Safety of egg membrane hydrolysate as a novel food pursuant to Regulation (EU) 2015/2283

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Safety of egg membrane hydrolysate as a novel food pursuant to Regulation (EU) 2015/2283

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Abstract

Following a request from the European Commission, the EFSA Panel on Dietetic Products, Nutrition and Allergies (NDA) was asked to deliver a scientific opinion on egg membrane hydrolysate as a novel food (NF) pursuant to Regulation (EU) 2015/2283. The NF is a water-soluble hydrolysate of egg membrane, produced by alkaline treatment of the thin layer lining the shells of chicken eggs. The main constituents of the NF are elastin, collagen and glycosaminoglycans. The information provided on the production process, batch-to-batch variability, composition and specifications of the NF is sufficient and does not raise safety concerns. The NF is proposed to be used as a food supplement for adults, at a maximum daily amount of 450 mg. The consumption of the NF is not nutritionally disadvantageous. One human study, which was not designed for safety but included a number of endpoints pertaining to safety, did not raise safety concerns. The Panel considers that taking into account the information provided and considering the nature, the source and the production process of the NF, there are no safety concerns for the NF at the proposed conditions of use. The Panel concludes that the NF, egg membrane hydrolysate, is safe as a food supplement at a dose of 450 mg/day. The target population for the NF is the general adult population.

Keywords: egg membrane hydrolysate, novel food, safety

Requestor: European Commission following an application by Biova, LLC (Iowa, USA)

Question number: EFSA-Q-2018-00103

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Summary

Following a request from the European Commission, the EFSA Panel on Dietetic Products, Nutrition and Allergies (NDA) was asked to deliver a scientific opinion on egg membrane hydrolysate as a novel food (NF) pursuant to Regulation (EU) 2015/2283. The assessment of the safety of the NF follows the methodology set out in the EFSA Guidance on the preparation and presentation of an application for authorisation of a novel food in the context of Regulation (EU) 2015/2283 and in the Commission Implementing Regulation (EU) 2017/2469.

The NF which is the subject of the application is a water-soluble hydrolysate of egg membrane, produced by alkaline treatment of the thin layer lining the shells of chicken eggs. The NF is a protein-based, water-soluble, off-white powder. Its main constituents are elastin, collagen and glycosaminoglycans. The NF has been marketed outside the European Union (EU) under the trade name of BiovaFlex™.

The information provided on the production process, batch-to-batch variability, composition and specifications of the NF is sufficient and does not raise safety concerns.

The NF is proposed to be used as a food supplement for adults, at a maximum daily amount of 450 mg.

Even though the alkaline treatment conditions employed during the manufacturing process will result in partial racemisation of the amino acids in the NF and, thus, their limited digestibility/bioavailability, taking into account the proposed conditions of use the Panel considers that the consumption of the NF is not nutritionally disadvantageous.

There are no concerns for genotoxicity of the NF.

Of the two human studies provided with the NF, one study reported on safety related endpoints. This study, even though not designed for safety but including a number of endpoints pertaining to safety, did not raise safety concerns.

The Panel considers that taking into account the information provided and considering the nature, the source and the production process of the NF, there are no safety concerns for the NF at the proposed conditions of use.

The Panel concludes that the NF, egg membrane hydrolysate, is safe at the proposed conditions of use, i.e. as a food supplement at a dose of 450 mg/day. The target population is the general adult population.

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1. Introduction

1.1. Background and Terms of Reference as provided by the European Commission

On 5 August 2016, the company Biova LLC submitted a request to the Danish Veterinary and Food Administration (DVFA) in accordance with Article 4 of Regulation (EU) 258/1997[1] to place on the market egg membrane hydrolysate as a novel food (NF).

On 7 June 2017, the DVFA forwarded to the Commission its initial assessment report, which came to the conclusion that egg membrane hydrolysate meets the criteria for acceptance of a NF defined in Article (3)1 of Regulation (EU) 258/1997.

On 12 June 2017, the Commission forwarded the initial assessment report to the other Member States (MS). Several MS raised objections or submitted comments.

