Guideline for making application dossiers for novel proteins

Novel food dossiers: from black box to tool box

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1 Introduction

1.1 Goal of the document

According to Regulation (EC) No 258/97, in order to market a novel protein in the European Union (EU), its safety needs to be assessed prior to market introduction. Novel proteins are proteins which have not been used for human consumption to a significant degree within the EU before 15 May 1997. Therefore, any person, producer or importer who wishes to market such a novel protein in the EU must submit an application dossier to a competent authority (CA) for novel foods of an EU member state for an assessment of safety. Commission Recommendation 97/618/EC provides general guidelines on the administrative and scientific contents of an application dossier. Many companies who want to market novel food products struggle with making such an application dossier however. This document aims to assist in making an application dossier for novel food proteins.

This document describes when a new protein intended to market for human consumption is considered to be a novel food protein (novel protein) and when it is not, when an application dossier for authorisation must be made and when, in general, an application dossier for notification might be sufficient. It describes in detail the items to be addressed in these application dossiers and gives references to guidance documents of CAs and provides examples. It also provides guidelines of what information for each item might consider being sufficient by CAs. However, for many items there are no clear-cut criteria. Furthermore, each application dossier for a novel protein will be different due to specific product related characteristics. Moreover, the opinion from member states' CAs or European Food Safety Authority (EFSA) cannot be predicted. The information in this document can, therefore, only be regarded as a guideline.

1.2 The goal of an application dossier for novel protein

Why do you have to make an application dossier for a novel food? It is good to keep in mind that you are not making an application dossier just to comply with demands from the government. ***You are making an application dossier to convince anybody, from consumers, business-to-business customers and media to health authorities that the product you aim to market is safe when the product is consumed by humans in the form and to the extent as you describe in the dossier.*** You should tell a convincing story in the application dossier substantiating that your new protein is safe for human consumption. You need to put all information which is necessary to prove this in the application dossier, more than this is not needed.

1.3 Application procedures for novel foods

Before going into detail about the information needed in an application dossier in the next chapters, this paragraph provides, in short, information about the application procedures for novel foods.
An applicant has to submit his request for placing a novel food product on the EU market to a CA for novel foods in one EU member[1]. Each EU member state has a CA for novel foods, which has the legal responsibility to execute Regulation (EC) No 258/97. The request to the first member state should contain an application dossier including all the necessary information, including copies of all studies carried out, and a summary.

[1] Application procedure is not unique for novel foods: comparable procedures are required for pesticides and veterinary medicines.

At the same time a copy of the request has to be sent by the applicant to the EC. The EC must forward the request, the name of the CA responsible for the initial safety assessment and the summary of the application dossier to the CAs of the other member states. The CA assesses the application dossier and makes an initial assessment report including a decision on whether an additional assessment is required or not. Some member states have a separate assessment body, which performs the assessments of application dossiers and advices the CA (Appendix I). The initial assessment report of the national CA is sent to the European Commission (EC). The EC forwards the initial assessment report to the CAs of all other member states for comments or reasoned objections. If no additional assessment was considered to be necessary by the first member state and no comments were made or objections were raised, the first member state informs the applicant that he is allowed to place the novel food product on the market. If an additional assessment was considered to be necessary or comments or objections were made, the application dossier is nowadays forwarded to EFSA for further assessment. In case of a positive opinion of EFSA, the EC drafts a proposal for authorisation of the novel food. If the Council and the European Parliament do not object to the proposal, the EC publishes the authorisation in the Official Journal of the European Union.

For novel foods that are substantially equivalent to existing foods or food ingredients as regards their composition, nutritional value, metabolism, intended use and levels of undesirable substances, the applicant should notify the EC. Nowadays, most applicants first submit such a notification, by a notification dossier, to the CA of a member state to obtain an opinion of the CA on the equivalence status of the product. This opinion is then included in the notification dossier that is sent to the EC. The EC forwards the notification to the CAs of all member states.

The procedures and organisations involved in the assessment of application dossiers submitted to the CA in the Netherlands are described in a decision tree developed by Wageningen UR which is available on the internet[2,3]. Although national CAs are different in the EU member states, the general procedures are similar.

An applicant has to pay a fee to the CA in the member state where the application dossier is submitted for the initial assessment. The fee is set by the member state, and the height of the fee depends on the kind of application dossier: notification or authorisation. Fees differ between countries (see Appendix II for fees of some member states). *Don't let the choice for submission to which member state be guided by the height of the fee alone.* Countries with a higher fee could have more experience in dealing with application dossiers and might be more willing to interact with the applicant during the making of an application dossier prior to submission. Such interaction could save money and time in making a correct application dossier, which could easily compensate the higher fee.

CAs or their assessment bodies in some countries, like the Netherlands, the UK, and Finland, have much experience in dealing with novel food applications and have shown to be open to an exploratory discussion on request of the applicant about the novel food product before official submission of an application dossier for first assessment. Such exploratory discussions are often free of charge.

[2] Authorisation procedure: http://eiwitinnovaties.fbresearch.nl/page/decision-tree-authorisation-novel-food
[3] Notification procedure: http://eiwitinnovaties.fbresearch.nl/page/decision-tree-notification-novel-food

Regulation in progress

Since 2008 the European Commission is working on a simpler, clearer and more efficient authorisation procedure. Recently the European Commission (18-12-2013) released a Draft Regulation on novel foods: Proposal COM (2013) 894 final[4]. This draft Regulation is not in force yet, and it probably will not enter into force before 2016.

Under the draft Regulation, novel food would enter an authorisation procedure centralised at EU level: this may lead to a reduction of the authorisation procedure (18 months instead of 3 years in average currently).

Authorisation will be generic, which will avoid the resubmission of new applications by other companies for the same novel food. Protection of innovation is covered by a 'data protection' regime, with the granting of an applicant linked authorisation for a maximum of 5 years.

Furthermore, special provisions are made for food which has not been marketed in the EU but which has a history of safe use in non-EU countries. If a history of safe food use in a third country for at least 25 years has been demonstrated by the applicant, the food may be included in the Union list. Those foods should have been consumed in the third country as a part of the customary diet within a large part of the population of the country and be confirmed with compositional data. The history of safe food use should not include non-food uses or uses not related to normal diets.

1.4 Reading guide

Chapter 2 provides information and background for when a novel protein is not to be considered a novel food, in which case no application dossier has to be submitted to a CA. Chapter 3 provides information and background for making an application dossier for authorisation. Finally, chapter 4 provides information and background for making an application dossier for notification for novel proteins considered to be substantially equivalent to an existing food protein that is already allowed on the EU market.

In this document we refer to texts of other documents. We do not copy the texts of these documents; instead we provide links to the website where to find the documents in a footnote on the page. For examples of specific topics in an already assessed application dossier, we provide the link to the website where to find the application dossier with a reference to the chapter concerned in the application dossier. If we use a figure or a table from another document, a link to its source is provided in a note to the figure or table.

[4] Proposal http://ec.europa.eu/food/food/biotechnology/novelfood/documents/novel-cloning_com2013-894_final_en.pdf

2 Is the novel protein a novel food?

2.1 When is a new protein not a novel food?

According to Regulation (EC) No 258/97[5] a new protein is a novel food if it has not been used for human consumption to a significant degree within the EU before 15 May 1997. The deadline of 15 May 1997 applies to all current member states, irrespective from the date of accession to the EU. To prove that a new protein is not a novel food, a person, producer or importer who aims to market it has to demonstrate 'human consumption to a significant degree within the EU'. Only consumption in the EU is evidence; consumption outside the EU is no evidence for significant consumption within the scope of Regulation (EC) No 258/97.

Figure 2.1 provides a decision tree for assessing human consumption to a significant degree. By following the questions in this decision tree and gathering the data to answer these, you can establish if the new protein is a novel food or not. If your new protein is exactly the same as a protein that is already on the EU market, and use of your protein will be the same, you need to prove that it is the same. Therefore, you need to specify the 1) full Latin name of the source organism (taxonomic name) and other names used in EU member states; 2) the parts of the source organism used before 15 May 1997; 3) the form and/or concentration of the protein (fluid, extract etc.) which were used; and 4) the intake of the protein compared to intake of the new protein. Previous use of the protein in food supplements only is not considered to be sufficient as evidence for a history of consumption. Table 2.1 provides a list of types of evidence of a history of human consumption you can use to substantiate history of consumption. The more concrete and detailed the information about sales and consumption in the EU, the better is the evidence. The document of the Belgian government 'Tools to prove that a food or food ingredient is not a novel food (.PDF)'[6] can also help to identify human consumption to a significant degree. In some member states the CA can be consulted to aid in this process of determining whether a protein is a novel food or not.
If a protein was consumed to a significant degree before 15 May 1997 in the EU, no application dossier has to be submitted to a national CA for novel foods. However, a CA or other government body could ask a person, producer or importer to show that the protein in question is not a novel food within the scope of Regulation (EC) No 258/97. Therefore, it is advisable to collect the evidence on human consumption to a significant degree in a dossier before marketing, this dossier can be shown upon request of official authorities.

5 http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=CONSLEG:1997R0258:20090807:EN:PDF
6 http://www.health.belgium.be/eportal/foodsafety/foodstuffs/novelfoods/index.htm?fodnlang=en

Table 2.1

Types of evidence of a history of human consumption of product in EU

Type of Evidence	Examples of type of evidence	Possible Weighting
Comprehensive Sales Information	Invoices etc., detailing sale of food, including evidence of large quantities of sale in the EU	Very Good Evidence, if purpose (food use) is indicated
Sales Information	Invoices etc., detailing sale of food	Good Evidence, if purpose (food use) is indicated
Government Import/Export Information	Official documents	Supporting Evidence, if purpose (food use) is indicated
Sales Information	Catalogues, Sales Brochures	Supporting Evidence, if purpose (food use) is indicated
Listed in recognised catalogues/documents		Supporting Evidence
Expert knowledge	Personal Testimonies	Supporting Evidence
Supporting Information	Magazine articles, Recipe Books etc.	Supporting Evidence
Other	Please Specify	

Source: http://ec.europa.eu/food/food/biotechnology/novelfood/documents/substantial_equivalenc_en.pdf.

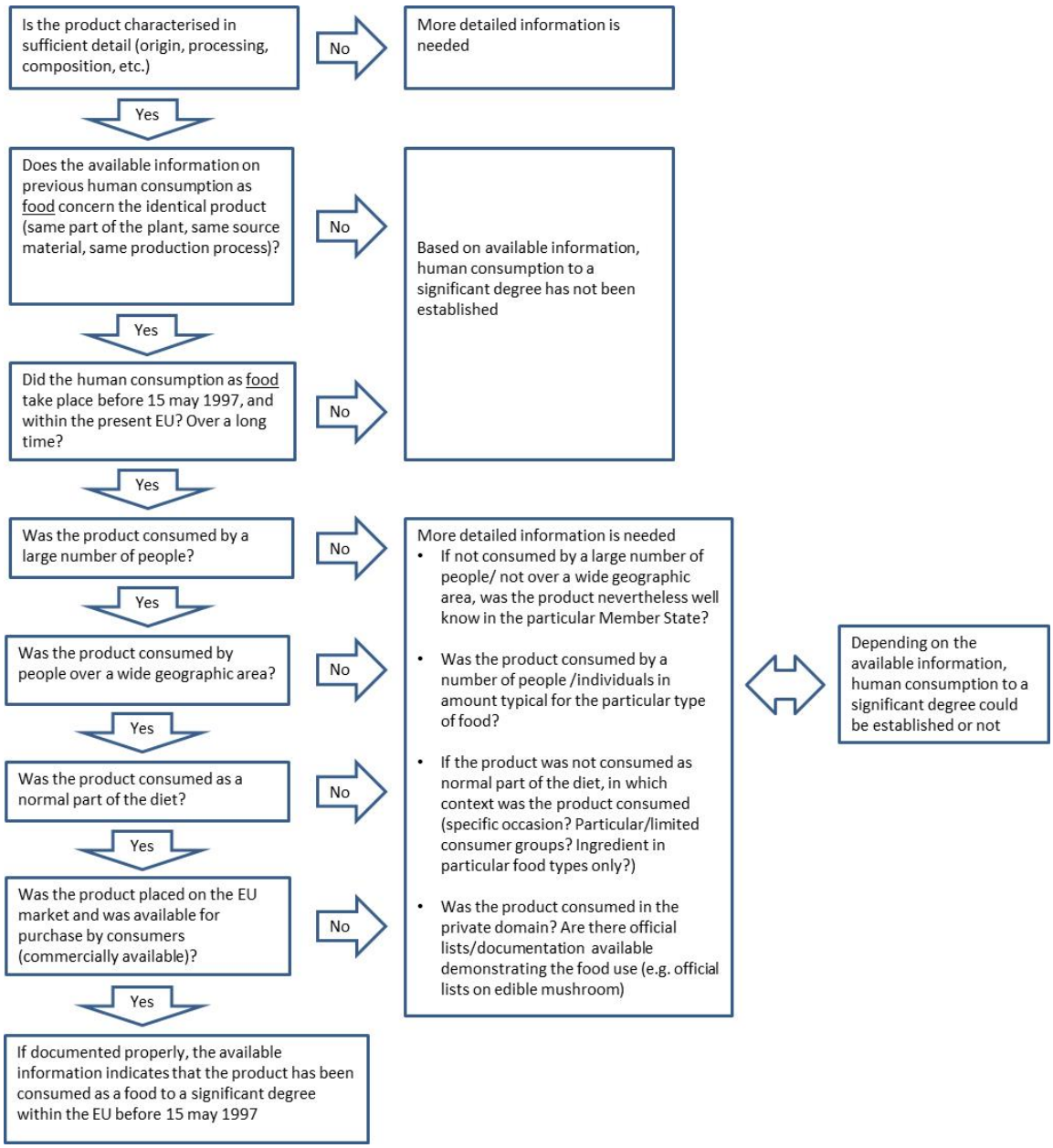

Figure 2.1 *Decision tree to identify whether a product is a novel food (source: http://ec.europa.eu/food/food/biotechnology/novelfood/documents/substantial_equivalenc_en.pdf).*

Figure 2.1 shows a decision tree to identify whether no significant consumption in the EU before 15 May 1997 can be established which means the product is a novel food. If more information is needed a novel food dossier has to be set up.

