrus tree, fig tree, persimmon tree, kiwi and blueberry crops. The reliable end points, appropriate for use in regulatory risk assessment, are presented. Missing information identified as being required by the regulatory framework is listed. Concerns are reported where identified.

Keywords: hydrolysed proteins, peer review, risk assessment, pesticide, attractant, MRL review

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Summary

Commission Implementing Regulation (EU) No 844/2012, as amended by Commission Implementing Regulation (EU) No 2018/1659, lays down the procedure for the renewal of the approval of active substances submitted under Article 14 of Regulation (EC) No 1107/2009. The list of those substances is established in Commission Implementing Regulation (EU) No 686/2012 as amended by Commission Implementing Regulation (EU) No 2016/183. Hydrolysed proteins is one of the active substances listed in that Regulation.

In accordance with Article 1 of Regulation (EU) No 844/2012, the rapporteur Member State (RMS), Spain, and co-rapporteur Member State (co-RMS), Greece, received an application from a task force (consisting of BIOIBÉRICA, S.A.U., N.G.STAVRAKIS – PHYTOPHYL and SICIT 2000 S.p.A.) and from PROALAN S.A. for the renewal of approval of the active substance hydrolysed proteins.

An initial evaluation of the dossier on hydrolysed proteins was provided by the RMS in the renewal assessment report (RAR), and subsequently, a peer review of the pesticide risk assessment on the RMS evaluation was conducted by EFSA in accordance with Article 13 of Commission Implementing Regulation (EU) No 844/2012, as amended by Commission Implementing Regulation (EU) No 2018/1659. The following conclusions are derived.

The uses of hydrolysed proteins according to the representative field foliar sprayer uses as an insect attractant on olive tree, deciduous fruit tree, stone fruit tree, pome fruit tree, walnut tree, citrus tree, fig tree, persimmon tree, kiwi and blueberry crops, as proposed at southern Europe (SEU) level result in a sufficient attractant efficacy against the target insects.

The assessment of the data package revealed no issues that could not be finalised or that need to be included as critical areas of concern with respect to **identity, physical and chemical properties and analytical methods**.

In the area of **mammalian toxicology**, hydrolysed proteins per se are likely to be of **low toxicological concern** and no risks to human health could be expected from the use as a plant protection product. However, it cannot be concluded if the proposed reference specifications are toxicologically acceptable for the active substance as manufactured by applicants N.G.STAVRAKIS – PHYTOPHYL and SICIT 2000 S.p.A.

In the **residues section**, an assessment was conducted for the representative uses and in parallel for authorised uses according to Article 12 of Regulation (EC) No 396/2005. Given the toxicological profile and that it would not be possible to distinguish protein and peptide components occurring naturally from those resulting by the use of hydrolysed protein as plant protection products, no consumers risk assessment was deemed necessary. No residue definition is proposed (neither for risk assessment nor for enforcement). At least one criterion established in the Guidance document on criteria for the inclusion of active substances into Annex IV of Regulation (EC) No 396/2005 (European Commission, 2015) is met. If hydrolysed proteins is agreed to be included into Annex IV of Regulation (EC) No 396/2005 by risk managers, no further data in relation to residues would be necessary.

The data available on environmental fate and behaviour were sufficient to carry out the required **environmental exposure assessments** at EU level for the representative uses.

In the area of **ecotoxicology**, a low risk to all groups of non-target organisms was concluded for the representative uses.

The active substance hydrolysed proteins **does not meet the criteria for endocrine disruption** 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.

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Background

Commission Implementing Regulation (EU) No 844/2012[1], as amended by Commission Implementing Regulation (EU) No 2018/1659[2], (hereinafter referred to as 'the Regulation'), lays down the provisions for the procedure of the renewal of the approval of active substances, submitted under Article 14 of Regulation (EC) No 1107/2009[3]. This regulates for the European Food Safety Authority (EFSA) the procedure for organising the consultation of Member States, the applicant(s) and the public on the initial evaluation provided by the rapporteur Member State (RMS) and/or co-rapporteur Member State (co-RMS) in the renewal assessment report (RAR), and the organisation of an expert consultation where appropriate.

In accordance with Article 13 of the Regulation, unless formally informed by the European Commission that a conclusion is not necessary, EFSA is required to adopt a conclusion on whether the active substance can be expected to meet the approval criteria provided for in Article 4 of Regulation (EC) No 1107/2009 within 5 months from the end of the period provided for the submission of written comments, subject to an extension of an additional 3 months where additional information is required to be submitted by the applicant(s) in accordance with Article 13(3). Furthermore, in accordance with Article 13(3a), where the information available in the dossier is not sufficient to conclude the assessment on whether the approval criteria for endocrine disruption are met, additional information can be requested to be submitted in a period of minimum 3 months, not exceeding 30 months, depending on the type of information requested.

In accordance with Article 1 of the Regulation, the RMS Spain and co-RMS Greece received an application from a task force, consisting of BIOIBÉRICA, S.A.U., N.G.STAVRAKIS – PHYTOPHYL and SICIT 2000 S.p.A., and from PROALAN S.A. for the renewal of approval of the active substance hydrolysed proteins. Complying with Article 8 of the Regulation, the RMS checked the completeness of the dossier and informed the applicants, the co-RMS (Greece), the European Commission and EFSA about the admissibility.

The RMS provided its initial evaluation of the dossier on hydrolysed proteins in the RAR, which was received by EFSA on 24 June 2020 (Spain, 2020). Furthermore, this conclusion also addresses the assessment required from EFSA under Article 12 of Regulation (EC) No 396/2005[4]. On 5 February 2021 EFSA invited the Member States and UK[5] to submit their Good Agricultural Practices (GAPs) that are authorised nationally, in the format of specific GAP forms. All the GAPs were collected by EFSA and they are made publicly available as a background document to this conclusion, in the format of a specific GAP overview file.