The concerns of a scientific nature raised by the MS can be summarised as follows:

- Further information was requested on the manufacturing process.
- Further details on the composition of the NF were requested.
- One MS questioned the applicant's rationale for not providing a full toxicological assessment ('based on the lack of toxicological effects of the source, i.e. egg membrane, which is occasionally consumed with boiled eggs').
- Concerns were raised by one MS concerning potential drug interactions between the NF and medication taken by people with joint pain (who were the targeted study subjects in the submitted human study and who might potentially be the target population for the NF).

Pursuant to Article 35(1) of Regulation (EU) 2015/2283[2], any request for placing a novel food on the market within the Union submitted to a Member State in accordance with Article 4 of Regulation (EC) No 258/97 of the European Parliament and of the Council concerning novel foods and novel foods ingredients and for which the final decision has not been taken before 1 January 2018, shall be treated as an application submitted under Regulation (EU) 2015/2283.

On 20 April 2018, the European Commission asked EFSA to provide a scientific opinion by carrying out the additional assessment for egg membrane as a novel food ingredient, in accordance with Article 10(3) of Regulation (EU) 2015/2283.

2. Data and methodologies

2.1. Data

The safety assessment of this NF is based on data supplied in the application, the initial assessment by the DVFA, the concerns and objections of a scientific nature raised by the other MS and the responses from the applicant thereto.

The information in support of this application has been submitted through the Commission e-submission portal (NF 2018/0124).

Administrative and scientific requirements for NF applications referred to in Article 10 of Regulation (EU) 2015/2283 are listed in the Commission Implementing Regulation (EU) 2017/2469[3].

A common and structured format on the presentation of NF applications is described in the EFSA guidance on the preparation and presentation of a NF application.[4] As indicated in this guidance, it is the duty of the applicant to provide all of the available (proprietary, confidential and published)

[1] Regulation (EU) No 258/97 of the European Parliament and of the Council of 27 January 1997 concerning novel foods and novel food ingredients. OJ L 43, 14.2.1997, p. 1–6.

[2] Regulation (EU) 2015/2283 of the European Parliament and of the Council on novel foods, amending Regulation (EU) No 1169/2011 of the European Parliament and of the Council and repealing Regulation (EC) No 258/97 of the European Parliament and of the Council and Commission Regulation (EC) No 1852/2001 (2013/0435 (COD). OJ L 327, 11.12.2015, p. 1–22.

[3] Commission Implementing Regulation (EU) 2017/2469 of 20 December 2017 laying down administrative and scientific requirements for applications referred to in Article 10 of Regulation (EU) 2015/2283 of the European Parliament and of the Council on novel foods. OJ L 351, 30.12.2017, pp. 64–71.

[4] EFSA NDA Panel (EFSA Panel on Dietetic Products, Nutrition and Allergies), Turck D, Bresson J-L, Burlingame B, Dean T, Fairweather-Tait S, Heinonen M, Hirsch-Ernst KI, Mangelsdorf I, McArdle H, Naska A, Neuhäuser-Berthold M, Nowicka G, Pentieva K, Sanz Y, Siani A, Sjödin A, Stern M, Tomé D, Vinceti M, Willatts P, Engel K-H, Marchelli R, Pöting A, Poulsen M, Salminen S, Schlatter J, Arcella D, Gelbmann W, de Sesmaisons-Lecarré A, Verhagen H and van Loveren H, 2016. Guidance on the preparation and presentation of an application for authorisation of a novel food in the context of Regulation (EU) 2015/2283. EFSA Journal 2016;14(11):4594, 24 pp. https://doi.org/10.2903/j.efsa.2016.4594

scientific data, including both data in favour and not in favour to supporting the safety of the proposed NF.

This NF application includes a request for the protection of proprietary data in accordance with Article 26 of Regulation (EU) 2015/2283. The data requested by the applicant to be protected comprise: detailed description of the manufacturing process, GRAS dossier (Biova, LLC, 2015), proteomic analysis, bacterial reverse mutation test (ST&T Consultants, 2009b, unpublished), *in vitro* micronucleus assay (Roy, 2016; unpublished), acute oral toxicity study (ST&T Consultants, 2009a, unpublished), human study (ST&T Consultants, 2009c, unpublished), RAST-inhibition assay (Food Allergy Research and Resource Program, 2008a, unpublished), quantitative egg allergen test (Food Allergy Research and Resource Program, 2008b, unpublished) and a guinea pig sensitisation assay (ST&T Consultants, 2009d, unpublished).