2.2 What to do if the protein is a novel food: authorisation or notification?

If for a protein no significant consumption in the EU before 15 May 1997 can be established, the person, producer, or importer who aims to market this protein, has to make an application dossier. The application dossier has to be submitted to a national CA for novel foods for assessment. In general, an application dossier for authorisation has to be made. Chapter 3 provides information, instructions, practical tips, and examples for application dossiers for authorisation (full application). If, however, substantial equivalence with an existing counterpart already allowed on the EU market can be established, an application dossier for notification can be sufficient. Chapter 4 provides information, instructions, tips, and examples for an application dossier for notification (the simplified procedure). Only after (1) the novel protein has been assessed to be safe; and (2) either the first member state informs you that you are allowed to place your product on the market; or (3) the EC has published the authorisation in the Official Journal of the European Union; or (4) has listed the notification on the DG SANCO website (http://ec.europa.eu/food/food/biotechnology/novelfood/index_en.htm), the protein can be placed on the EU market.

3 Application dossier for authorisation

If a new protein is a novel food within the scope of Regulation (EC) No 258/97, in most cases an application dossier for authorisation has to be made. This chapter provides information, instructions, tips, and examples for application dossiers for authorisation (full application). When substantial equivalence with an existing counterpart already allowed on the EU market can be established, an application dossier for notification can be sufficient. Chapter 4 provides information, instructions, tips, and examples for an application dossier for notification. According to Part II of Recommendation 97/618/EC[7], an application dossier for authorisation should contain the following six chapters:

1. Administrative data.
2. General description.
3. Identification of essential information requirements.
4. Consultation of structured schemes.
5. Evaluation and conclusion by the applicant.

Box 1: The public part of application dossiers for authorisation of Chia seeds and Touchi extract of soybean

Chia seeds
The application dossier for authorisation is available at http://www.food.gov.uk/multimedia/pdfs/applicdosschiacompany.pdf.

Touchi extract of soybean
The application dossier for authorisation is available at http://www.food.gov.uk/multimedia/pdfs/touchiapplication.pdf.

3.1 Administrative data

The administrative chapter should contain the following information:

- Name, postal and email address, telephone, and fax of the applicant of the application dossier.
- Name, postal and email address, telephone, and fax of the producer of the novel protein.
- Name, postal and email address, telephone, and fax of the person responsible for the application dossier.
- Date of the application.

3.2 General description

According to Chapter 4 of Recommendation 97/618/EC the applicant must, with a scientific justification, assign the novel protein to one of three classes/subclasses[9]:

7 http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:1997:253:0001:0036:EN:PDF
8 http://acnfp.food.gov.uk/assess/
9 Classes 3, 4 and 5 referred to genetically modified organisms and are no longer within the scope of the Regulation (EC) No 258/97.

Class 1: Pure chemicals or simple mixtures from non-GM sources. This class comprises foods and food components that are single chemically defined substances or mixtures of these which are not obtained from plants, animals, or microorganisms that have been genetically modified. Two sub-classes can be identified:

1.1 the source of the novel food has a history of food use in the EU;

1.2 the source of the novel food has no history of food use in the EU.

Class 2: Complex novel food from non-GM source. This class comprises complex novel food which are not, or are derived from sources which have not, been genetically modified. Intact plants, animals, and microorganisms used as foods as well as food components (e.g. complex carbohydrates, fats, proteins or those substances collectively described as dietary fibre) are included. Two sub-classes can be identified:

2.1 the source of the novel food has a history of food use in the EU;

2.2 the source of the novel food has no history of food use in the EU.

Class 6: Foods produced using a novel process. This class comprises foods and food ingredients which have been subjected to a process not currently used in food production. Novel processes for food production may encompass, for example, new types of heat processing, non-thermal preservation methods, new processes to chill or freeze products, to dehydrate products, and the application of new processes catalyzed by enzymes. According to the scope of Regulation (EC) No 258/97, the resulting product is only considered to be a novel food, if the process results in changes in the chemical composition or structure of the food or food ingredient, which affect its nutritional value, metabolism, or level of undesirable substances.

3.3 Identification of essential information requirements

Based on the class/subclass allocation, the applicant can identify in table 3.1 (Table II from Recommendation 97/618/EC) what information is needed in the application dossier.

Table 3.1

Structured schemes for identification of the class and subclass of a novel protein.

Structured scheme		Class of novel protein				
		1.1	1.2	2.1	2.2	6
I.	Specification of the novel protein	x[a]	x	x	x	x
II.	Effect of the production process applied to the novel protein	x	x	x	x	x
III.	History of the organism used as source of the novel protein	x	x	x	x	x
IX.	Anticipated intake/extent of use of the novel protein	x	x	x	x	x
X.	Information from previous human exposure to the novel protein or its source	x		x		x
XI.	Nutritional information on the novel protein	x	x	x	x	x
XII.	Microbiological information on the novel protein	x	x	x	x	x
XIII.	Toxicological information on the novel protein	x	x	x	x	x

[a] x = The information mention in this structured scheme is needed in the dossier.

Source: Table II from Recommendation 97/618/EC.

So, there are hardly any differences in data requirements for the different protein classes. Even for item X. information from previous human exposure, applies that if a novel protein does have a history of food use outside the EU, it is recommended to include information on this in the dossier.

3.4 Consultation of structured schemes

The data needed to answer the questions in the structured schemes in Recommendation 97/618/EC form the main body of an application dossier for authorisation. The data needed for each structured scheme are explained in detail in the following paragraphs.

3.4.1 Specification of the novel protein

Figure 3.1 (Scheme I of Recommendation 97/618/EC) refers to the specification of the source and the composition of the novel protein. Table 3.2 provides the questions in scheme I, and information and suggestions for answering each question. For the composition, all parameters relevant to characterise the product from a safety and nutritional point of view must be analysed. The information in the application dossier should be representative for the novel protein produced on a commercial scale. The taxon of the source of the novel protein must be specified as detailed as possible (e.g. class, order, family, genus, species, subspecies, variety, cultivar, etc.)

Table 3.2

Specification of the novel protein: composition, representativeness for commercial production and taxonomic identity

Question from scheme I (Figure 3.1)	Information and suggestions
Depending on the derivation and composition of the Novel Food, is appropriate analytical information available on potentially toxic inherent constituents, external contaminants and nutrients?	Use at least four different batches for compositional analyses. The batches must be representative for the product to be placed on the EU-market. Preferably, let analyses be performed by accredited laboratories. If possible, use official sampling methods and (criteria for) methods of analysis Indicate the method of analysis per parameter Provide data on composition like (note that not all parameters are applicable to all products): Appearance; Crude composition: moisture, total protein, total fat, ash, total carbohydrates, crude fibre; Amino acid profile, fatty acid profile; For isolated proteins: purity of the protein, solubility, pH 2% solution, amino acid composition, molecular mass, isoelectric point, absorption spectra, protease sensitivity, heat stability; Micronutrients: vitamins (A, B1, B2, B3, B5, B6, B8, B9, B12, C, D, E, K1), minerals (Ca, Mg, P, Na, K, Zn, Fe, Cu, Mn, Cl), other relevant substances; Inherent plant or animal toxins and/or antinutritional substances; Heavy metals (Cd, Pb, As, Hg, Ni), pesticide residues, mycotoxins, other contaminants (like dioxins, dioxin-like PCBs, PCBs, PAHs, etc); Substances used in processing (like solvents); Substances formed during processing; Microbiology: total bacteria (standard plate count), aerobic bacteria, *Enterobacteriaceae*, bacteria mentioned in Regulation (EC) 2073/2005, yeasts and moulds. Add copies of full laboratory reports (appendix). Add copies of the accreditation certificate of the labs (appendix). Give specifications of each of the parameters mentioned (e.g. minimum, maximum, range, >, <). Compare results of compositional analysis with your specifications and if applicable with legal limits in products (Table 3.3).
Is the information representative of the novel food when produced on a commercial scale?	Provide compositional information from batches that are representative for the product to be placed on the EU market. State where and when the batches used in the analyses were produced. If necessary, perform studies to show compositional stability of product during storage.
Is there an appropriate specification (including species, taxon, etc. for living organisms) to ensure that the novel food marketed is the same as that evaluated?	Use the Latin name (scientific nomenclature) to uniquely identify the source of the novel protein. Provide the taxon minimally up to the level of species, sub-species and variety (for example a chicken is *Gallus gallus domesticus*).

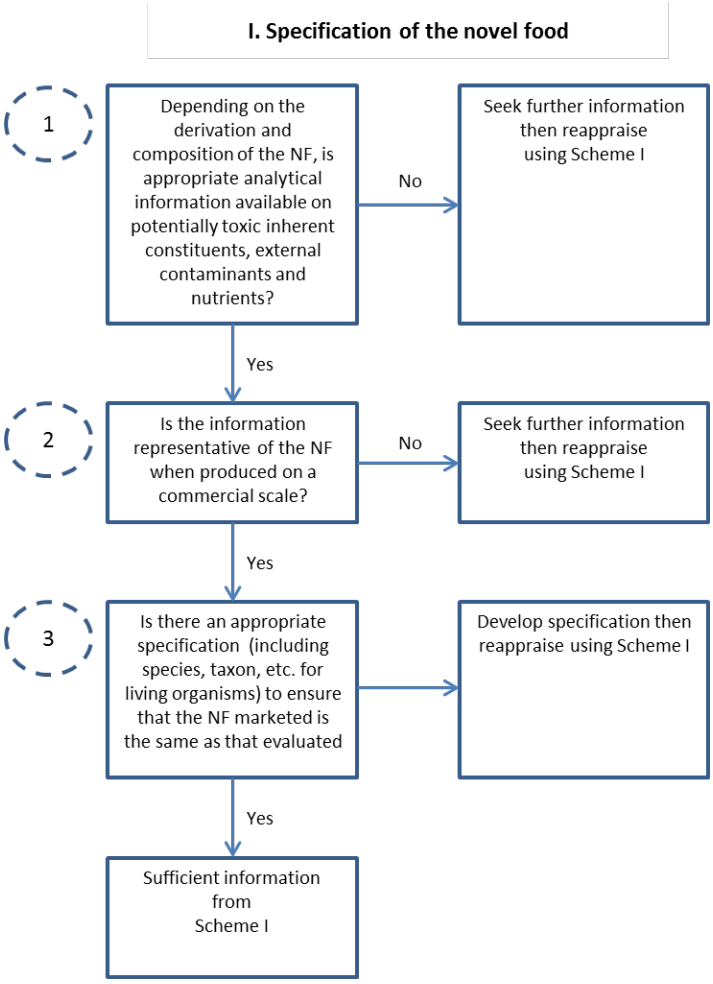

Figure 3.1 *Scheme I for specification of the novel food (NF) (Source: Recommendation 97/618/EC).*

Details on information and suggestions about questions in Scheme I for specification of the novel food
The chemical, microbial and physical characteristics of the novel protein have to be specified. In general, four or more samples of the novel protein should be analysed to determine average level, standard deviation, and minimum and maximum levels of each of the compounds. The novel protein and its composition must be representative of the protein when produced at a commercial scale. The potential influence of the proposed production processes, transport, and storage during the entire proposed shelf life of the novel protein on the characteristics should be taken into account. If the length of the storage time is expected to vary significantly, storage studies may be necessary to investigate the stability of the novel protein until the maximum expected storage time. If the source of the novel protein is produced at different locations in the world, it may be necessary to analyse batches of the novel protein derived from sources from different locations in order to gain insight into the variation in the composition of the novel protein. The type of substances of the composition needed to be analysed, depends on the novel protein. Some guidelines for this are:

- Appearance, crude composition (moisture, total protein, total fat, ash, total carbohydrates, crude fibre), key micro-nutrients (vitamins A, B1, B2, B3, B5, B6, B8, B9, B12, C, D, E, K1, minerals Ca, Mg, P, Na, K, Zn, Fe, Cu, Mn, Cl, other relevant substances), anti-nutritional substances and inherent plant or animal toxins may have to be determined depending on (the source of) the novel food. Information on key nutrients, anti-nutrients and toxins characteristic for some specific crop plant species (such as sugar beet, soybean and maize) and the extent of natural variation of these substances are provided in OECD consensus documents[10].
- Information on the presence of micro-organism should be provided (like on total bacteria using a standard plate count, aerobic bacteria, *Enterobacteriaceae*, moulds and yeasts). The selection of micro-organisms sought for should be determined based on the characteristics of the product (and production process), and should include those bacteria, moulds and yeasts that cannot be excluded to be present. If the novel food or its source resembles a product mentioned in Regulation (EC) No 2073/2005, it is advisable to include the micro-organisms mentioned in this regulation for this food product in the analysis.
- Those contaminants introduced at primary production (like mycotoxins, pesticide residues), those formed during processing, transport, and storage, and those substances used in processing (like solvents) may have to be analysed.
- Heavy metals (Cd, Pb, As, F, Hg, Ni), pesticide residues, mycotoxins, and other contaminants such as dioxins, dioxin-like PCBs, PCBs, PAHs, may have to be determined.
- For protein products, analysis of the amino acid composition is advisable as this can be used to determine the nutritional value of the protein. The UK based ACNFP has provided guidelines[11] for identifying and quantifying protein levels. Determination of a fatty acid profile for pure proteins is not required. However, for whole food products that contain fat, a fatty acid profile is helpful in the assessment of the nutritional value.
- Parameters for isolated proteins may be: purity of the protein, solubility, pH 2% solution, amino acid composition, molecular mass, isoelectric point, absorption spectra, protease sensitivity, and heat stability.