In accordance with Article 12 of the Regulation, EFSA distributed the RAR to the Member States and the applicants, the task force (consisting of BIOIBÉRICA, S.A.U., N.G.STAVRAKIS – PHYTOPHYL and SICIT 2000 S.p.A.) and PROALAN S.A., for consultation and comments on 29 January 2021. EFSA also provided comments. In addition, EFSA conducted a public consultation on the RAR. EFSA collated and forwarded all comments received to the European Commission on 31 March 2021. At the same time, the collated comments were forwarded to the RMS for compilation and evaluation in the format of reporting table. In addition, the applicants were invited to respond to the comments received. The comments and the applicants' 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 applicants in accordance with Article 13(3) of the Regulation were considered in a telephone conference between EFSA and the RMS on 30 June 2021. On the basis of the comments received, the

[1] Commission Implementing Regulation (EU) No 844/2012 of 18 September 2012 setting out the provisions necessary for the implementation of the renewal procedure for active substances, as provided for in Regulation (EC) No 1107/2009 of the European Parliament and of the Council concerning the placing of plant protection products on the market. OJ L 252, 19.9.2012, p. 26–32.

[2] Commission Implementing Regulation (EU) No 2018/1659 of 7 November 2018 amending Implementing Regulation (EU) No 844/2012 in view of the scientific criteria for the determination of endocrine-disrupting properties introduced by Regulation (EU) 2018/605.

[3] 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.

[4] Regulation (EC) No 396/2005 of the European parliament and of the council of 23 February 2005 on maximum residue levels of pesticides in or on food and feed of plant and animal origin and amending council Directive 91/414/EEC OJ L 70, 16.3.2005, p. 1–16.

[5] The United Kingdom withdrew from EU on 1 February 2020. In accordance with the Agreement on the Withdrawal of the United Kingdom from the EU, and in particular with the Protocol on IE/NI, the EU requirements on data reporting are also applicable to NI.

applicants' response to the comments and the RMS's evaluation thereof, it was concluded that additional information should be requested from the applicants, and that EFSA should conduct an expert consultation in the areas of identity, physical/chemical/technical properties and methods of analysis, mammalian toxicology and ecotoxicology.

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.

A final consultation on the conclusions arising from the peer review of the risk assessment and on the Article 12 MRL review of Regulation (EC) No 396/2005 took place with Member States via a written procedure in December 2022–January 2023.

This conclusion report summarises the outcome of the peer review of the risk assessment of the active substance and the representative formulation, evaluated on the basis of the representative uses of hydrolysed proteins as an insect attractant on olive tree, deciduous fruit tree, stone fruit tree, pome fruit tree, walnut tree, citrus tree, fig tree, persimmon tree, kiwi and blueberry crops, as proposed by the applicants. In accordance with Article 12(2) of Regulation (EC) No 1107/2009, risk mitigation options identified in the RAR 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 for hydrolysed proteins 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, 2022), 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 RAR;
- the reporting table (5 July 2021);
- the evaluation table (5 April 2023);
- 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;
- the Good Agricultural Practice (GAP) overview.

Given the importance of the RAR, including its revisions (Spain, 2022), 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 formulated product

The active substance 'hydrolysed proteins' is a mixture consisting mainly of polypeptides, peptides and amino acids, obtained by the hydrolysis of animal by-products or by the hydrolysis of urea enriched beet molasses. The naming of this active substance was discussed in the Pesticide Peer Review Experts' Teleconference (TC) 74 (April 2022). Experts proposed that the non-ISO common name 'hydrolysed proteins' should be used in combination with the specific names: 'urea enriched beet molasses, hydrolysed' for the active substance as manufactured by N.G.STAVRAKIS – PHYTOPHYL; 'collagen protein hydrolysate' for the active substance as manufactured by SICIT 2000 S.p.A. and PROALAN S.A.; and 'animal tissues hydrolysate excluding ruminants hides and skins' for the active substance as manufactured by BIOIBÉRICA, S.A.U.

The representative formulated products for this evaluation were 'BIOCEBO' (notified by BIOIBÉRICA, S.A.U.) containing 263 g/kg (300 g/L) of hydrolysed proteins–animal tissues hydrolysate

excluding ruminants hides and skins; 'ENTOMELA 50SL/ENT50' (notified by N.G.STAVRAKIS – PHYTOPHYL) containing 100 g/kg of hydrolysed proteins–urea enriched beet molasses (135 g/L), hydrolysed and 160 g/kg of urea (216 g/L); 'NUTREL' (notified by SICIT 2000 S.p.A.) and 'SVA14-004' (notified by PROALAN S.A.) containing 300 g/kg (378 g/L) and 295 g/L (254.3 g/kg) of hydrolysed proteins–collagen protein hydrolysate, respectively. All representative products are soluble concentrates (SLs).

The representative uses evaluated comprise field foliar spraying in southern Europe (SEU) as an insect attractant on olive tree, deciduous fruit tree, stone fruit tree, pome fruit tree, walnut tree, citrus tree, fig tree, persimmon tree, kiwi and blueberry crops. Full details of the GAP can be found in the list of end points in Appendix B.

Data were submitted to conclude that the uses of hydrolysed proteins according to the representative uses proposed at EU level result in a sufficient attractant efficacy of the target organisms, following the guidance document SANCO/2012/11251-rev. 4 (European Commission, 2014b). It is noted that by the time of the peer review process the product 'SVA14-004' (notified by PROALAN S.A.) was not authorised in the EU, the submitted product efficacy data were previously assessed by the co-RMS within the context of a SEU zonal assessment and co-RMS concluded a non-authorisation due to efficacy issues. On that basis RMS proposed that 'SVA14-004' should not be considered as an appropriate representative product for the renewal of hydrolysed proteins (Table 1).