2.2. Methodologies

The assessment follows the methodology set out in the EFSA guidance on NF applications and the principles described in the relevant existing guidance documents from the EFSA Scientific Committee. The legal provisions for the assessment are laid down in Article 11 of Regulation (EU) 2015/2283 and in Article 7 of the Commission Implementing Regulation (EU) 2017/2469.

This assessment concerns only risks that might be associated with the consumption of the NF under the proposed conditions of use, and it is not an assessment of the efficacy of the NF with regard to any claimed benefit.

3. Assessment

3.1. Introduction

The NF which is the subject of the application is a water-soluble hydrolysate of egg membrane, produced by alkaline treatment of the thin layer lining the shells of chicken eggs. The powder is proposed to be used as a food supplement. The NF has been marketed outside the EU under the trade name of BiovaFlex™.

3.2. Identity of the NF

The NF, i.e. egg membrane hydrolysate, is a protein-based, water-soluble, off-white powder. Its main constituents are elastin, collagen and glycosaminoglycans.

The NF is derived from the eggs of farmed chicken hens (*Gallus domesticus*).

3.3. Production process

The NF is produced according to Good Manufacturing Practice (GMP) and Hazard Analysis Critical Control Points (HACCP) principles.

The starting material for the production of the NF is eggshells from farmed chicken eggs produced for human consumption. Information on the supplier of the eggshells has been provided. It is a United States Department of Agriculture (USDA)-inspected egg-breaking facility located in the US.

The eggshells undergo hydromechanical separation in order to obtain the egg membranes, which are then further processed using a patented solubilisation method. For the processing, pH and temperature are increased and the egg membranes are kept under these conditions for a specified amount of time. No solvents other than water are used. Details on the manufacturing process including flow charts have been provided. Following the solubilisation process, the solution is filtered, concentrated, spray-dried and packaged.

The Panel notes that the conditions employed during the manufacturing process (heat treatment under alkaline pH) are expected to result in the formation of lysinoalanine as well as partial racemisation of amino acids in the NF. However, taking into account the proposed daily intake of the NF (i.e. 450 mg) and considering the dietary background intake from other processed protein-based foods, the potential intake of lysinoalanine or D-amino acids via the NF is not considered to be of safety concern.

The Panel considers that the production process is sufficiently described and does not raise safety concerns.

3.4. Compositional data

The NF consists primarily of proteins, peptides and amino acids (about 90%), with the remainder being moisture (≤ 9%), ash (≤ 8%), fat (~ 1.8%), fibre (2%) and traces of carbohydrates (< 0.01%).

The most abundant proteins in the NF are elastin (~ 25%) and collagen (~ 22%). Also the fraction of glycosaminoglycans constitutes a sizable part (~ 18%) of the NF (values are the means of the batches provided).

In order to confirm that the manufacturing process is reproducible and adequate to produce on a commercial scale a product with certain characteristics, the applicant provided analytical information for three batches of the NF (see Table 1).

Information was provided on the accreditation (i.e. ISO/IEC 17025:2005 – general requirements for the competence of testing and calibration laboratories) of the laboratory that conducted the analyses.