The measured levels of contaminants and residues should be compared to the legal limits for these compounds. EU and Dutch legislation on legal limits for contaminants and residues is listed in Table 3.3.

Preferably, laboratory analyses for all compounds and organisms should be performed by accredited laboratories. Methods of analysis used should preferably be accredited and validated as far as possible, and, if possible, comply with EU rules on official methods of analysis and criteria for such methods. Accredited laboratories and methods in the Netherlands can be found at http://www.rva.nl/search/. EU legislation on official methods of analysis for contaminants and residues in food products is listed in Table 3.3. If available, samples to be analysed for contaminants and residues should preferably be taken using official methods mentioned in EU legislation (Table 3.3). Note that it is not always necessary to perform all analyses. The composition of the novel protein can be compared to compositions of similar proteins in published scientific observations. Like the levels of contaminants and residues, the levels of toxins and anti-nutrients in the novel protein can also be compared with those of substances in comparable common food sources which are already consumed in similar quantities, to show that the novel protein is safe.

[10] http://www.oecd.org/fr/env/ess/biotrack/consensusdocumentsfortheworkonharmonisationofregulatory oversightinbiotechnology.htm

[11] http://www.food.gov.uk/multimedia/pdfs/proteinsinnovelfoodsissuesforconsid.pdf

Table 3.3

Legal limits in food and official methods of analysis sampling.

Contaminant(s) / residues	Legal limits in food in EU and the Netherlands[a]	Official methods of analysis (and sampling)
Dioxins, furans and dioxin-like PCBs, and non-dioxin-like PCBs in food	Regulation (EC) No 1881/2006	Regulation (EU) No 252/2012
Pd, Cd, Hg, inorganic tin, 3-MCPD, and PAHs in food	Regulation (EC) No 1881/2006	Regulation (EC) No 333/2007
Mycotoxins in food	Regulation (EC) No 1881/2006	Regulation (EC) No 401/2006
Nitrate in food	Regulation (EC) No 1881/2006, Warenwetregeling verontreinigingen in levensmiddelen	Regulation (EC) No 1882/2006
Residues of plant protection products	Regulation (EC) No 396/2005	Guideline SANCO/12495/2011, (Sampling: Directive 2002/63/EC)
Residues of veterinary drugs	Regulation (EU) No 37/2010	Decision 2002/657/EC, (Sampling: Decision 98/179/EC)
(Residues of) extraction solvents	Directive 2009/32/EC, Warenwetregeling extractiemiddelen	
Lysino-alanine	Warenwetbesluit Eiwitproducten	

a The latest consolidated versions of EU legislation can be found at http://eur-lex.europa.eu/en/index.htm. Dutch legislation can be found at www.overheid.nl. Plant protection products' MRLs can also be found in the Plant Pesticide Database http://ec.europa.eu/food/plant/pesticides/pesticides_database/index_en.htm

The source of the novel protein has to be specified using scientific nomenclature and should include the Latin name. Taxonomic identity of the novel protein established should be according to referenced and internationally accepted principles, for example the International Code of Nomenclature for algae, fungi, and plants (ICN) and International Code of Zoological Nomenclature (ICZN). Any deviation from such principles should be explained. In general, providing the taxon to the level of species, subspecies, and variety is sufficient to uniquely identify the source of the novel protein. Possible databases for taxonomic identity are:

- The 2010 EU Common Catalogue of Varieties of Agricultural Plant Species (http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:C:2010:337A:0001:0660:EN:PDF).
- http://www.eu-nomen.eu/portal/
- http://www.catalogueoflife.org/col/info/databases
- http://www.ncbi.nlm.nih.gov/taxonomy
- http://www.ipni.org/ipni/plantnamesearchpage.do

Examples of the specification of the novel protein in application dossiers for authorisation

Box 2 provides examples of how the specification of a novel protein can be described in an application dossier for authorisation. The application dossier of the Touchi extract of soybean provides an example about how to present information about the stability of the novel food during storage.

Box 2: The specification of a novel food in the application dossiers for authorisation of Chia seeds and Touchi extract of soybean

Chia seeds

The specification is presented in chapter 'I. Specification of the Novel Food' of the application dossier (http://www.food.gov.uk/multimedia/pdfs/applicdosschiacompany.pdf) in the paragraphs:

- Description: Latin name of Chia is *Salvia hispanica L.* belonging to the *Labiatae* family.
- Composition of …
- Potentially toxic inherent constituents, external contaminants and nutrients
- Samples and specification representative of commercial scale and traceable

Touchi extract of soybean

The specification is presented in the chapter 'I. Specification of the Novel Food' of the application dossier (http://www.food.gov.uk/multimedia/pdfs/touchiapplication.pdf) in the paragraphs:

I.A Identity: Latin name: '… small soybeans (*Glycine max.)* fermented with the fungus *Aspergillus Oryzae*'.

I.A.1 Proposed Names

I.A.2 Trade Names

I.B Specification (table I.B-1))

I.C Analytical Information (presents batches used)

I.C.1 Potentially Toxic Inherent Constituents and External Contaminants (Pesticides, heavy metals, dioxins and dioxin-like PCB's, Polycyclic Aromatic Hydrocarbons (PAHs), mycotoxins, 3-Monochloropropane-1,2-diol (3-MCPD))

I.C.2 Nutrients (Nutrient profile, Isoflavone Aglycones Content, Enzyme Inhibitory Activity)

I.D Representative Commercial Scale Batch Data

I.E Formulation Data

I.F Stability Data (in time, conditions)

I.F.1 Stability of the Bulk Powder

I.F.2 Stability Formulated Products

3.4.2 Effect of the production process applied to the novel protein

Figure 3.2 (Scheme II of Recommendation 97/618/EC) refers to the effect of the production process applied to the novel protein. Table 3.4 provides the questions in scheme II, and information and suggestions to answer each question.

Table 3.4

Effect of the production process applied to the novel protein.

Question from scheme II (Figure 3.2)	Information and suggestions
Does the novel food undergo a production process?	Provide a detailed description of the production process, process conditions, and of intermediate products Describe the proposed methods to maintain effective control to comply with the specifications (Quality Management Systems such as HACCP, GMP, ISO, GlobalGAP). Add copies of certificates of these Quality Management Systems, if available.
Is there a history of use of the production process for the food?	Compare the process of the novel food with processes used for an existing food product.
Does the process result in a significant change in the composition or structure of the novel food compared to its traditional counterpart?	Compare the composition and/or structure of novel protein to the composition and/or structure of the protein in the source from which it was derived, or with comparable proteins in sources already consumed in the EU.
Is information available to enable identification of the possible toxicological, nutritional and microbiological hazards arising from use of the process?	See scheme I (figure 3.1), question 1.
Are the means identified for controlling the process to ensure that the novel food complies with its specification?	Describe agreed methods and specifications to maintain effective control thereby ensuring a high standard of food safety throughout the production process (QMS based on HACCP, traceability) Add copies of details and certificates HACCP etc.
Has the process the potential to alter the levels in the novel food of substances with an adverse effect on public health?	See question 4
After processing is the novel food likely to contain microorganisms of adverse public health significance?	See question 4
After processing is the novel food likely to contain microorganisms of adverse public health significance?	See question 4

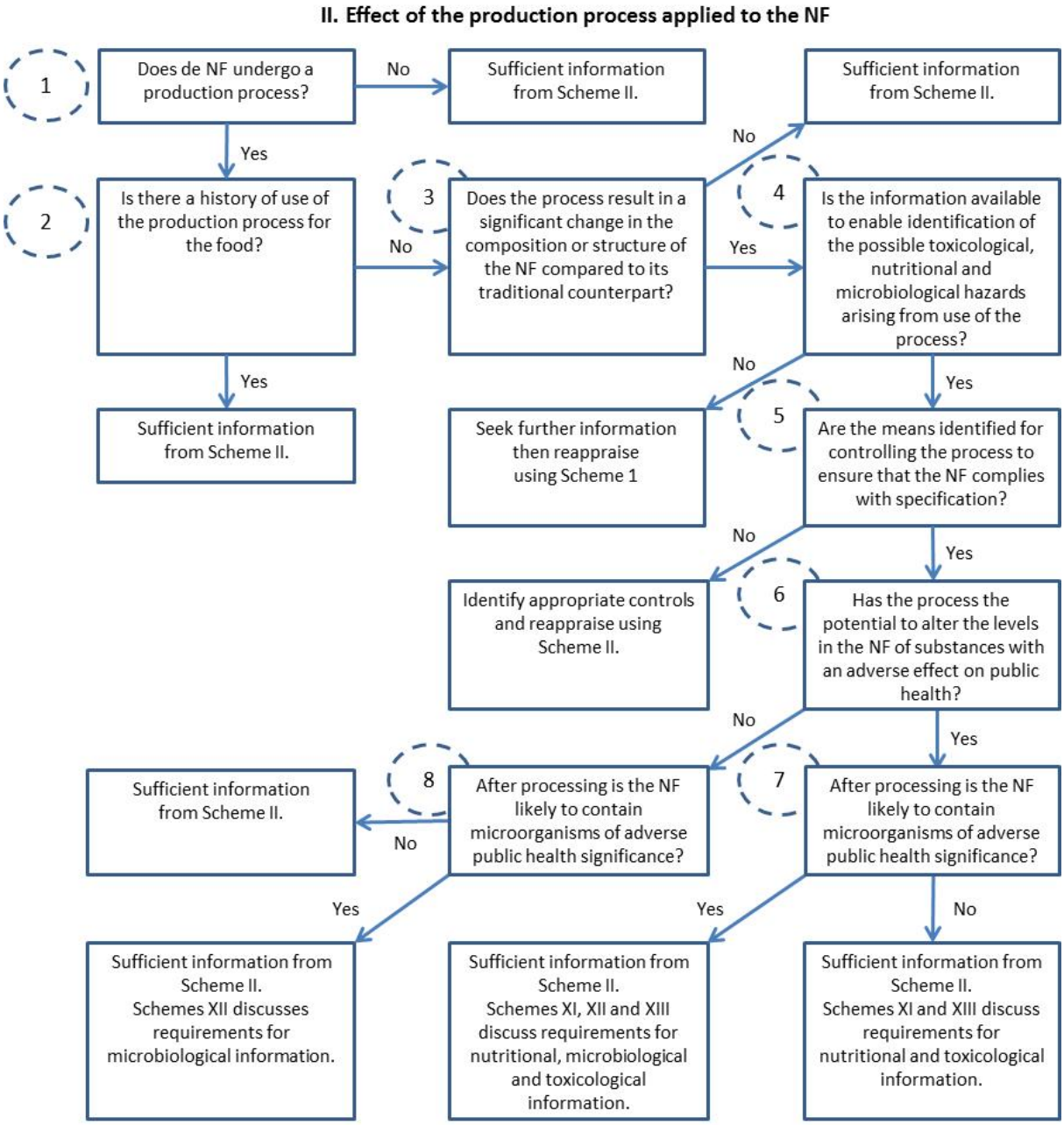

Figure 3.2 *Scheme II for the effect of the production process applied to a novel food (Source: Recommendation 97/618/EC).*

Details of information and suggestions about the questions in Scheme II for the effect of the production process applied to a novel protein

A detailed description of the production processes and conditions used and of the intermediate products of the novel protein has to be provided. This includes possible transport and storage phases. The description in the application dossier should convince assessors that any residues or contaminants derived from apparatus and equipment and from chemical, physical or biological aids are controlled. The application dossier should describe how the product is monitored and how safety and quality are controlled during the production process including transport and storage based on a Quality Management System, e.g. HACCP, GMP, ISO, GLOBALGAP, to be put in place. The application dossier should provide evidence that the process would not result in an adverse impact on essential nutritional, toxicological and microbiological parameters of the novel protein. To do so, the processes of the novel protein could be compared to processes already used for existing food products to show that these do not result in food safety risk.

Examples of the effect of the production process applied to the novel food in application dossiers for authorisation

Box 3 provides examples of how the effect of the production process applied to the novel food can be described in an authorisation dossier.