Table 1: Notifiers, active substances, and related representative products

Notifier	**N.G.STAVRAKIS – PHYTOPHYL**	**BIOIBÉRICA, S.A.U.**	**PROALAN S.A.**	**SICIT 2000 S.p.A.**
Hydrolysed proteins specific name	Urea enriched beet molasses, hydrolysed	Animal tissues hydrolysate excluding ruminants hides and skins)	Collagen protein hydrolysate	
Hydrolysed proteins content in TK	On dry weight basis is 110 g/kg (content of the active substance in TK 90–110 g/kg)	On dry weight 708 g/kg (content of the active substance in TK 400–434 g/kg	On a dry weight 582 g/kg (content of the active substance in TK 249–262 g/kg)	No 5-batch data
Representative formulation	'ENTOMELA 50SL/ ENT50'	BIOCEBO	SVA14-004	NUTREL

Conclusions of the evaluation

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

The following guidance document were followed in the production of this conclusion: European Commission (2000).

The principles of setting the reference specifications and the expression of purity were discussed in the Pesticide Peer Review Experts' TC 74 (April 2022). It was agreed to propose individual reference specifications for each specific naming group of hydrolysed proteins. All applicants manufacture hydrolysed proteins as a technical concentrate (TK). Based on batch data from industrial scale production the proposed minimum purity on dry weight basis is 110 g/kg for hydrolysed proteins-urea enriched beet molasses, hydrolysed (content of the active substance in TK 90–110 g/kg); 708 g/kg for hydrolysed proteins–animal tissues hydrolysate excluding ruminants hides and skins (content of the active substance in TK 400–434 g/kg); and 582 g/kg for hydrolysed proteins–collagen protein hydrolysate (content of the active substance in TK 249–262 g/kg). A **data gap** was identified for SICIT 2000 S.p.A for five-batch data (see Section 9); consequently, the proposed reference specifications for 'hydrolysed proteins–collagen protein hydrolysate' were based on batch data provided by the applicant PROALAN S.A. (issue not finalised for SICIT 2000 S.p.A., see Section 9). Lead, cadmium, arsenic and mercury were considered relevant impurities only for hydrolysed proteins-collagen protein hydrolysate and were specified at levels set according to regulation (EU) 2019/1009[6]

[6] Regulation (EU) 2019/1009 of the European Parliament and of the Council of 5 June 2019 laying down rules on the making available on the market of EU fertilising products and amending Regulations (EC) No 1069/2009 and (EC) No 1107/2009 and repealing Regulation (EC) No 2003/2003 (Text with EEA relevance).

(see Section 2). No relevant impurities were identified for hydrolysed proteins animal tissues hydrolysate excluding ruminants hides and skins manufactured by BIOIBÉRICA, S.A.U. Biuret and formaldehyde were considered relevant impurities only for hydrolysed proteins-urea enriched beet molasses, hydrolysed (notified by N.G.STAVRAKIS – PHYTOPHYL); biuret was specified at levels set according to regulation (EU) 2019/1009 and formaldehyde at 1 g/kg (see Section 2). A **data gap** was set for applicant N.G.STAVRAKIS – PHYTOPHYL to provide 5-batch analysis data on the content of the potential relevant impurities and a potential significant impurity in the TK (see Section 9 and confidential evaluation table for N.G.STAVRAKIS – PHYTOPHYL). Consequently, specifications for hydrolysed proteins-urea enriched beet molasses, hydrolysed cannot be finalised. It is suggested to update the reference specifications to the proposed specifications, as the specification for the first approval did not consider relevant impurities. The proposed reference specifications are supported by the toxicologically assessment for the active substance as manufactured by PROALAN S.A. (hydrolysed proteins–collagen protein hydrolysate) and BIOIBERICA (hydrolysed proteins–animal tissues hydrolysate excluding ruminants hides and skins) (see Section 2). However, it cannot be concluded if the proposed reference specifications for the active substance as manufactured by N.G.STAVRAKIS – PHYTOPHYL (hydrolysed proteins–urea enriched beet molasses, hydrolysed) are supported by the toxicologically assessment (see Section 2). The current reference specifications are supported by the (eco)toxicologically assessment for the active substance as manufactured by all applicants (see Sections 2 and 5). There is no FAO specification available for hydrolysed proteins.

The assessment of the data package revealed no issues that need to be included as critical areas of concern with respect to the identity, physical, chemical and technical properties of hydrolysed proteins or the representative formulations. **Data gaps** were identified for the applicant SICIT 2000 S.p.A. to provide physical, chemical and technical property data (excluding persistent foaming) for the representative formulation 'NUTREL' and identification information for the component named 'inert' and contained in this formulation (see Section 10). No data were provided on the content of the relevant impurity formaldehyde before and after storage of the formulation 'ENTOMELA 50SL/ENT50' (see Section 10). The main data regarding the identity of hydrolysed protein and its physical and chemical properties are given in Appendix B.

Methods of analysis are available for the determination of the active substance and the relevant impurities in the technical materials and in the representative formulations. **Data gaps** were identified to demonstrate the applicability of the proposed analytical methods, in terms of specificity, for the determination of urea, formaldehyde, biuret and one significant impurity in the TK as manufactured by the notifier N.G.STAVRAKIS – PHYTOPHYL (see Section 10). A transparent evaluation of the analytical methods provided for the determination of the relevant impurities lead, cadmium, arsenic and mercury in the TK manufactured by PROALAN is missing (see Section 10).