Table 1: Batch-to-batch analysis of the NF

Parameter	Batch results of three commercial lots		
	P3095	P4132	P4252-1
Chemical			
Total nitrogen-containing compounds (%)	90.79	89.69	89.47
Collagen (%)	20	22	25
Elastin (%)	26	26	22
Total glycosaminoglycans (%)	12.7	19.8	21
Calcium (%)	0.14	0.36	0.42
Physical			
pH	6.6	6.9	6.8
Ash (%)	5.28	6.68	5.69
Moisture (%)	6.6	6.95	7.4
Water activity	0.207	0.246	0.244
Solubility (in water)	Soluble	Soluble	Soluble
Bulk density (g/cc)	0.66	0.66	0.63
Heavy metal(s)			
Arsenic (mg/kg)	0.02	0.02	0.02
Lead (mg/kg)	0.02	0.03	0.09
Cadmium (mg/kg)	0.01	0.01	0.01
Mercury (mg/kg)	0.01	0.01	0.01
Microbiology			
Aerobic plate count (CFU/g)	150	60	90
Escherichia coli (MPN/g)	< 3	< 3	< 3
Salmonella (in 25 g)	negative	negative	negative
Coliforms (MPN/g)	< 3	< 3	< 3
Staphylococcus aureus (CFU/g)	< 10	< 10	< 10
Mesophilic spore count (CFU/g)	20	20	20
Thermophilic spore count (CFU/10 g)	< 10	< 10	< 10
Yeast (CFU/g)	< 10	< 10	< 10
Mould (CFU/g)	< 10	< 10	10

CFU: colony forming units; MPN: most probable number.

Additionally, the applicant provided the analytical results for a number of pesticides, dioxins and antibiotics in the NF, which were all below the limit of detection.

Following a request from a MS for more details on the characterisation of the NF, the applicant submitted information on the total amino acid composition of the NF and, in addition, compared it to that of native egg membrane. Differences in the content of a number of amino acids were observed, which might be owing to the hydrolysation step that occurs during the manufacturing process of the NF. For example, the amide groups of glutamine and asparagine residues are partially hydrolysed during the manufacturing process, increasing the content of glutamic acid and aspartic acid in the NF

compared to native egg membrane. Furthermore, the drying step might dehydrate part of the hydroxyproline in the native egg membrane to proline, leading to an increase of proline and a decrease of hydroxyproline in the NF. The observed decrease of cystine in the NF might be owing to a loss during processing prior to amino acid analysis.

The Panel considers that the information provided on the composition of the NF is sufficient and does not raise safety concerns.

3.4.1. Stability

In order to demonstrate the stability of the NF over the intended shelf life, specified as a period of 48 months in a cool and dry environment, the applicant provided the results of real-time stability testing for one batch over 48 months at warehouse room temperature (relative humidity not provided). The results for the parameters analysed (i.e. nitrogen-containing compounds, collagen, elastin and total glycosaminoglycans; moisture, water activity, microbial growth) remained within the limits set in the specifications.

Following a request from a MS for additional information concerning the stability of the NF, the applicant provided the results of two additional batches, even though only up to 19.9 and 25.5 months, respectively. Over this time frame, the analysed parameters remained within the limits set in the specifications.

The Panel considers that the data provided sufficient information with respect to the stability of the NF up to 20 months.

3.5. Specifications

The specifications of the NF are indicated in Table 2. They comprise the content of collagen, elastin, and total glycosaminoglycans as well as other physicochemical parameters, limits for contaminants such as heavy metals and microbiological specifications.

Table 2: Specifications of the NF

Parameter	Limits	Method
Chemical		
Total nitrogen-containing compounds	≥ 88%	Combustion according to AOAC 990.03 and AOAC 992.15
Collagen	≥ 15%	Sircol™ Soluble Collagen Assay (ELISA)
Elastin	≥ 20%	Fastin™ Elastin Assay (ELISA)
Total glycosaminoglycans	≥ 5%	USP26 (chondroitin sulphate K0032 method)
Calcium	≤ 1%	AOAC 965.17/985.01 mod.
Physical		
pH	6.5–7.6	10% solution of NF at 25°C
Ash	≤ 8%	AOAC 942.05
Moisture	≤ 9%	AOAC 934.01
Water activity	≤ 0.3	Vapour pressure at 25°C
Solubility (in water)	soluble	10% solution at 25°C
Bulk density	≥ 0.6 g/cc	USP 616
Heavy metals		
Arsenic	≤ 0.5 mg/kg	ICP-MS according to AOAC 986.15
Microbiological		
Aerobic plate count	≤ 2,500 CFU/g	CMMEF, 4th Ed., 2001, Method 7.6
Escherichia coli	≤ 5 MPN/g	FDA BAM 8th Ed., ch4
Salmonella	Negative (in 25 g)	AOAC 2003.09
Coliforms	≤ 10 MPN/g	FDA BAM 8th Ed., ch4
Staphylococcus aureus	≤ 10 CFU/g	FDA BAM 8th Ed., ch12
Mesophilic spore count	≤ 25 CFU/g	AACC 4240
Thermophilic spore count	≤ 10 CFU/10 g	AACC 4240