Box 3: The effect of the production process applied to a novel food in the application dossiers for authorisation of Chia seeds and Touchi extract of soybean

Chia seeds

The production process is presented in the chapter 'II. Effects of the Production Process Applied to the Novel Food' of the application dossier (http://www.food.gov.uk/multimedia/pdfs/applicdosschiacompany.pdf) in the paragraphs:

- Growing of the crop
- Harvest
- Post-harvest
- Storage
- Transport

Touchi extract of soybean

The production process is presented in the chapter 'II. EFFECT OF THE PRODUCTION PROCESS APPLIED TO THE NOVEL FOOD' of the application dossier (http://www.food.gov.uk/multimedia/pdfs/touchiapplication.pdf) in the paragraphs:

II.A Production Process
- II.A.1 Production of Fermented Black Beans
- II.A.2 Production of Touchi Extract

II.B History of the Production Process

II.C Identification of Potential Hazards
- II.C.1 Toxicological Hazards
- II.C.2 Nutritional Hazards
- II.C.3 Microbiological Hazards

II.D Control of the Production Process
- II.E Potential for Adverse Effect on Public Health or Micro-organism Contamination

3.4.3 History of the organism used as source of the novel protein

Figure 3.3 (Scheme III of Recommendation 97/618/EC) refers to the history of the organism used as the source of the novel protein. Table 3.5 provides the questions in scheme III, and information and suggestions to answer each question.

Table 3.5

Effect of the history of the organism used as the source of the novel protein.

Question from scheme III (Figure 3.3)	Information and suggestions
Is the novel food obtained from a biological source, i.e. a plant, animal, or microorganism?	Yes, proteins have a biological source.
Is the source organism characterised?	For a biological source such as a novel protein, this is the taxon from scheme I, question 3.
Is there information to show that the source organism and/or foods obtained from it are not detrimental to human health?	If available, provide evidence on human consumption of the source or existing products derived from this source in the EU and outside the EU. The more concrete and detailed information about sales and consumption is available, the better the evidence (see Table 2.1 for types of evidence). If available, provide evidence on the safe use of the source or existing products derived from this source in other applications, such as in personal care products, or safe human handling of the source (including skin contact), for example in a production process. If available, provide evidence on safe consumption by mammals or other animals of the source or existing products derived from the source. This evidence may be indicative for the novel protein not being detrimental to human health. If available, provide information on known food safety aspects of human consumption of the source or products derived from it.
Is there information on the mean levels and ranges of the detrimental substances in the novel food derived from the organism?	Provide the results of analysis for hazardous substances in the novel protein as asked in Scheme I, question 1.
Does the information reflect extremes in production and processing conditions for the novel food?	The composition of the novel protein as asked in scheme I, question 1 should be representative for the novel protein when produced for the commercial market and should reflect extremes in production and processing conditions. Provide description of quality control system to show how you deal with extremes in production and processing conditions.
Is the information sufficient to assess potential consumer risk?	If you can fill in scheme XI and XIII, this is yes.

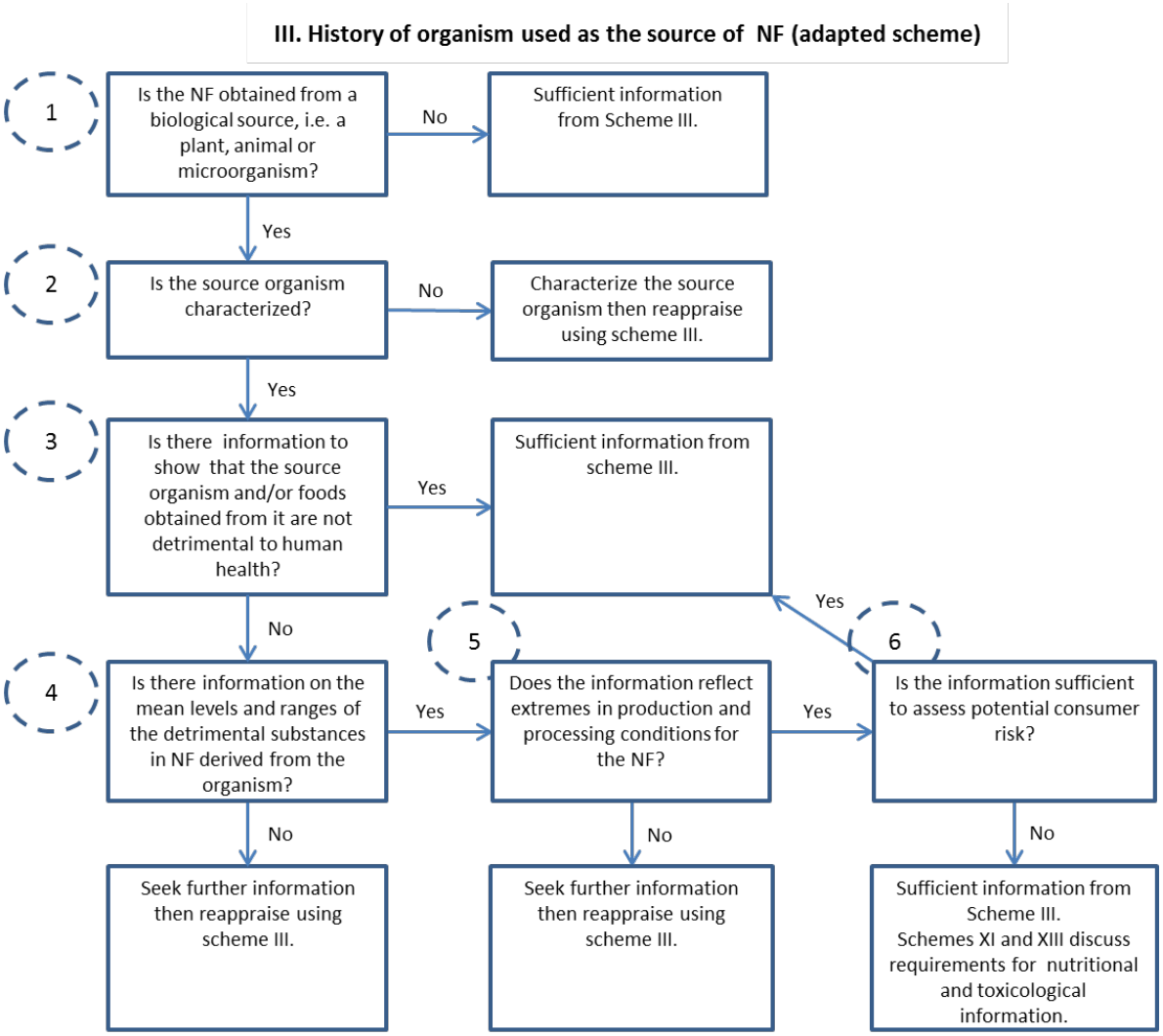

Figure 3.3 *Scheme III for history of the source organism of a novel food (Source: adapted version of the decision tree in Recommendation 97/618/EC. The questions about genetically modified organisms have been deleted, because these are no longer within the scope of the Regulation (EC) No 258/97).*

Details of information and suggestions about the questions in Scheme III for the history of the source organism of a novel protein

The source of the novel protein has to be identified in scientific nomenclature, which is also asked in scheme I, question 3.

To show that the source of the novel protein is not detrimental to human health, evidence of human exposure to the source or existing derived products inside the EU or outside the EU can be used. An important part of human exposure is consumption. The types of evidence of a history of human consumption to establish substantial equivalence (see Table 2.1) can also be used to show human consumption of the source or derived products. The more concrete and detailed information about consumption and sales is available, the better the evidence. Next to the historical use of the source or existing derived products in human consumption, the historical use in animal nutrition and in other applications, such as in personal care products, can be part of the evidence that the novel protein is safe.

Examples of the effect of history of the source organism of the novel protein in application dossiers for authorisation

Box 4 provides examples of how the effect of the history of the source organism of the novel protein can be described in an application dossier for authorisation.

Box 4: The history of the source organism of a novel food in the application dossiers for authorisation of Chia seeds and Touchi extract of soybean

Chia seeds

The history of the organism used as source is presented in the chapter 'III. History of the Source Organism' of the application dossier (http://www.food.gov.uk/multimedia/pdfs/applicdosschiacompany.pdf) in the paragraphs:

- Chia seed Source, GM Status, and Taxonomy
- Information on Detrimental Health Effects

Touchi extract of soybean

The history of the organism used as source is presented in the chapter 'III. HISTORY OF THE ORGANISM USED AS THE SOURCE OF THE NOVEL FOOD ' of the application dossier (http://www.food.gov.uk/multimedia/pdfs/touchiapplication.pdf) in the paragraphs:

III.A. Source of Touchi Extract
- III.A.1 Identity of the Soybean
- III.A.2 Cultivation of the Soybean
- III.A.3 Fermentation of the Soybean

III.B GM Status of Touchi Extract
- III.C Characterisation of the Small Soybean
- III.D Characterisation of Aspergillus Oryzae

III.E Potential for Detrimental Effects on Human Health
- III.E.1 Source Soybeans
- III.E.2 Aspergillus Oryzae

3.4.4 Anticipated intake/extent of use of the novel protein

Figure 3.4 (Scheme IX of Recommendation 97/618/EC) refers to the anticipated extent of use and intake of the novel protein. Table 3.6 provides the questions in scheme IX, and information and suggestions to answer each question.

Table 3.6

Effect of the anticipated extent of use and intake of the novel protein.

Question from scheme IX (Figure 3.4)	Information and suggestions
Is there information on the anticipated uses of the novel food based on its properties?	Describe the intended use and purpose of the novel protein. The intended use can for example be use as food as such (like an apple), use as a food ingredient or use as an ingredient of a food supplement. The intended purpose can be nutritional (e.g. use as a source of protein), functional, or for beneficial effects.
Is there information to show anticipated intakes for groups predicted to be at risk?	Describe the intended quantity of inclusion in food products, diets or food supplements. Estimate levels of intake of the novel protein based on the intended quantity of inclusion in the human diet. Distinguish in intake of different population groups (like male, female, young, old), and include groups whose intake might be different from general population groups due to deviating consumption habits (e.g. vegetarian, vegan, halal, etc.). If necessary also take into account more vulnerable subpopulations (e.g. with deviating functioning of the immune system, genetically challenged, etc). If available, use data from food consumption surveys to estimate the potential intakes of your novel protein. If available, use consumption data from multiple member states to assure coverage of differences in intake levels due to differences in diets between member states. If possible, assess mean and 90^{th}, 95^{th}, and 97.5^{th} percentile levels of intake. Include worst-case scenarios of consumers with the highest intakes in EU. Preferably, use the most recent consumption survey data. If you did identify special consumer groups (like vegan, vegetarian, etc), consumption data for these groups might be lacking. If this is the case, use literature or expert information to estimate intake levels.
Will introduction of the novel food be restricted geographically?	Describe region of market introduction in the EU. In most cases this will be the EU.
Do intake figures reflect this limited distribution of the NF?	Are figures from question 2 representative for region of question 3? In most cases no limited distribution is intended and this question is thus not applicable.
Will the novel food replace other foods in the diet?	Describe which foods or food ingredients the novel protein will replace and in what percentages or amount the novel protein will replace an existing protein/product. Note that this information should be used in the intake assessment of the novel protein.
Are any of the replaced foods significant nutritional resources?	If you answer question 4 in Scheme XI, you have answered this question as well.
Does the probable level of substitution have a nutritional significance for any population groups?	If you answer question 4 in Scheme XI, you have answered this question as well.

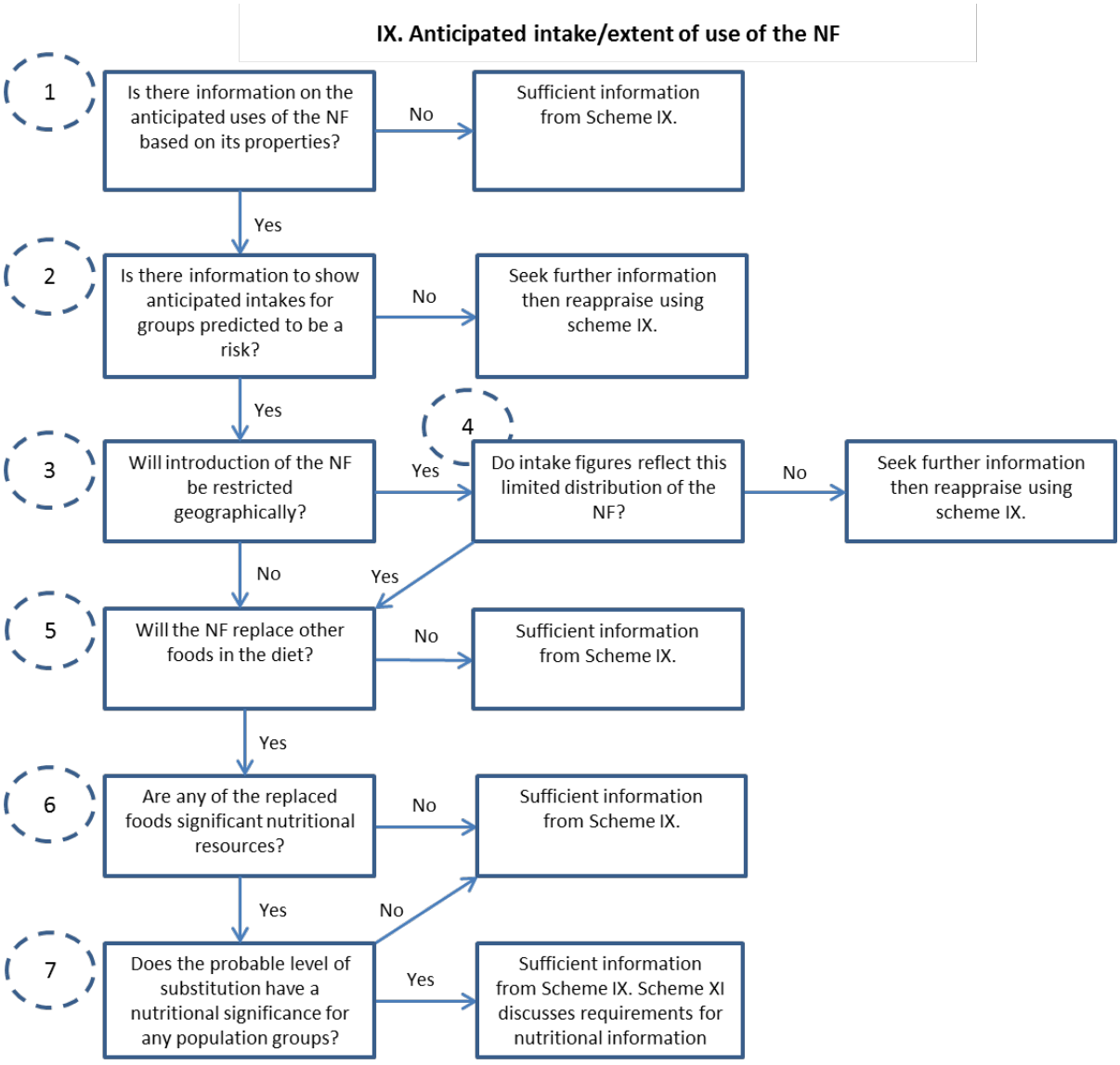

Figure 3.4 *Scheme IX for anticipated extent of use and intake of the novel protein (Source: Recommendation 97/618/EC).*