Analytical methods for the determination of residues in food and feed of plant origin, in food of animal origin, body fluids and tissues and in environmental compartments are not required due to the fact that no residue definitions are proposed.

2. Mammalian toxicity

The following guidance documents were used in the production of this conclusion: European Commission (2003, 2012), EFSA (2014), EFSA PPR Panel (2012) and ECHA (2017). The active substance hydrolysed proteins was discussed at the Pesticide Peer Review Experts' TC 73 in April 2022.

The representativeness of the toxicological batches and the validity of the related analytical methods could not be assessed as no toxicological studies with active substance were available. However, the proposed and current reference specifications are toxicologically acceptable for the active substance as manufactured by PROALAN S.A. (relevant impurities below the maximum acceptable concentration limits) and BIOIBERICA (no relevant impurities identified), but it cannot be concluded if the proposed reference specifications are toxicologically acceptable for the active substance as manufactured by applicants N.G.STAVRAKIS – PHYTOPHYL (see data gap set for 5-batch analysis data on the content of potential relevant impurities, Section 1) and SICIT 2000 S.p.A (see data gap for 5-batch data, Section 1) (**data gap** as regard the relevance of the impurities leading to an issue not finalised, see Section 9).

Toxicological relevant **impurities** are identified in the technical materials from applicants N.G. STAVRAKIS – PHYTOPHYL**,** i.e. biuret and formaldehyde, and PROALAN S.A., i.e. heavy metals (lead, cadmium, arsenic and mercury). At the concentration proposed in the reference specifications of hydrolysed proteins, no toxicological concern has been identified. Biuret and heavy metals (lead,

cadmium, arsenic and mercury) are not exceeding the limit set in Regulation (EU) 2019/1009, laying down rules on the making available on the market of EU fertilising product. Formaldehyde is classified for human health as Acute Tox.3, Skin Corr. 1B, Skin Sens 1, Muta. 2 and Carc. 1B;[7] however, the specific concentration limits for classification are not exceeded in the technical material.

Hydrolysed proteins derived from hydrolysis of living vegetal or animal organisms' tissues are widely used for several purposes and approved under different regulations, i.e. as cosmetic ingredients, feed and food additives and fertilisers. Based on the available information and on the history of safe use in both humans and animals, no toxicological concern is expected from the hydrolysates subjected to the current renewal process. However, considering that hydrolysed proteins is applied as a plant protection product by spraying, that is a condition requiring acute inhalation toxicity assessment according to Regulations (EU) No 283/2013[8] and No 284/2013[9], and in the absence of an appropriate study or a robust justification further data for supporting the waiving of an inhalation toxicity study are requested (outstanding **data gap,** see Section 10).

As regards **human data**, although no surveillance programs or monitoring studies are available, no concern or incident has been reported with hydrolysed proteins during any phase of development, production or use of the active substance. It is also acknowledged that the sources used for the manufacturing of the hydrolysed proteins under assessment are not among the list of food allergens listed in Regulation No 1169/2011[10].

No reference values, i.e. acceptable daily intake (**ADI**), (acute) acceptable operator exposure level (**A**) (**AOEL**) or acute reference dose (**ARfD**), are considered needed. The active substance hydrolysed proteins is of low toxicological concern as hydrolysed proteins are natural occurring at high levels in organic molecules of living organisms' tissues and their use is approved under different regulations as above-mentioned. The **dermal absorption** values for the representative formulations notified by the applicants are 10% and 50% (default values) for the undiluted and diluted product, respectively.

In the absence of toxicological reference values, the **non-dietary risk assessment** for operators, workers, bystanders and residents is not required for hydrolysed proteins.

The representative formulation notified by N.G. STAVRAKIS – PHYTOPHYL contains two active substances, hydrolysed proteins and urea. Urea is an active substance included in Annex I to Directive 91/414/EEC and deemed to be approved under Regulation (EC) No 1107/2009; as such it was discussed at the Pesticide Peer Review Experts' TC 73 in April 2022.[11] It was concluded that, being a low-risk substance, no reference values are needed for urea; however, a semi-quantitative risk assessment to confirm that exposure to urea resulting from its use as a plant protection product would be very limited was required to the RMS and included in the assessment of urea.

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).

According to the representative uses, it is not excluded that the edible parts of the treated crops and/or their by-products destined for animal consumption will be in contact with the hydrolysed proteins from their use as an 'insect attractant'. Nevertheless, these active substances have been assessed as not presenting toxicological concern and setting toxicological reference values for them has not been deemed necessary (see Section 2). Given the toxicological profile of low concern for the active substance and that it would not be possible to distinguish protein and peptide components

[7] Regulation (EC) No 1272/2008 of the European Parliament and of the Council of 16 December 2008 on classification, labelling and packaging of substances and mixtures, amending and repealing Directives 67/548/EEC and 1999/45/EC, and amending Regulation (EC) No 1907/2006. OJ L 353, 31.12.2008, p. 1–1355.

[8] Commission Regulation (EU) No 283/2013 of 1 March 2013 setting out the data requirements for active substances, in accordance with Regulation (EC) No 1107/2009 of the European Parliament and of the Council concerning the placing of plant protection products on the market Text with EEA relevance.

[9] Commission Regulation (EU) No 284/2013 of 1 March 2013 setting out the data requirements for plant protection products, in accordance with Regulation (EC) No 1107/2009 of the European Parliament and of the Council concerning the placing of plant protection products on the market Text with EEA relevance.

[10] Complete list of allergens, Annex II of Regulation (EU) No 1169/2011 of the European Parliament and of the Council of 25 October 2011 on the provision of food information to consumers, amending Regulations (EC) No 1924/2006 and (EC) No 1925/2006 of the European Parliament and of the Council, and repealing Commission Directive 87/250/EEC, Council Directive 90/496/EEC, Commission Directive 1999/10/EC, Directive 2000/13/EC of the European Parliament and of the Council, Commission Directives 2002/67/EC and 2008/5/EC and Commission Regulation (EC) No 608/2004.