Parameter	Limits	Method
Yeast	≤ 10 CFU/g	AACC 9th Ed., 42-50
Mould	≤ 200 CFU/g	AACC 9th Ed., 42-50

AACC: American Association for Clinical Chemistry; CFU: colony forming units; CMMEF: Compendium of Methods for the Microbiological Examination of Foods; ELISA: enzyme-linked immunosorbent assay; FDA BAM: United States Food and Drug Administration's Bacteriological Analytical Manual; ICP-MS: inductively coupled mass spectrometry; MPN: most probable number; USP: United States Pharmacopeia.

The Panel considers that the information provided on the specifications of the NF is sufficient and does not raise safety concerns.

3.6. History of use of the NF and/or of its source

3.6.1. History of use of the source

The NF is produced from chicken eggs (*Gallus domesticus*), which have a long history of food use within the EU.

Even though not consumed as a food as such, egg membranes may incidentally be consumed with boiled eggs.

3.6.2. History of use of the NF

In 2009, the NF was notified as a New Dietary Ingredient (NDI) in the United States. Since then approximately 17,000 kg of the NF have been sold (under the tradename of BiovaFlex®) in the US.

In 2015, the NF (i.e. BiovaFlex®) was notified by the applicant to be Generally Recognized as Safe (GRAS) for use in food and food supplements (Biova LLC, 2015).

According to the information provided, no adverse reactions to egg membrane products on the US market have been reported to date under the US FDA's MedWatch adverse event reporting programme.

3.7. Proposed uses and use levels

3.7.1. Target population

The target population proposed by the applicant is adults above 35 years of age.

3.7.2. Proposed uses and use levels

The applicant proposed to use the NF as an ingredient in food supplements, at a maximum dose of 450 mg per day.

3.8. Absorption, distribution, metabolism and excretion (ADME)

No ADME data have been provided on the NF.

3.9. Nutritional information

The applicant provided a nutritional analysis of the NF, which comprises information on the content of nitrogen-containing compounds, fibre, sodium, carbohydrates, fatty acids, vitamins and minerals in the NF.

The NF is primarily (about 90%) composed of nitrogen-containing compounds (i.e. proteins, peptides and amino acids). The proposed daily amount of 450 mg of the NF would result in an additional intake of approximately 400 mg nitrogen-containing compounds per day.

The Panel notes that the alkaline treatment conditions employed during the manufacturing process will result in partial racemisation of the amino acids in the NF and, consequentially, in limited digestibility/bioavailability of such amino acids.

However, taking into account the proposed conditions of use (i.e. 450 mg/day), the Panel considers that the consumption of the NF is not nutritionally disadvantageous.

3.10. Toxicological information

3.10.1. Genotoxicity

The applicant provided a bacterial reverse mutation assay (ST&T Consultants, 2009b, unpublished) and an *in vitro* micronucleus assay (Roy, 2016, unpublished).

The bacterial reverse mutation assay (ST&T Consultants, 2009b, unpublished) was described as following a non-GLP protocol. Reference was made to the publications by Ames et al. (1975) and Maron and Ames (1983). For the assay five different strains of *Salmonella* Typhimurium were used, i.e. TA97a, TA98, TA100, TA102 and TA1535. The NF, which was found to be completely soluble in sterile water at 50 mg NF/mL (used as a stock solution), was tested at concentrations up to 5,000 μg/plate. The testing included negative (i.e. solvent) and positive controls and was carried out with and without metabolic activation (i.e. S9-mix from rat liver derived from Aroclor™-treated rats). All tests were carried out in triplicate. The spontaneous reversion rates remained within accepted values for each strain. All the five strains were sensitive to the mutagens used for the positive controls. No cytotoxicity was observed. There was no increase in the number of revertant colonies following exposure to the NF at concentrations up to 5,000 μg/plate in the presence or absence of metabolic activation.