Details of information and suggestions about the questions in Scheme IX about the anticipated extent of use and intake of the novel protein

Indicate the intended use, purpose and quantity of consumption of the novel protein. The intended uses can for example be: use as a food product, use as a food ingredient or use as or in a food supplement. The purpose can be nutritional (source of protein), functional, or beneficial effects. The quantity indicates the maximum amount (in grams) of the novel protein a person will ingest (e.g. per day). Table 3.7 provides an example of how to present intended use categories and the maximum intended usage levels per category.

Table 3.7:

Example of intended use and purpose and the maximum intended usage levels per category.

Food category	Proposed food use	Maximum use-level (mg/serving)	Serving size (g)	Maximum use-level (mg/100g)
Milk and milk products	Ice cream			
	Milk beverages			
	Yoghurts			

The intended use levels for all products in which the novel protein is proposed to be used should be taken as a starting point of the intake assessment. This assessment should be based on food consumption data of consumers from multiple EU member states, since diets differ between the member states. Using data from recent food consumption surveys is advisable. Food consumption data for different EU member states can be found in the EFSA Comprehensive European Food Consumption Database available at the EFSA website[12]. These food consumption survey data can be used to assess mean and higher percentile levels (90^{th}, 95^{th}, 97.5^{th}) of intake. If specific consumer groups might have a higher risk, e.g. due to age or gender, the intake of these specific consumer groups should also be estimated. For special consumer groups and groups with high intakes, intake estimates could also be derived from literature or based on expert judgement (if no other sources are available). For 'worst-case' high estimates, intake estimates should be on the 'safe' side. A worst-case scenario for the highest intake in the EU is advisable, especially if in this scenario the intake is far below the intake where adverse effects might be noted. Table 3.8 provides an example of estimated daily intake in different population groups in (m)g per person per day and in (m)g per kg body weight per day. Another model for estimating daily intakes is the model[13] DEEM-FCID of the Environmental Protection Agency in the USA (DEEM-FCID: Dietary Exposure Evaluation Model-Food Commodity Intake Database). Although developed to estimate the dietary exposure to pesticides residues, this model could also be used as an example of an estimation of the intake.
When a novel protein is to be used as a novel source of protein in the diet, a crude estimate of the intake may suffice. In this case, the novel protein should be assumed to replace a common other protein in all products in which this common protein is present.
For food supplements, the recommended intake of the supplement determines the maximum intake. It is recommended to define different dose levels for different age groups or genders.

Table 3.8

Example of estimated daily intake in population groups (UK population groups based on the NDNS consumption data).

Population group	Age group (years)	% user	Actual # of total users	All person consumption				All users consumption			
				Mean (mg)	Percentile (mg)			Mean (mg)	Percentile (mg)		
					90^{th}	95^{th}	97.5^{th}		90^{th}	95^{th}	97.5^{th}
Children	1.5-4.5										
Young people	4-10										
Female teenagers	11-18										
Male teenagers	11-18										
Female adults	16-64										
Male adults	16-64										

Examples of anticipated extent of use and intake of the novel protein in application dossiers for authorisation

Box 5 provides examples of the description of anticipated extent of use and intake of the novel protein in an application dossier for authorisation.

[12] http://www.efsa.europa.eu/en/datexfoodcdb/datexfooddb.htm
[13] http://www.epa.gov/oppfead1/cb/csb_page/updates/2013/deem.html

Box 5: The anticipated extent of use and intake of a novel food in the application dossiers for authorisation of Chia seeds and Touchi extract of soybean

Chia seeds

Anticipated extent of use and intake is presented in the chapter 'IX Anticipated Intake/Extent of Use' of the application dossier (http://www.food.gov.uk/multimedia/pdfs/applicdosschiacompany.pdf) in the paragraphs:

- Intended Uses
- Current Position
  - Anticipated Intake
- 100% Chia seed as a Consumer Product
- Intake for Groups Predicted to be at Risk
- Geographic restriction of Chia seed Release
- Will Chia seed replace other foods in the diet?
- Labelling

Touchi extract of soybean

Anticipated extent of use and intake is presented in the chapter 'IX ANTICIPATED INTAKE/EXTENT OF USE OF THE NOVEL FOOD' of the application dossier (http://www.food.gov.uk/multimedia/pdfs/touchiapplication.pdf) in the paragraphs:

IX.A Anticipated Food Uses and Maximum Use Level

IX.A.1 Intended Use and Use-Levels

IX.A.2 Consumer Awareness

IX.A.3 Exposure Estimates

3.4.5 3.4.5. Information from previous human exposure to the novel protein or its source

Figure 3.5 (Scheme X of Recommendation 97/618/EC) refers to the information of previous human exposure of the novel protein or its source. Table 3.9 provides the questions in scheme X, and information and suggestions to answer each question.

Table 3.9

Information of previous human exposure to the novel protein or its source.

Question from scheme X (Figure 3.5)	Information and suggestions
Is there information from previous direct, indirect, intended, or unintended human exposure to the novel food or its source which is relevant to the Community situation with respect to production, preparation, population, lifestyles and intakes?	Provide detailed information on previous human exposure to source of the novel protein inside the EU and outside the EU, if available. This is the same information as asked in Scheme III, question 3. Provide detailed information on previous human exposure to the novel protein outside EU, if available. Exposure can be oral, but also dermal like via skin contact during handling or use in other applications such as personal care products, or via inhalation. If available, provide evidence on safe consumption by mammals or other animals of the source or existing products derived from the source. This evidence may be indicative for the novel protein not being detrimental to human health. Provide evidence of human exposure across the world, if available.
Is there information to demonstrate that exposure to the novel food is unlikely to give rise to nutritional, microbiological, toxicological and/or allergenicity problems?	Provide information about nutritional, microbiological, toxicological and/or allergenicity problems that have occurred due to exposure (oral, dermal, via inhalation) to the source of novel protein, to existing products derived from the source of the novel protein, and to the novel protein.

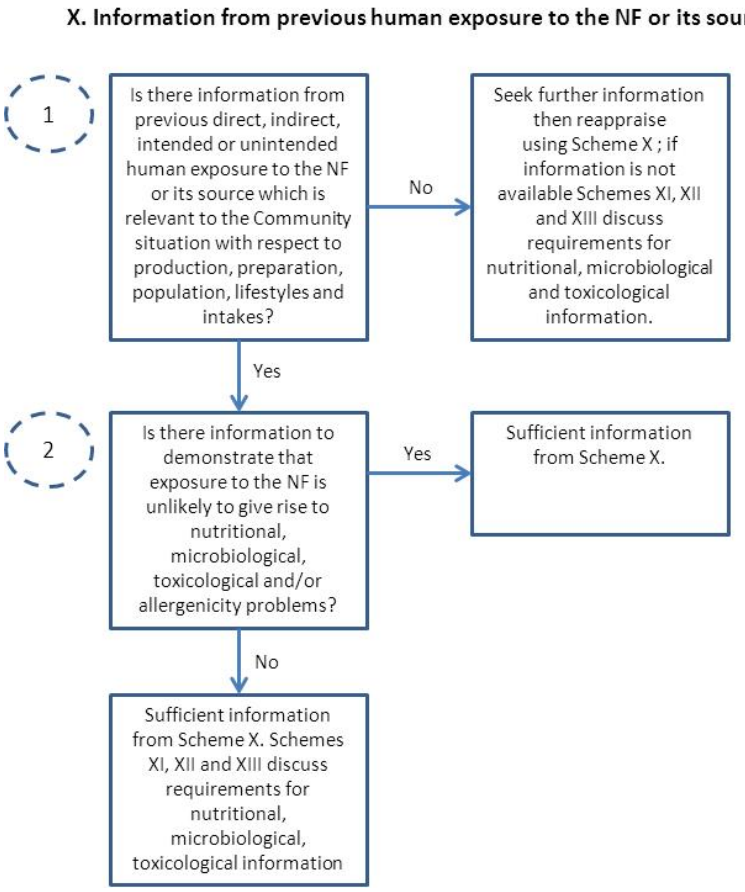

Figure 3.5 *Scheme X for information of previous human exposure to a novel food or its source (Source: Recommendation 97/618/EC).*

Details of information and suggestions about the questions in Scheme X about the information of previous human exposure to a novel protein or its source

In this chapter, the results of a thorough search of documented use of the NF by humans in third countries or the documented use of the source organism by humans in the EU and in third countries have to be provided. This has overlap with Scheme III, question 3 about the history of the source organism of the novel protein, in which information must be provided on human exposure to the source of the novel protein. In this chapter, the information provided in Scheme III, question 3 can be referred to, and information about human exposure to the novel protein itself outside the EU can be added. The types of evidence of a history of human consumption to establish substantial equivalence (see Table 2.1) can also be used to show human consumption of the source or derived products. The more concrete and detailed information about sales and consumption is available, the better the evidence. In addition to the historical use of the source or existing derived products in human consumption, the historical use in other applications, such as in personal care products, can be part of the evidence that the novel protein is safe.

Examples of information of previous human exposure to a novel food or its source in application dossiers for authorisation

Box 6 provides examples of the information on previous human exposure to a novel food or its source for an application dossier for authorisation.

Box 6: The information on previous human exposure to a novel food or its source in the application dossiers for authorisation of Chia seeds and Touchi extract of soybean

Chia seeds

Information about previous human exposure is presented in the chapter 'X. Information on Previous Human Exposure' of the application dossier (http://www.food.gov.uk/multimedia/pdfs/applicdosschiacompany.pdf) in the paragraphs:

- Recent Human Exposure to Chia seed
- Consumption Recent History
- Global Regulatory Approvals for Chia Seed
- Investigation into Allergic Reactions to Chia
- Conclusion on Previous Human Exposure
- Nutritional, Microbiological, and Toxicological Information related to Chia seed Exposure

Touchi extract of soybean

Information about previous human exposure is presented in the chapter 'X. Specification of the Novel Food' of the application dossier (http://www.food.gov.uk/multimedia/pdfs/touchiapplication.pdf) in the paragraphs:

X. INFORMATION FROM PREVIOUS HUMAN EXPOSURE TO THE NOVEL FOOD OR ITS SOURCE
X.A Previous Human Exposure
X.B Allergenicity of Touchi Extract

3.4.6 Nutritional information on the novel protein

Figure 3.6 (Scheme XI of Recommendation 97/618/EC) refers to the nutritional information on the novel protein. Table 3.10 provides the questions in scheme XI, and information and suggestions to answer each question.

Table 3.10

Nutritional information on the novel protein.

Question from scheme XI (Figure 3.6)	Information and suggestions
Is there information to show that the novel food is nutritionally equivalent to existing foods that it might replace in the diet?	Provide the nutritional information of the novel protein as presented in Scheme I question 1, and compare this with the composition of the existing protein you aim to replace in the diet. In case of (very) low intake levels compared to total dietary protein intake it might be possible to draw the conclusion that intake would not be nutritiously disadvantageous without taking into consideration parameters like amino acid composition or digestibility of the protein.
Is there information to show that the novel food does not affect the bioavailability of nutrients from the diet or have any adverse physiological effects?	Nutritional consequences should be established at normal and maximum levels of consumption, comparable to scheme IX, question 2.
Is information available to allow a balance to be made between risks and benefits?	Most of the times no specific information will be available. You can make some general remarks on the increased sustainability of the source of your novel protein or other beneficial aspects of the novel protein.
Is there information to allow an assessment to be made of the nutritional impact of the introduction of the novel food?	Provide information on potential shifts in intake in (micro)nutrients in (sub)populations due to introduction of your novel protein in the diet based on intake levels of the novel protein (Scheme IX, question 2) and nutrient levels in the novel protein (Scheme XI, question 1).