[11] Report of pesticide peer review TC 73, UREA – AIR IV (April 2022): see Open point at Experts' consultation 2.3. https://www.efsa.europa.eu/sites/default/files/2021-09/high-level-report-mammalian-toxicity.pdf

occurring naturally from those resulting from the use of hydrolysed protein as plant protection products, a consumers' risk assessment was deemed not necessary. Residue definitions for enforcement and risk assessment are not proposed and not required.

This conclusion also addresses the assessment required from EFSA under Article 12 of Regulation (EC) No 396/2005. EFSA invited the Member States to submit their GAPs that are authorised nationally, in the format of specific GAP forms. All the GAPs were collected by EFSA and they are made publicly available as a background document to this conclusion, in the format of a specific GAP overview file. All uses in this collection of GAPs can be either covered by the representative uses (spray applications) or are uses in traps for which direct exposure of the edible parts of the treated crops and/or their by-products destined for animal consumption can be considered negligible.

Detailed analysis of the criteria according to the Guidance document on criteria for the inclusion of active substances into Annex IV of Regulation (EC) No 396/2005 (European Commission, 2015) is provided below for the active substances as manufactured by PROALAN S.A. and by BIOIBÉRICA, S.A.U.

Criterion 1: The active substance is approved as a basic substance under Regulation (EC) No 1107/2009. Criterion is **not met** since the substance is not approved as a basic substance.

Criterion 2: The compound is listed in Annex I of Regulation (EC) No 396/2005. Criterion is **not met** since the active substance is not foodstuff.

Criterion 3: The compound has no identified hazardous properties. Criterion is **met**. Toxicological reference values (ADI or ARfD) have not been derived for this active substance and it does not show any of the following properties: carcinogenic, mutagenic, toxic to reproduction, sensitising, very toxic or toxic, corrosive, endocrine disruptors, neurotoxic, immunotoxicity (see Section 2). The active substance and relevant metabolites are not expected to produce any adverse effect in the toxicological studies if were performed up to the test guideline limit doses.

Criterion 4: The consumer exposure to residues of hydrolysed proteins linked to use as plant protection product is considered as negligible compared to other uses in the food chain and/or natural background. Criterion **not fully assessed** with available data. However, due to the nature of the active substance, it is reasonable to expect it would be met in case it was assessed.

Criterion 5 is not needed to be considered since one of the four criteria above is considered met.

If the active substance hydrolysed proteins is agreed to be included into Annex IV of Regulation (EC) No 396/2005 by risk managers, no further data in relation to residues in food and feed would be necessary, neither to complete the risk assessment to consumers nor to establish MRLs for enforcement purposes.

The appropriateness of including hydrolysed proteins produced by SICIT 2000 S.p.A. and N.G.STAVRAKIS–PHYTOPHYL in Annex IV of Regulation (EC) No 396/2005 will need to be assessed once the data gaps for five-batch analysis are addressed by these applicants and assessed by MSs and EFSA.

4. Environmental fate and behaviour

The degradation of hydrolysed proteins results in amino acids. No specific studies on the fate and behaviour of hydrolysed proteins in the environment were conducted. However, due to the nature of hydrolysed proteins and their biodegradability, their persistence in the environment is very low without tendency for bioaccumulation.

The mobility of hydrolysed proteins was estimated deriving adsorption endpoints for each amino acids using the KOCWIN v2.00 MCI method and log K_{ow} method and published data.

The necessary surface water and sediment exposure assessments (predicted environmental concentration (PEC) calculations) were carried out for hydrolysed proteins using the FOCUS (FOCUS, 2001) step 1 and step 2 approach (version 3.2 of the Steps 1–2 in FOCUS calculator) for all representative uses, except for the sediment exposure assessment for the representative uses on citrus and persimmon (**data gap**).

The necessary groundwater exposure assessments were appropriately carried out using FOCUS (European Commission, 2014a) scenarios and the models PEARL 4.4.4, PELMO 5.5.3 and MACRO 5.5.4.[12] Attractants and repellents are not defined as pesticides in Council Directive 98/83/EC[13], therefore the parametric drinking water limit of 0.1 μ/L for pesticides and their relevant metabolites as

[12] Simulations utilised the agreed Q10 of 2.58 (following EFSA, 2008) and Walker equation coefficient of 0.7.

[13] Council Directive 98/83/EC of 3 November 1998 on the quality of water intended for human consumption. OJ L 330, 5.12.1988, p. 32–54.

defined by the drinking water directive 98/83/EEC[13] is not applicable for hydrolysed proteins. The groundwater exposure assessments for hydrolysed proteins for the representative uses on citrus and persimmon were not provided (**data gap**).

The applicant provided appropriate information to address the effect of water treatments processes on the nature of the residues that might be present in surface water and groundwater, when surface water or groundwater are abstracted for drinking water. The conclusion of this consideration was that hydrolysed proteins would be expected to undergo any substantial transformation due to oxidation at the disinfection stage of usual water treatment processes.

The PEC in soil, surface water, sediment, and groundwater covering the representative uses assessed can be found in Appendix B of this conclusion.

5. Ecotoxicology

The active substance hydrolysed proteins was discussed at the Pesticide Peer Review Experts' TC 77 in May 2022.

The only ecotoxicity data available were performed with the products thus the validity of the analytical methods cannot be assessed. It cannot be concluded if the proposed reference specifications are acceptable for the active substance as it is manufactured by applicants N.G.STAVRAKIS – PHYTOPHYL and SICIT 2000 S.p.A. (**data gap**, see Section 10).