The *in vitro* micronucleus assay (Roy, 2016, unpublished), which was conducted in compliance with US FDA GLP Regulations, was carried out in a lymphocytic cell line (TK6) of human origin. The batch of the NF used in the study was within the specifications set in section 3.5. As vehicle water was used. In a preliminary test, the TK6 cells were exposed to vehicle alone and to nine different concentrations of the NF with half-log dose spacing. Based on the findings of the pretest, the doses of the NF chosen for the definitive assay were 100, 240, 350 and 500 μg/mL for each treatment condition. For the assay, the cells were exposed to the NF for 4 h with and without S9-activation system, and for 27 h without the S9-mix. No cytotoxicity (defined as ≥ 50% decrease in population doubling relative to vehicle control) was observed at any dose level. The dose levels selected for microscopic analysis were 240, 350 and 500 μg/mL for each treatment condition. A minimum of 1,000 mononucleate cells from each culture were examined and scored for the presence of micronuclei. The frequency of micronuclei in cells exposed to the NF was not significantly increased at any dose level with or without metabolic activation.

The Panel considers that taking into account the test results provided and considering the nature, the source and the production process of the NF there are no concerns regarding genotoxicity of the NF.

3.10.2. Toxicity studies

The applicant submitted one acute oral toxicity study (ST&T Consultants, 2009a, unpublished), which was carried out in Sprague–Dawley albino rats. The rats (5/sex per group) were administered a single oral dose of the NF at a dose of 5,000 mg/kg body weight (bw). The animals were observed at 1, 3, 6 and 24 h after treatment, and daily thereafter for a total of 14 days. All animals survived the 14-day observation period. The oral median lethal dose was thus concluded to be greater than 5,000 mg/kg bw.

No other toxicity studies were provided.

3.10.3. Human data

Two human studies with the NF were provided (ST&T Consultants, 2009c, unpublished; Jensen et al., 2015) one of which reported on safety related endpoints (ST&T Consultants, 2009c, unpublished).

This trial (ST&T Consultants, 2009c, unpublished) was an open-label uncontrolled pilot study conducted in 42 subjects of at least 18 years with a history of arthritic-type joint pain or connective tissue disorder with a reduced range of knee motion. The study subjects were instructed to consume for 6 weeks 450 mg/day of the NF. The primary endpoint of the study was to assess a potential effect of the NF on pain, stiffness, and discomfort of knee-associated musculoskeletal disorders. As secondary endpoint the safety of the NF was investigated. Health evaluations of the study subjects were performed at baseline and at weeks 2, 4 and 6. Adverse events and compliance were recorded by study subjects in diaries and were reviewed at each visit. As part of the safety protocol, blood chemistry, haematology and allergen antibody assays (i.e. concentration of immunoglobulin E (IgE) antibodies to egg allergens) were performed. The haematology analysis included complete blood cell

counts and concentrations of haematocrit and haemoglobin as well as cell morphology. The blood chemistry analysis comprised non-fasting glucose, sodium, potassium, chloride, carbon dioxide, urea nitrogen, creatinine, calcium, alkaline phosphatase, total protein, albumin and globulin. In addition, aspartate aminotransferase (AST), alanine aminotransferase (ALT) and total bilirubin concentrations were analysed to monitor liver function. Twelve subjects dropped out from the study. The reasons were provided (i.e. personal (5), loss-to-follow up (2), high blood pressure (2), egg allergy (2) and 'pressure' (1)). The blood parameters analysed were all within normal ranges. No statistically significant changes from baseline were observed. No significant increases in the concentration of IgE antibodies to egg allergens were noticed in any subject. No adverse events were reported.