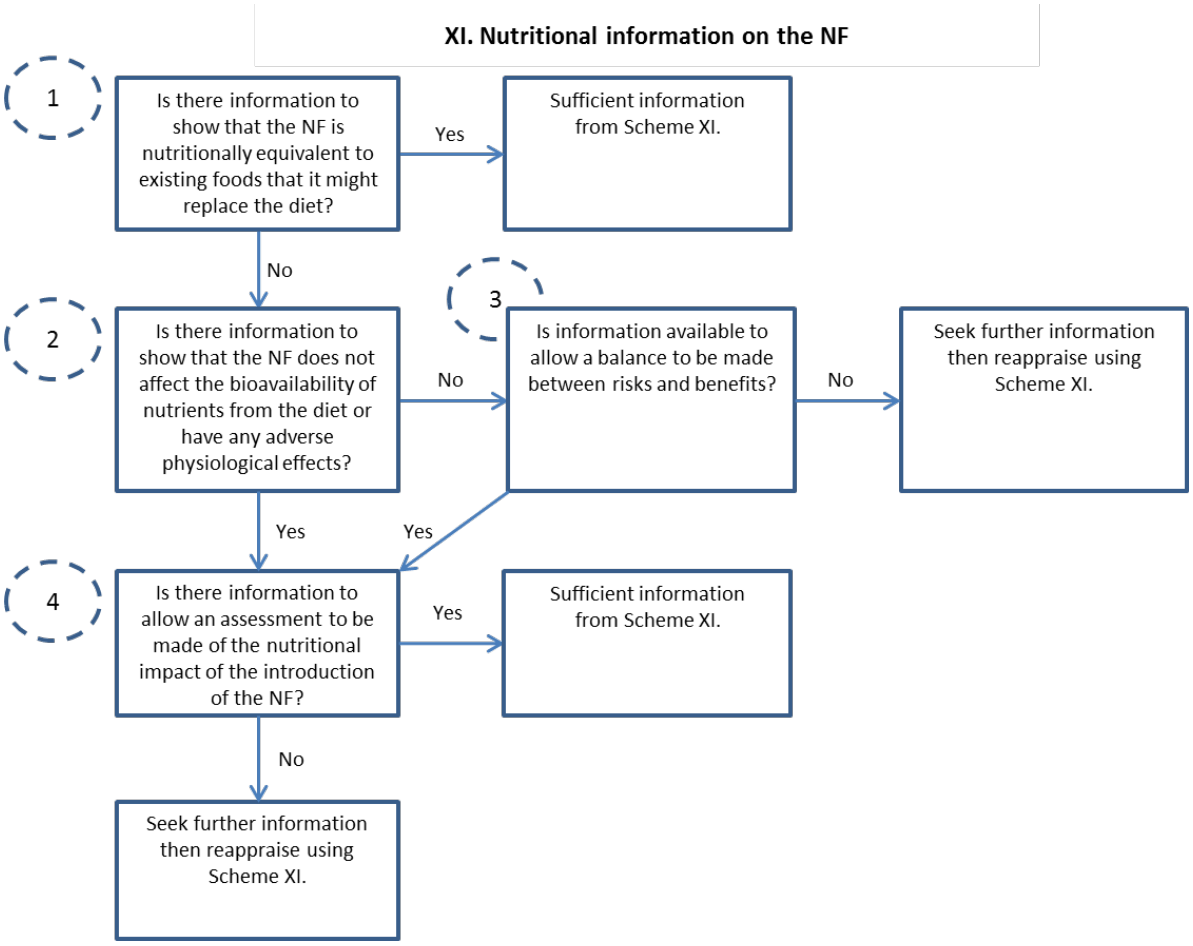

Figure 3.6 *Scheme XI for the nutritional information on a novel food (Source: Recommendation 97/618/EC).*

Details of information and suggestions about the questions in Scheme XI about the nutritional information on a novel protein

Nutritional effects are not to be expected if novel protein intake levels are estimated to be low and the change in human diet is minimal. Thus, in case of (very) low estimated intakes, this reasoning will be sufficient to conclude that there will be no nutritional impact. If the novel protein is meant to replace an existing protein in the diet, estimates of intakes will be higher. In this case, the analytical data on the composition (see Scheme I) and estimated intake (see Scheme IX) can be used to compare intake of proteins, amino acids, and other (macro and micro) nutrients in diets containing the novel protein to intake of nutrients from the 'old' diet to assess the nutritional impact. Recommended daily intake/amounts or reference values for nutrient intake could also be used to evaluate the nutritional impact.

Nutritional studies in animals are hardly ever considered to be necessary by CAs of EU member states. However, if you want to test your novel protein in nutritional studies in experimental or farm animals, the novel protein should be compared to a similar protein that is commonly used in animal diets. The only difference between the novel and common diets should be the protein used (thus protein content and also amino acid composition of the diets with the novel protein and the similar protein should be the same). Furthermore, diets should be used that are not nutritiously disadvantageous for animals.

Examples of the nutritional information on a novel food in application dossiers for authorisation

Box 7 provides examples of the nutritional information in an application dossier for authorisation.

Box 7: The nutritional information in the application dossiers for authorisation of Chia seeds and Touchi extract of soybean

Chia seeds

Nutritional information is presented in the chapter 'XI. Chia Nutritional Profile' of the application dossier (http://www.food.gov.uk/multimedia/pdfs/applicdosschiacompany.pdf) in the sub-chapters:

- Statement of Nutritional Profile
- Chia seed Nutritional Equivalence to Food it Might Replace
- Bioavailability of Nutrients and Nutritional Impact of Chia seed
- Heavy Metals and Chemical Contaminants

Touchi extract of soybean

Nutritional information is presented in the chapter 'XI. NUTRITIONAL INFORMATION ON THE NOVEL FOOD' of the application dossier (http://www.food.gov.uk/multimedia/pdfs/touchiapplication.pdf) in the sub-chapters:

XI.A Comparison of Touchi Extract to Traditional Counterparts
XI.A.1 Soy Proteins
XI.A.2 Soy Isoflavones
XI.A.3 Alpha-glucosidase Inhibitory Action
XI.B Labelling of Touchi Extract

3.4.7 Microbiological information on the novel protein

Figure 3.7 (Scheme XII of Recommendation 97/618/EC) refers to the microbiological information on the novel protein. Table 3.11 provides the questions in scheme XII, and information and suggestions to answer each question.

Table 3.11

Microbiological information on the novel protein.

Question from scheme XII (Figure 3.7)	Information and suggestions
Is the presence of any microorganisms or their metabolites due to the novelty of the product/process?	The source of your novel protein or the way of processing might be indicative of the presence or introduction of certain micro-organisms. Refer to scheme I specifications of your product (microbiological part).
Is there information to show that the NF is unlikely to contain microorganisms and/or their metabolites of adverse public health significance?	Mention if sterilisation or sufficiently high temperatures are used in the process because then it is unlikely that the product will contain micro-organisms. Add the information about microbiological content measured in Scheme I, question 1.
Is the NF likely to be confused with existing foods?	Refer to scheme I, question 1 and use the appearance in your specification (method visual).
Is information available to allow the development of procedures to ensure that the NF is appropriately handled, cooked or processed before consumption?	Provide the information you aim to provide to buyers of the novel protein on how to handle and use the novel protein. Describe how you provide the information mentioned in the first bullet to your buyers.
Are the procedures for handling, cooking or processing the existing food adequate to ensure safety if applied to the NF?	If the novel protein is similar to an existing protein, you can also mention that the safety procedures for the existing protein will also work for the novel protein. Describe how you provide the information mentioned in the first bullet to your buyers.

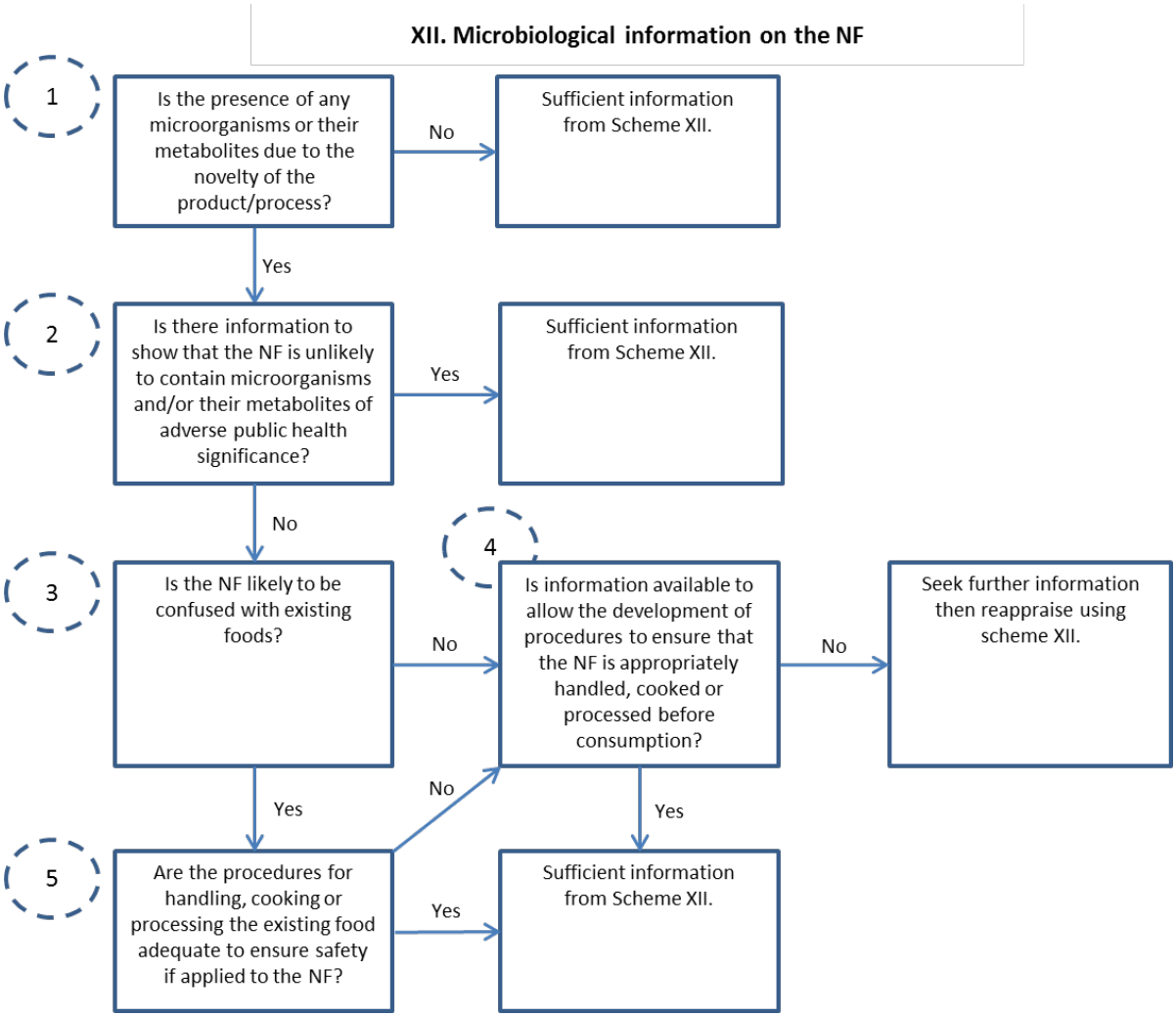

Figure 3.7 *Scheme XII for the microbiological information on a novel food (Source: Recommendation 97/618/EC).*

Details of information and suggestions about the questions in Scheme XII about the microbiological information on a novel protein

Applicants should provide data on microbiological tests performed on at least four batches of the novel protein taking into account, if appropriate, at least the micro-organisms and methods listed in Regulation (EC) No 2073/2005.

If the analysis in Scheme IX, question 2 included micro-organisms, referring to the results of Scheme IX, question 2 is sufficient here. It is also possible to describe the hazard analysis used to identify microbiological hazards, and the way these hazards are controlled in your HACCP system. This description should also include the stages of storage and transport.

The storage, handling, and processing of the novel protein should be specified to ultimately ensure the microbiological safety of the consumer products that contain the novel protein.

Examples of the microbiological information on a novel food in application dossiers for authorisation

Box 8 provides examples of microbiological information in an application dossier for authorisation.

Box 8: The microbiological information in the application dossiers for authorisation of Chia seeds and Touchi extract of soybean

Chia seeds
Microbiological Information of the Chia Seed is presented in the chapter 'XII. Microbiological Information of the Chia Seed' of the application dossier (http://www.food.gov.uk/multimedia/pdfs/applicdosschiacompany.pdf).

Touchi extract of soybean
Microbiological information is presented in the chapter 'XII. MICROBIOLOGICAL INFORMATION ON THE NOVEL FOOD' in sub-chapter 'XII.A Information on Microorganisms and their Metabolites' of the application dossier (http://www.food.gov.uk/multimedia/pdfs/touchiapplication.pdf).

3.4.8 Toxicological information on the novel protein

Figure 3.8 (Scheme XIII of Recommendation 97/618/EC) refers to the toxicological information of the novel protein. Table 3.12 provides the questions in scheme XIII, and information and suggestions to answer each question.

Table 3.12

Toxicological information of the novel protein.