For **birds and terrestrial vertebrates** no studies have been performed on the active or representative formulations. Each applicant submitted a statement to justify that the studies on birds and terrestrial vertebrates are waived since the exposure resulting from the proposed uses is above background exposure limits. Despite hydrolysed proteins being widely used as fertilisers or plant protection products, there are not available bibliographic information regarding the effects of hydrolysed proteins in birds and other terrestrial vertebrates. Considering the available evidence, the acute and long-term risk for birds and mammals from the representative uses of hydrolysed proteins are expected to be low. No metabolite has been identified for which a risk assessment was required, given the properties of the active substance.

For **aquatic organisms**, during the current review of the approval for the active substance, studies were requested, in agreement with the current data requirement (Regulation (EU) 283/2013 and 284/2013). Studies on acute fish (*Oncorhynchus mykiss*) and aquatic invertebrates (*Daphnia magna*) acute toxicity, and algal (*Pseudokirchneriella subcapitata*) growth inhibition were available with the representative formulations BIOCEBO, ENTOMELA 50SL and NUTREL and the analytical verification of the test items was discussed and was accepted by the experts.[14] A quantitative risk assessment has been performed for aquatic organisms and overall, a low risk was identified when uses are made according to the intended GAP.

No reliable endpoint was available to address the risk for **honey bees**, **non-target arthropods other than bees**, **soil macro-** and **microorganisms**, **biological methods for sewage treatment**, and **non-target terrestrial plants**. However, a low risk was concluded for all representative uses with a weight of evidence approach that considered the following lines of evidence: (i) hydrolysed proteins are naturally occurring compounds whose degradation leads to simple metabolites (i.e. amino acids) that are abundant organic molecules; (ii) the levels of nitrogen supplied to the environment of uses hydrolysed proteins as insects attractant are far below the levels of nitrogen typically applied in fertiliser applications; (iii) exposure to the active substances is low when it is used according to the proposed GAP; (iv) there is no available bibliographic information regarding the effects of the active substance in non-target arthropods and bees; (v) no adverse effect is expected due to the nature of hydrolysed proteins and their characteristics.

6. Endocrine disruption properties

With regard to the assessment of the endocrine disruption potential of hydrolysed proteins **for humans** and non-target organisms according to the ECHA/EFSA guidance (2018), although no (eco) toxicological data are available to assess the endocrine-disrupting properties, this does not appear scientifically necessary for the following reasons:

[14] Report of Pesticide Peer Review TC 77 (May 2022): see Experts' consultation point 5.1.

- The physico-chemical characteristics and the expected metabolism of hydrolysed proteins from different sources, as reported in this evaluation, indicate that these hydrolysed proteins will be transformed in a mixture of amino acids and peptides for which there is no evidence of biological activity.
- Hydrolysed proteins from different sources, as reported in the current evaluation, are widely used for several purposes and approved in different regulatory processes (i.e. as cosmetic ingredients, food additives, fertilisers).
- Available evidence from the literature review indicates no concern for endocrine disruptive properties for the hydrolysed proteins.

Based on the available information, it can be concluded that hydrolysed proteins do not meet the criteria for endocrine disruption 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.

7. Overview of the risk assessment of compounds listed in residue definitions triggering assessment of effects data for the environmental compartments (Tables 2–5)

Table 2: Soil

Compound (name and/or code)	Ecotoxicology
Hydrolysed proteins	Low risk

Table 3: Groundwater[(a)]

Compound (name and/or code)	> 0.1 μg/L at 1 m depth for the representative uses[(b)] Step 2	Biological (pesticidal) activity/ relevance Step 3a	Hazard identified Steps 3b and 3c	Consumer RA triggered Steps 4 and 5	Human health relevance
Hydrolysed proteins	0.016–0.356 mg/L	Not applicable[(c)]	–	–	Yes

(a): Assessment according to European Commission guidance of the relevance of groundwater metabolites (2003).
(b): FOCUS scenarios or a relevant lysimeter. Ranges indicated for FOCUS scenarios include the result from the model giving the highest concentration at each scenario, as needed to comply with European Commission (2014a) guidance.
(c): Attractants and repellents are not defined as pesticides in Council Directive 98/83/EC[13].

Table 4: Surface water and sediment

Compound (name and/or code)	Ecotoxicology
Hydrolysed proteins	Low risk

Table 5: Air

Compound (name and/or code)	Toxicology
Hydrolysed proteins	Not available (data gap)

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).

No particular conditions are proposed for the representative uses evaluated.

9. Concerns and related data gaps

9.1. 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[15] 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 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:

1) The proposed reference specification cannot be concluded for the active substance as manufactured by applicants N.G.STAVRAKIS – PHYTOPHYL and SICIT 2000 S.p.A.. Therefore, the assessment of their toxicological acceptability cannot be finalised (relevant for all representative uses of ENTOMELA 50SL/ENT50 and NUTREL, see Sections 1 and 2).

   - Five-batch analysis data on the content of the potential relevant impurities and a potential significant impurity in the technical material (see confidential evaluation table for N.G.STAVRAKIS – PHYTOPHYL) were not provided by the applicant N.G.STAVRAKIS – PHYTOPHYL (see Section 1).
   - Analysis data of at least five representative batches from recent and current industrial scale production of the active substance, analysed for content of pure active substance, impurities, additives and each further component other than additives, as appropriate, (see confidential evaluation table for SICIT 2000 S.p.A.) were not provided by the applicant SICIT 2000 S.p.A. (see Section 1).
   - Toxicological relevance of impurities, if any, is not assessed (see Section 2).

9.2. 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.

[15] 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.

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.

The following critical areas of concern 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:

Critical areas of concern were not identified.