3.11. Allergenicity

In order to determine the allergenic potential of the NF, a radioallergosorbent test (RAST)-inhibition assay was performed (Food Allergy Research and Resource Program, 2008a, unpublished), which is a competitive radioimmunoassay that uses serum from egg-allergic individuals and which detects IgE-binding (as described by Hefle et al., 1994). The RAST-inhibition curve of the NF was rather flat when compared to the curve of a whole egg sample (slope of 1.65 vs 23.42 for whole egg), indicating little inhibition (i.e. binding) of egg specific-IgE by the NF.

The allergenicity of the NF was further investigated using the Neogen Veratox® Quantitative Egg Allergen Test, which is specific for egg white. In three batches of the NF analysed, the amount of egg white was below the limit of detection (i.e. 2.5 mg/kg). In a control sample of concentrated egg membrane not having undergone solubilisation, the amount of egg white was 2,370 mg/kg (Food Allergy Research and Resource Program, 2008b, unpublished).

The applicant also submitted a guinea pig sensitisation assay (Buehler), in which the topical application of the NF to the skin of 12 Hartley albino guinea pigs for three weeks did not result in any evidence of skin irritation or sensitisation (ST&T Consultants, 2009d, unpublished).

The applicant informed that notwithstanding the above results the NF will be labelled in accordance with Regulation No 1169/2011[5], which requires labelling for substances or products with a potential to cause allergies or intolerances (such as eggs and products thereof).

The Panel notes that the source of the NF is a recognised allergen and that, therefore, the NF is potentially allergenic.

4. Discussion

The NF which is the subject of the application is a hydrolysate of egg membrane.

The information provided on the composition, the specifications, the production process and the batch-to-batch variability of the NF is sufficient and does not raise safety concerns.

The intention is to market the NF as a food supplement to adults, with a proposed maximum intake of 450 mg/day.

The human study, which was not designed for safety but included a number of endpoints pertaining to safety, did not raise safety concerns.

There are no concerns for genotoxicity of the NF.

The Panel considers that taking into account the information provided and considering the nature, the source and the production process of the NF, there are no safety concerns for the NF at the proposed conditions of use.

5. Conclusions

The Panel concludes that the NF, egg membrane hydrolysate, is safe at the proposed conditions of use, i.e. as a food supplement at a dose of 450 mg/day. The target population is the general adult population.

The Panel could not have reached its conclusion on the safety of the NF under the proposed conditions of use without the detailed description of the manufacturing process for which data protection was requested by the applicant.

[5] 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. Official Journal of the European Union 2011, 54: 18–63.

Steps taken by EFSA

1) Letter from the European Commission to EFSA with the request for a scientific opinion on the safety of egg membrane as a NF. Ref. Ares(2018)2115205, dated 20 April 2018.
2) The information in support of this application has been submitted through the Commission e-submission portal (NF 2018/0124).
3) On 13 March 2018 and on 23 March 2018, during validation of the application, EFSA asked the applicant to provide missing information to complement the application.
4) On 20 April 2018, the validity of the application was confirmed and the scientific evaluation started.
5) During its meeting on 27 June 2018, the NDA Panel, having evaluated the data, adopted a scientific opinion on the safety of egg membrane hydrolysate as a NF pursuant to Regulation (EU) 2015/2283.

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Abbreviations

AACC	American Association for Clinical Chemistry
ADME	absorption, distribution, metabolism and excretion
ALT	alanine aminotransferase
AST	aspartate aminotransferase
bw	body weight
CFU	colony forming units
CMMEF	Compendium of Methods for the Microbiological Examination of Foods
DVFA	Danish Veterinary and Food Administration
ELISA	enzyme-linked immunosorbent assay
FDA BAM	United States Food and Drug Administration's Bacteriological Analytical Manual

GLP	Good Laboratory Practice
GMP	Good Manufacturing Practice
GRAS	Generally Recognized as Safe
HACCP	Hazard Analysis Critical Control Points
ICP-MS	inductively coupled mass spectrometry
IgE	immunoglobulin E
MPN	most probable number
MS	Member State
NDA	EFSA Panel on Dietetic Products, Nutrition and Allergies
NDI	New Dietary Ingredient
NF	novel food
RAST	radioallergosorbent test
USDA	United States Department of Agriculture
USP	United States Pharmacopeia