Question from scheme XIII (Figure 3.8)	Information and suggestions
Is there a traditional counterpart to the NF that can be used as a baseline to facilitate the toxicological assessment?	If possible, use the existing protein that you aim to replace as traditional counterpart. Alternatively, you can use a product from a taxonomically related food source.
Is there information from a range of toxicological studies appropriate to the NF to show that the NF is safe under anticipated conditions of preparation and use?	Include here all data you can find on the history of the safety of the source, on the composition / specifications of your novel protein, and on the use in food or feed, demonstrating no adverse effects on human or mammal health when consumed in a comparable way, supported by any existing toxicological studies. The specifications of your product (Scheme I) might waiver the supply of toxicological studies.
Compared to the traditional counterpart, does the NF contain new toxicants or changed levels of existing toxicants?	Provide the information of the novel protein as presented in Scheme I question 1, and compare this with the composition of the existing protein you aim to replace in the diet. If applicable compare levels of toxicants (contaminants, residues, anti nutritional substances,, toxins, etc) with legal limits.
Is there information which suggests that the NF might pose an allergenic risk to humans?	At present, validated testing methods to predict the allergenicity of a novel protein are not available. Some information on the potential allergenicity can be derived from: Literature data on the allergenicity of the source of the novel protein due to consumption, skin contact, or inhalation. Literature data on the allergenicity of species related to the source of the novel protein. A search for amino acid sequence and/or structural similarities between the novel proteins(s) and known allergens in in international databases.
Is there sufficient information to allow the potential allergenicity of the NF to be monitored?	In case the novel protein is related to existing proteins with a known allergenic risk, propose labelling of products containing your novel protein.
Has the level of allergenicity been determined in controlled trials?	Most likely there are no controlled trials but if trials have been performed, describe them.
Are the levels in the NF of these new toxicants or existing toxicants no higher than those found in other foods with a history of food use in the Community?	Compare levels of antinutritional constituents and contaminants (as in Scheme 1) to legal limits or levels of these substances in other foods that are already on the market. Refer to the information provided in question 3 of this Scheme.
Is there information to show that the consumption of the NF will not raise intakes of the toxicants to unacceptable levels?	Intake levels of toxic substances should be established at normal and maximum consumption levels, comparable to scheme IX, question 2. Compare the results on intake of the first bullet with Acceptable Daily Intake (ADI), Tolerable Daily Intakes (TDI), Acute Reference Dose (ARfD) or other human health limits established for the specific toxic substances.
Is there information to show that the presence of these toxicants in the NF will not be a cause for concern?	See question 8 of this Scheme.
Is there information which suggests that the NF might pose an allergenic risk to humans?	See question 4 of this Scheme.

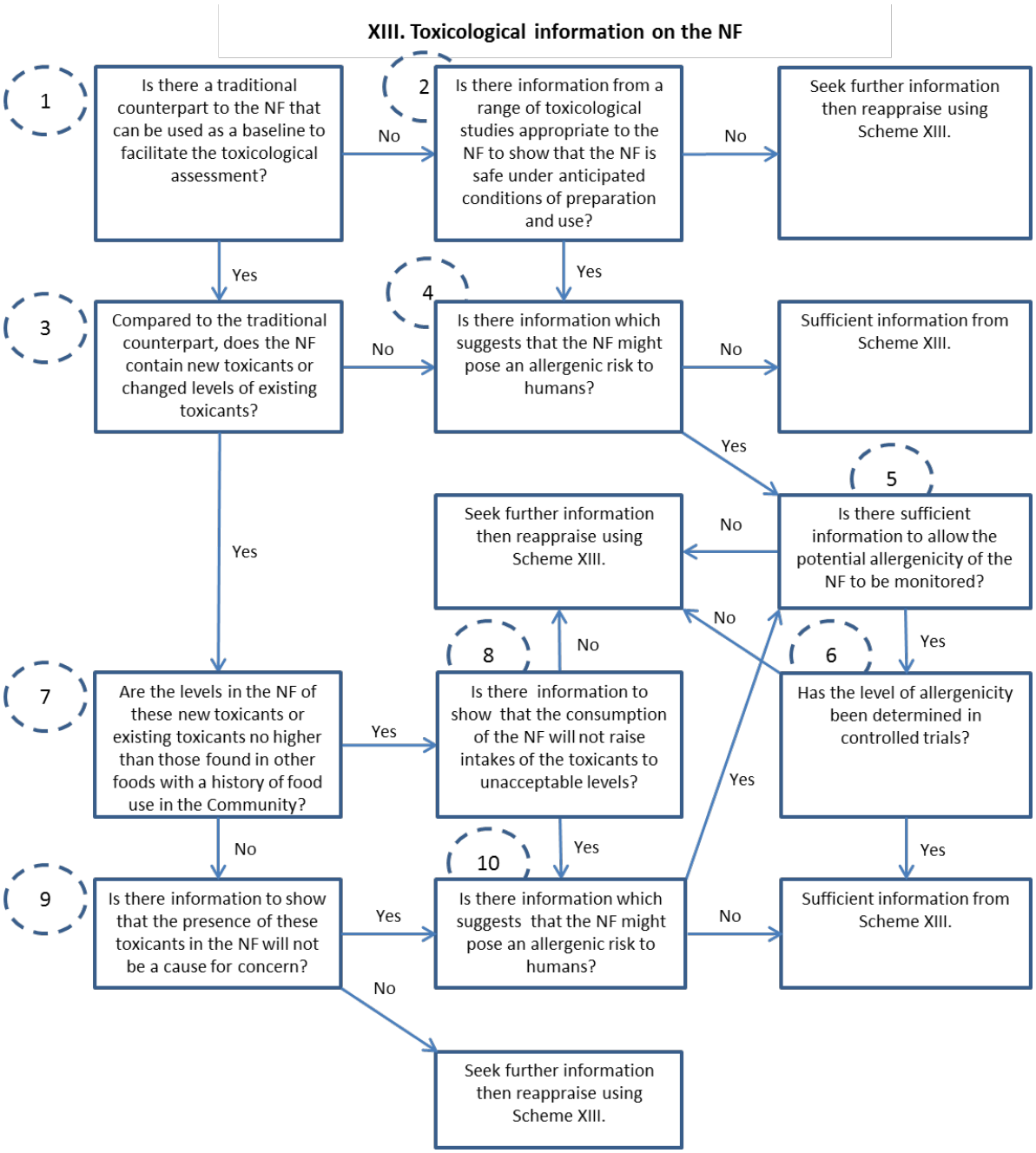

Figure 3.8 *Scheme XIII for the toxicological information on a novel food (Source: Recommendation 97/618/EC).*

Details of information and suggestions about the questions in Scheme XIII about the toxicological information on a novel protein

For novel proteins to be used as a source of protein, toxicity studies in experimental animals are hardly required by CAs of member states. A detailed and adequate analysis of the composition (including naturally occurring substances, contaminants formed during processing, and other substances known to be toxic) and an adequate description of the source of the protein, will usually be sufficient.

Some applicants may wish to place novel proteins on the market bearing claims of beneficial effects. This guideline does not describe the substantiation of claims. However, if efficacy studies in humans are performed, parameters addressing potential adverse effects could be included making these studies more valuable for the safety assessment.

If studies in experimental animals are performed, the applicant should make sure that OECD (http://www.oecd-ilibrary.org/environment/oecd-guidelines-for-the-testing-of-chemicals-section-4-health-effects_20745788) or other international guidelines for these studies are taken into account, that studies are performed under Good Laboratory Practices conditions, and that the material tested is described properly (and is identical or highly equivalent to the novel food product). An applicant should provide complete copies of the study reports (including individual animal data).

A thorough and adequate search of scientific literature on reported (adverse) effects of the source of the novel protein in humans and animals, (levels of) contaminants, toxins, anti-nutritional substances etc. should be included to substantiate safety of the novel protein. Complete copies of all relevant literature should be included in your application dossier. Estimated intakes of those hazardous substances in the novel protein can be compared to human health limits (like Acceptable Daily Intakes (ADI), Tolerable Daily Intakes (TDI), and Acute Reference Dose (ARfD)) established by EFSA, or other risk assessment bodies such as Joint FAO/WHO Expert Committee on Food Additives (JECFA), Joint FAO/WHO Meeting on Pesticide Residues (JMPR), Environmental Protection Agency (EPA) in the USA, and Food and Drug Administration in the USA (FDA). Lower estimated intakes than established health limits can be evidence of safety of the novel protein.

Allergenic potential of proteins

For assessing the allergenic potential of proteins, ACNFP (2011)[14] advices to use the EFSA guide 'Scientific Opinion on the assessment of allergenicity of GM plants and microorganisms and derived food and feed' (EFSA, 2010)[15].

Allergic reactions can be expected when the novel protein or the source of the novel protein is similar to food products that already need to be labelled due to their allergenicity (as listed in Annex IIIa of Directive 2000/13/EC). When an allergic reaction is expected, the applicant should include a labelling proposition in the novel food dossiers.

For those novel proteins that are supposed to be used in a hydrolysed form, peptide lengths in the hydrolysed product should be determined with adequate analysis methods. Only if the size of the peptides makes it very unlikely that a sensitised person will react to the product, labelling can be wavered.

If an appropriate literature search does not reveal any indications of allergic reactions to the source of the product (including search for contact dermatitis in those handling the product), and other products from related source families, then this will suffice to conclude the novel protein is not allergenic. However, very often, the source will be related to other sources known to induce allergies. In this case, it may be necessary to perform a homology search for all proteins in the products with known allergens in international databases, such as the allergen online database[16]. A possibility is to derive amino acid sequences from the DNA sequence of the source organism and to compare these with a databank of known allergens.

Examples of the toxicological information on a novel food in application dossiers for authorisation

Box 9 provides examples of toxicological information on a novel food in an application dossier for authorisation.

[14] http://www.food.gov.uk/multimedia/pdfs/proteinsinnovelfoodsissuesforconsid.pdf.
[15] http://www.efsa.europa.eu/en/efsajournal/doc/1700.pdf.
[16] Allergen online database available at http://www.allergenonline.org/.

Box 9: The toxicological information in the application dossiers for authorisation of Chia seeds and Touchi extract of soybean

Chia seeds
Toxicological information is presented in the chapter 'XIII. Toxicological Information of the Chia Seed' of the application dossier (http://www.food.gov.uk/multimedia/pdfs/applicdosschiacompany.pdf) in sub-chapter 'Allergy'.

Touchi extract of soybean
Toxicological information is presented in the chapter 'XIII. TOXICOLOGICAL INFORMATION ON THE NOVEL FOOD' of the application dossier (http://www.food.gov.uk/multimedia/pdfs/touchiapplication.pdf) in the sub-chapters:

- XIII.A Experimental Animal Data
  - XIII.A.1 Acute Toxicity
  - XIII.A.2 Subacute / Subchronic Toxicity
  - XIII.A.3 Reproductive/Developmental Toxicity
  - XIII.A.4 Mutagenicity/Genotoxicity
  - XIII.A.5 Chronic Toxicity
  - XIII.A.6 Other Preclinical Studies
- XIII.B Human Data

3.5 Evaluation and conclusion by the applicant

The applicant has to evaluate all the information provided in the former chapters and conclude on the safety for human consumption of the novel protein. The evaluation and the conclusion you draw can only be based on information presented in the application dossier. Box 10 provides examples of the conclusion in an application dossier for authorisation.

Box 10: The conclusion in the application dossiers for authorisation of Chia seeds and Touchi extract of soybean

Chia seeds
The conclusion is presented in the chapter 'Conclusions' of the application dossier (http://www.food.gov.uk/multimedia/pdfs/applicdosschiacompany.pdf).

Touchi extract of soybean
The conclusion is presented in the chapter 'OVERALL CONCLUSIONS' of the application dossier (http://www.food.gov.uk/multimedia/pdfs/touchiapplication.pdf).

3.6 Summary by the applicant

The applicant has to summarise all the information provided in the former chapters and draw conclusions on the safety for human consumption of the novel protein. Box 11 provides examples of the summary in an application dossier for authorisation.

Box 11: The summary in the application dossiers for authorisation of Chia seeds and Touchi extract of soybean

Chia seeds

The summary is presented in the chapter 'Executive summary' of the application dossier (http://www.food.gov.uk/multimedia/pdfs/applicdosschiacompany.pdf).

Touchi extract of soybean

The summary is presented in the chapter 'EXECUTIVE SUMMARY' of the application dossier (http://www.food.gov.uk/multimedia/pdfs/touchiapplication.pdf).

4 Application dossier for notification (substantial equivalence)

Article 5 of Regulation (EC) No 258/97 on novel foods and novel food ingredients provides a simplified procedure for a person, producer, or importer to bring a novel protein to the market that is 'substantially equivalent' to an existing counterpart (product) already allowed on the EU market. Substantial equivalence has to be demonstrated in an application dossier for notification. This dossier has to be submitted to a local CA for novel foods in an EU member state. This chapter handles instructions, practical tips, and examples for application of dossiers for notification.

Applicants of an application dossier for notification could use the guidelines from the UK's ACNFP[17] and the Dutch Gezondheidsraad[18] (in Dutch), which provide information to prove the substantial equivalence of a novel food to an existing counterpart. The main structure of the chapters of an application dossier for notification of a novel protein is: 1. basic administrative information; 2. general description and composition; 3. nutritional value; 4. metabolism; 5. intended use; 6. level of undesirable substances, and 7. any other relevant information on the novel protein.

Previously approved applications dossiers for notification can aid in making an application dossier for a novel protein. Box 12 provides examples of application dossiers for notification of refined Buglossoides oil, Chia seeds and DHA-rich algal oil from *Schizochitrium* Sp.ONC-T18 assessed by the UK's ACNFP. The examples show the public parts of the application dossiers. More application dossiers for notification of novel foods assessed by the ACNFP can be found on their website[19] under 'Simplified procedure'.