9.3. Overview of the concerns identified for each representative use considered (Table 6)

To be noted that the technical material specification cannot be concluded for SICIT 2000 S.p.A. and N.G.STAVRAKIS-PHYTOPHYL.

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		Deciduous fruit trees, citrus, olive trees	Olive crop	Olive, pome fruits, stone fruits, walnut, citrus, fig, *Actinidia* and blueberries	Citrus, Persimmon
		Patch spray	Low and very low volume spot bait sprays	Foliar spray	Foliar spray
Operator risk	Risk identified				
	Assessment not finalised				
Worker risk	Risk identified				
	Assessment not finalised				
Resident/bystander risk	Risk identified				
	Assessment not finalised				
Consumer risk	Risk identified				
	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				
Groundwater exposure to metabolites	Legal parametric value breached[(a)]				
	Parametric value of 10 µg/L[(b)] breached				
	Assessment not finalised				

The superscript numbers relate to the numbered points indicated in Sections 9.1 and 9.2. Where there is no superscript number, see Sections 2–7 for further information.

(a): When the consideration for classification made in the context of this evaluation under Regulation (EC) No 1107/2009 is confirmed under Regulation (EC) No 1272/2008 of the European Parliament and of the Council of 16 December 2008.

(b): 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, 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.

These data gaps refer only to the representative uses assessed and are listed in the order of the sections:

- Physical, chemical and technical property data (excluding persistent foaming) for the representative formulation NUTREL were not provided by the applicant SICIT 2000 S.p.A. (relevant for the representative uses of NUTREL; see Section 1).
- A transparent evaluation of the analytical methods provided for the determination of the relevant impurities lead, cadmium, arsenic and mercury in the TK manufactured by PROALAN is missing (see Section 1).
- Identification information for the component named 'inert' and contained in the formulation NUTREL was not provided by the applicant SICIT 2000 S.p.A. (relevant for the representative uses of NUTREL; see Section 1).
- No data were provided on the content of the relevant impurity formaldehyde before and after storage of the formulation 'ENTOMELA 50SL/ENT50' (relevant for the representative uses of ENTOMELA 50SL/ENT50; see Section 1).
- Data to demonstrate the applicability of the method ISO 19746/2017, in terms of specificity, for determination of urea in the TK were not provided by the applicant N.G.STAVRAKIS – PHYTOPHYL.
- Data to demonstrate the applicability of the proposed analytical methods, in terms of specificity, for determination of a significant impurity in the TK were not provided by the applicant N.G.STAVRAKIS – PHYTOPHYL.
- Data to demonstrate the applicability of the method 82/434/EEC, in terms of specificity, for determination of formaldehyde in the TK were not provided by the applicant N.G.STAVRAKIS – PHYTOPHYL.
- Data to demonstrate the applicability of the method ISO 18643.2016, in terms of specificity, for determination of biuret in the TK were not provided by the applicant N.G.STAVRAKIS – PHYTOPHYL.
- Information to conclude on the acceptability of the proposed reference specifications for the active substance as it is manufactured by applicants N.G.STAVRAKIS – PHYTOPHYL and SICIT 2000 S.p.A.
- Acute inhalation toxicity assessment was not available for hydrolysed proteins, further data for supporting the waiving of an inhalation toxicity study for inhalation toxicity are requested (relevant for all the representative uses evaluated; see Section 2).
- PEC_{soil} calculations for multiple applications were not provided by the applicant PROALAN S.A. (relevant for the representative uses on citrus and persimmon; see evaluation table's Section 4).
- Comparison between PEC_{soil} and the representative agricultural background soil concentrations of hydrolysed proteins was not provided by the applicant PROALAN S.A. (relevant for the representative uses on citrus and persimmon; see evaluation table's Section 4).
- PEC_{gw} calculations for hydrolysed proteins were not provided by the applicant PROALAN S.A. (relevant for the representative uses on citrus and persimmon; see Section 4)
- PEC_{sed} calculations for hydrolysed proteins were not provided by the applicant PROALAN S.A. (relevant for the representative uses on citrus and persimmon; see Section 4).
- Information on the timing/growth stage of crop, the max number of applications (per use and/ or per crop/season) and, if relevant, the minimum interval between applications were not provided by the applicant PROALAN S.A. (relevant for the representative uses on citrus and persimmon; see evaluation table's Section 4).

References

ECHA (European Chemicals Agency), 2017. Guidance on the Application of the CLP Criteria; Guidance to Regulation (EC) No 1272/2008 on classification, labelling and packaging (CLP) of substances and mixtures. Version 5.0 July 2017. Reference: ECHA-17-G-21-EN; ISBN: 978–92–9020-050-5. Available online: https://echa.europa.eu/guidance-documents/guidance-on-clp

ECHA and EFSA (European Chemicals Agency and European Food Safety Authority) with the technical support of the Joint Research Centre (JRC), Andersson N, Arena M, Auteri D, Barmaz S, Grignard E, Kienzler A, Lepper P, Lostia AM, Munn S, Parra Morte JM, Pellizzato F, Tarazona J, Terron A and Van der Linden S, 2018. Guidance for the identification of endocrine disruptors in the context of Regulations (EU) No 528/2012 and (EC) No 1107/2009. EFSA Journal 2018;16(6):5311, 135 pp. https://doi.org/10.2903/j.efsa.2018.5311

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 2008;6(1):622, 32 pp. https://doi.org/10.2903/j.efsa.2008.622

EFSA (European Food Safety Authority), 2012. Conclusion on the peer review of the pesticide risk assessment of the active substance hydrolysed proteins. EFSA Journal 2012;10(2):2545, 41 pp. https://doi.org/10.2903/j.efsa.2012.2545

EFSA (European Food Safety Authority), 2014. Guidance on the assessment of exposure of operators, workers, residents and bystanders in risk assessment for plant protection products. EFSA Journal 2014;12(10):3874, 55 pp. https://doi.org/10.2903/j.efsa.2014.3874

EFSA (European Food Safety Authority), 2022. Peer review report to the conclusion regarding the peer review of the pesticide risk assessment of the active substance hydrolysed proteins. Available online: www.efsa.europa.eu

EFSA PPR Panel (EFSA Panel on Plant Protection Products and their Residues), 2012. Guidance on dermal absorption. EFSA Journal 2012;10(4):2665, 30 pp. https://doi.org/10.2903/j.efsa.2012.2665

European Commission, 2000. Technical material and preparations: guidance for generating and reporting methods of analysis in support of pre- and post-registration data requirements for Annex II (Part A, Section 4) and Annex III (Part A, Section 5) of Directive 91/414. SANCO/3030/99-rev. 4, 11 July 2000.

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, 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, 2012. Guidance document on the assessment of the equivalence of technical materials of substances regulated under Regulation (EC) No 1107/2009. SANCO/10597/2003-rev. 10.1, 13 July 2012.

European Commission, 2014a. 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, 2014b. Guidance document on the renewal of approval of active substances to be assessed in compliance with Regulation (EU) No 844/2012. SANCO/2012/11251-rev. 4, 12 December 2014.

European Commission, 2015. Guidance document on criteria for the inclusion of active substances into Annex IV of Regulation (EC) N° 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.

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.

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. Available online: www.oecd.org

Spain, 2020. Renewal Assessment Report (RAR) on the active substance hydrolysed proteins prepared by the rapporteur Member State Spain, in the framework of Commission Implementing Regulation (EU) No 844/2012, June 2020. Available online: www.efsa.europa.eu

Spain, 2022. Revised Renewal Assessment Report (RAR) on hydrolysed proteins prepared by the rapporteur Member State Spain in the framework of Commission Implementing Regulation (EU) No 844/2012, June 2022. Available online: www.efsa.europa.eu

Abbreviations

a.s.	active substance
ADI	acceptable daily intake
AAOEL	acute acceptable operator exposure level
AOEL	acceptable operator exposure level

ARfD	acute reference dose
ECHA	European Chemicals Agency
EEC	European Economic Community
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
InChiKey	International Chemical Identifier Key
ISO	International Organization for Standardization
IUPAC	International Union of Pure and Applied Chemistry
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)
MRL	maximum residue level
OECD	Organisation for Economic Co-operation and Development
PEC	predicted environmental concentration
PEC_{gw}	predicted environmental concentration in groundwater
PEC_{sed}	predicted environmental concentration in sediment
PEC_{soil}	predicted environmental concentration in soil
PEC_{sw}	predicted environmental concentration in surface water
SEU	southern Europe
RAR	Renewal Assessment Report
SC	suspension concentrate
SMILES	simplified molecular-input line-entry system
WHO	World Health Organization

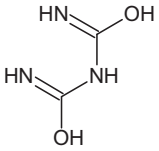
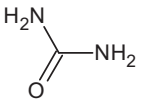
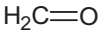
Appendix A – Consideration of cut-off criteria for hydrolysed proteins according to Annex II of Regulation (EC) No 1107/2009 of the European Parliament and of the Council

Properties		Conclusion
CMR	Carcinogenicity (C)	The active substance hydrolysed proteins is not considered to be mutagenic, carcinogenic or toxic for reproduction according to points 3.6.2, 3.6.3 and 3.6.4 of Annex II of Regulation (EC) 1107/2009.
	Mutagenicity (M)	
	Toxic for Reproduction (R)	
Endocrine-disrupting properties		The active substance hydrolysed proteins is not considered to meet the criteria for endocrine disruption for human health and non-target organisms 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.
POP	**Persistence**	The active substance hydrolysed proteins is not considered to be a persistent organic pollutant (POP) according to point 3.7.1 of Annex II of Regulation (EC) 1107/2009.
	Bioaccumulation	
	Long-range transport	
PBT	**Persistence**	The active substance hydrolysed proteins is not considered to be a persistent, bioaccumulative and toxic (PBT) substance according to point 3.7.2 of Annex II of Regulation (EC) 1107/2009.
	Bioaccumulation	
	Toxicity	
vPvB	**Persistence**	The active substance hydrolysed proteins is not considered to be a very persistent, very bioaccumulative substance according to point 3.7.3 of Annex II of Regulation (EC) 1107/2009.
	Bioaccumulation	

Appendix B – List of end points for the active substance and the representative formulation

Appendix B can be found in the online version of this output ('Supporting information' section): https://doi.org/10.2903/j.efsa.2023.8079

Appendix C – Used compound codes

Code/trivial name[(a)]	IUPAC name/SMILES notation/InChiKey[(b)]	Structural formula[(c)]
Biuret	triimidodicarbonic acid N=C(O)NC(=N)O OHJMTUPIZMNBFR-UHFFFAOYSA-N	
Urea	Urea NC(N) = O XSQUKJJJFZCRTK-UHFFFAOYSA-N	
Formaldehyde	Formaldehyde C=O WSFSSNUMVMOOMR-UHFFFAOYSA-N	

IUPAC: International Union of Pure and Applied Chemistry; SMILES: simplified molecular-input line-entry system; InChiKey: International Chemical Identifier Key.
(a): The compound name in bold is the name used in the conclusion.
(b): ACD/Name 2021.1.3 ACD/Labs 2021 Release (File version N15E41, Build 123232, 7 July 2021).
(c): ACD/ChemSketch 2021.1.3 ACD/Labs 2021 Release (File version C25H41, Build 123835, 29 August 2021).