Box 12: The public part of application dossiers for notification of Refined Buglossoides oil, Chia seeds and DHA-rich algal oil from *Schizochitrium* Sp.ONC-T18

Refined Buglossoides oil
The application dossier for notification is available at
http://www.food.gov.uk/multimedia/pdfs/buglossoides-arvensis-application.pdf.

Chia seeds
Two application dossiers for notification are available at
http://www.food.gov.uk/multimedia/pdfs/chiaappinvagrop.pdf and
http://www.food.gov.uk/multimedia/pdfs/chiaappinfood.pdf.

DHA-rich algal oil from *Schizochitrium* Sp.ONC-T18
The application dossier for notification is available at

17 http://www.food.gov.uk/multimedia/pdfs/seguidelines.pdf
18 Instructions on page 31 of 'Veiligheidsbeoordeling van nieuwe voedingsmiddelen (2)' available at http://www.cbg-meb.nl/NR/rdonlyres/4B55FA07-6E31-4037-A0D4-F62ABE0FC237/0/200723.pdf
19 http://acnfp.food.gov.uk/assess/.

4.1 Administrative data

The following administrative data are needed:

- Name, postal and email address, telephone and fax of the applicant of the application dossier.
- Name, postal and email address, telephone and fax of the producer of the novel protein.
- Name, postal and email address, telephone and fax of the person responsible for the application dossier.
- Date of the application.
- Name of the novel protein.

4.2 General description and composition

The application dossier for notification should contain a specification of the novel protein, including information on the source organism, methods used for preparation, the composition of the final product and specification (minimum, maximum, average) of levels of contaminants, residues, and, if applicable, endogenous toxins. The composition of the novel equivalent product should be compared to the composition of one existing counterpart. This counterpart should be described in the same level of detail. The novel protein and the existing counterpart should be derived from the same or very similar species, and if applicable, grown and harvested under similar conditions. This requirement may be less strictly, if the products are refined extracts that contain only a limited number of defined chemical components.

4.2.1 Information on source organism

Taxonomic identity of the source of the novel protein has to be specified in scientific nomenclature using the Latin name. This should be established according to referenced and internationally accepted principles (for example the International Code of Nomenclature for algae, fungi, and plants (ICN) and International Code of Zoological Nomenclature (ICZN)). Any deviation from such principles should be explained. In general providing the taxon to the level of species, subspecies, and variety is sufficient to uniquely identify the source of the novel protein. Possible databases for taxonomic identity are:

- The 2010 EU Common Catalogue of Varieties of Agricultural Plant Species (http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:C:2010:337A:0001:0660:EN:PDF).
- http://www.eu-nomen.eu/portal/
- http://www.catalogueoflife.org/col/info/databases
- http://www.ncbi.nlm.nih.gov/taxonomy
- http://www.ipni.org/ipni/plantnamesearchpage.do

Box 13 provides four examples of Chia seeds, DHA-rich algal oil from *Schizochitrium* Sp.ONC-T18, Refined Buglossoides oil and Saskatoon berry to present taxonomic information in an application dossier for notification.

Box 13: Taxonomic information in the application dossiers for notification of Chia seeds, DHA-rich algal oil from *Schizochitrium* Sp.ONC-T18, refined Buglossoides oil and Saskatoon berry

Chia seeds
Appendix 6 of the application dossier for notification (http://www.food.gov.uk/multimedia/pdfs/chiaappinfood.pdf).

DHA-rich algal oil from *Schizochitrium* Sp.ONC-T18
Chapter '3.1 Compositional equivalence' and figure 3, Annex 3 and Annex 4 of the application dossier for notification (http://www.food.gov.uk/multimedia/pdfs/dhaoilont.pdf).

Refined Buglossoides oil
Chapter 'B1 Identity of the source' of the application dossier for notification (http://www.food.gov.uk/multimedia/pdfs/buglossoides-arvensis-application.pdf).

Saskatoon berry (*Amelanchier alnifolia*)
'Appendix 1. Taxonomy of saskatoon berry and blueberry' of the application dossier for notification (http://www.food.gov.uk/multimedia/pdfs/saskatoon.pdf).

4.2.2 History of use

Evidence of human exposure to the source or existing derived products can be used to show that the source of the novel protein is not detrimental to human health. This concerns human exposure inside and outside the EU. The exposure to humans will be dosed via oral consumption. Table 2.1 provides types of evidence of a history of human consumption. The more concrete and detailed information on sales and consumption is available, the better the evidence. Exposure via skin contact or use in other applications, such as personal care products, can also be part of the evidence that the novel protein is safe. If available, detailed information on use of the source of the novel protein or existing derived products in animal feed for mammals or other animals should be provided. This could give indications for the novel protein being not detrimental to human health. Box 14 provides an example of history of use of Chia seeds in the application dossier for notification.

Box 14: The history of use in the application dossier for notification of Chia seeds

Chapter '4.B History of use' of the application dossier for notification (http://www.food.gov.uk/multimedia/pdfs/chiaappinfood.pdf).

4.2.3 Product specification

The proposed product specification should be compared to the product specification of the existing counterpart. Box 15 provides an example of the product specification of refined Buglossoides oil compared to that of Echium Oil in the application dossier for notification.

Box 15: Product specification of refined Buglossoides oil compared to that of Echium oil in the application dossier for notification

Chapter 'B2 Product specification' of the application dossier for notification (http://www.food.gov.uk/multimedia/pdfs/buglossoides-arvensis-application.pdf).

4.2.4 Production process

The application dossier should contain a specification of the preparation method, manufacture process, and chain for both the novel protein and the existing counterpart. A process diagram can be used to explain the process. Box 16 provides an example of the production process of refined Buglossoides oil compared to that of other edible oils in the application dossier for notification.

Box 16: The description of the production process of refined Buglossoides oil compared to that of other edible oils in the application dossier for notification

Chapter 'B3 Preparation method' of the application dossier for notification (http://www.food.gov.uk/multimedia/pdfs/buglossoides-arvensis-application.pdf).

4.2.5 Composition of product

The novel protein should not contain significant levels of substances that are not present in the existing counterpart. If such substances are present, in general an application for notification will not be sufficient and an application for authorisation must be submitted.
Compositional analyses should be reported for at least four batches of the novel protein and of the existing counterpart. The batches and composition must be representative for the product to be placed on the EU market. The analyses should be performed by accredited labs, preferably using accredited and validated methods of analysis. If available, official sampling methods should be used. Data has to include the average, standard deviation, and minimum and maximum limits of each of the substances. The results of analyses of the novel protein and of the existing counterpart should be compared by appropriate statistical methods. Copies of full laboratory reports and copies of the accreditation certificate of the labs should be added to the application dossier for notification in appendices.

Provide data on the composition such as (note that not all parameters are applicable to all products):

- Appearance;
- Crude composition: moisture, total protein, total fat, ash, total carbohydrates, crude fibre;
- Amino acid profile, fatty acid profile;
- For isolated proteins: purity of the protein, solubility, pH 2% solution, amino acid composition, molecular mass, isoelectric point, absorption spectra, protease sensitivity, heat stability;
- Micronutrients: vitamins (A, B1, B2, B3, B5, B6, B8, B9, B12, C, D, E, K1), minerals (Ca, Mg, P, Na, K, Zn, Fe, Cu, Mn, Cl), other relevant substances;
- Inherent plant or animal toxins and/or antinutritional substances;
- Heavy metals (Cd, Pb, As, F, Hg, Ni), pesticide residues, mycotoxins, other contaminants (like dioxins, dioxin-like PCBs, PCBs, PAHs, etc);
- Substances used in processing (like solvents);
- Substances formed during processing;
- Microbiology: total bacteria (standard plate count), aerobic bacteria, *Enterobacteriaceae*, bacteria mentioned in Regulation (EC) 2073/2005, yeast and mould.

Box 17 provides an example of the composition of refined Buglossoides oil compared to Echium oil in the application dossier for notification.

Box 17: The composition of refined Buglossoides oil compared to that of Echium oil in the application dossier for notification

Chapter 'B.5 Nutrient composition' and 'Appendix 1 - Summary of analytical results' of the application dossier for notification (http://www.food.gov.uk/multimedia/pdfs/buglossoides-arvensis-application.pdf).

4.3 Nutritional value

If the composition of the novel protein does not differ from its existing counterpart, it is unlikely that there will be significant differences in its nutritional value. Nevertheless, the applicant should consider this possibility and provide results of any relevant studies in the application dossier. The nutritional composition of the novel protein and the existing counterpart should be compared. Reference to the results of the composition of the novel protein and the existing protein can be made as described in paragraph 4.2.3. (Very) low intake levels compared to total dietary protein intake might imply that intake would not be nutritiously disadvantageous, without taking into consideration parameters like amino acid composition, mineral or ash levels in the product or digestibility of the protein. Box 18 provides an example of general nutritional description of Chia seeds in the application dossier for notification.

Box 18: The general nutritional description in the application dossier for notification of Chia seeds

Chapter '4.A General description' of the application dossier for notification (http://www.food.gov.uk/multimedia/pdfs/chiaappinfood.pdf).

4.4 Metabolism

If the composition of the product does not differ from its existing counterpart, it is unlikely that there will be significant differences in its metabolism. Nevertheless, the application should consider this possibility and provide results of any relevant studies. These might include the results of bioavailability studies and stability tests to show that the novel product does not degenerate during storage or use.

4.4.1 Bioavailability

The bioavailability of nutrients in the novel protein should be demonstrated. When the novel protein is consumed as intended within the proposed diet, the bioavailability of nutrients should not change when the existing counterpart is replaced by the novel protein. Data about the bioavailability from the existing counterpart can be used from literature, if the composition of the product or diet in which the novel protein is replaced does not change from its existing counterpart. Box 19 provides an example of bioavailability in the application dossier for notification.

Box 19: The bioavailability in the application dossier for notification of Chia seeds

Chapter '5.A Bioavailability' of the application dossier for notification (http://www.food.gov.uk/multimedia/pdfs/chiaappinfood.pdf).

4.4.2 Stability of the product

The compositional stability of the novel protein during the whole storage period has to be demonstrated. If data are available, you could show this with a literature research. Otherwise, you could perform storage experiments to show compositional stability. Box 20 provides an example of stability of the product in the application dossier for notification.

Box 20: The stability of the product in the application dossier for notification of Chia seeds

Chapter '5.B Stability of the product' of the application dossier for notification (http://www.food.gov.uk/multimedia/pdfs/chiaappinfood.pdf).

4.5 Intended use

The application dossier for notification should describe the uses of the existing counterpart and explain which of those are relevant to the novel protein. This may include use in food supplements, use as a food, and use as a food ingredient in a list of specified food categories. In general, new uses for a novel protein cannot be included in an application for notification, particularly if the use is likely to result in consumption of the protein by a wider range of the population or at higher levels, compared with the existing counterpart. For example, the novel protein cannot be assessed as 'substantially equivalent' if it is intended for use as an ingredient in foods and the existing counterpart is only consumed in the form of food supplements.

The anticipated levels of intake should be specified in the dossier, based on the proposed level of substitution in the diet. Specific consumer groups at increased risk should be distinguished as well as differences in diet across the EU. Where the application covers use in food supplements, it should include information on the recommended dosage of the new protein and the existing counterpart. For further detailed information about the estimation of anticipated levels of intake, see paragraph 3.4.4. Box 21 provides examples of intended use of Chia seeds and refined Buglossoides oil in the application dossiers for notification.

Box 21: Intended use of Chia seeds and refined Buglossoides oil in the application dossiers for notification

Chia seeds
Chapter '6 Intended use' of the application dossier for notification (http://www.food.gov.uk/multimedia/pdfs/chiaappinfood.pdf).

Refined Buglossoides oil
Chapter 'E Intended use' and 'Table 2 – Intended food uses' of the application dossier for notification (http://www.food.gov.uk/multimedia/pdfs/buglossoides-arvensis-application.pdf).

4.6 Level of undesirable substances

The application dossier should include an analysis of the potentially present undesirable substances, such as environmental contaminants, mycotoxins, allergens, naturally occurring toxins and anti-nutrients, and pathogenic microorganisms. A detailed literature search could be performed to identify any undesirable substances that could be associated with the novel protein and its source. Box 22 provides an example of such a literature study for refined Buglossoides oil. Analytical data should be provided for at least four representative batches of the novel protein and the existing counterpart to show that the levels of these substances are comparable between the novel protein and existing counterpart, and that levels are below maximum limits. If the potentially present undesirable substances are described in the composition of the novel protein and of the existing protein in paragraph 4.2.3, the substances can be referred to that chapter. Different chapters or paragraphs about chemical contaminants and heavy metals, microbiological content, and toxicity and safety studies can be included, as well as a detailed description of the Quality Management System proposed to use for the novel protein.

Box 22: Literature study for the presence of undesirable substances in the application dossier for notification of refined Buglossoides oil

Chapter 'F Level of undesirable substances' of the application dossier for notification (http://www.food.gov.uk/multimedia/pdfs/buglossoides-arvensis-application.pdf).

4.6.1 Chemical contaminants and heavy metals

In this paragraph the results of the analysis on external chemical contaminants and heavy metals should be provided. At least four batches of the novel protein and the existing counterpart should be analysed. For further information, see paragraph 4.6 and paragraph 3.4.1. Box 23 provides examples of chemical contaminants and heavy metals in the application dossier for notification.

Box 23: Chemical contaminants and heavy metals in the application dossier for notification of Chia seeds and of refined Buglossoides oil

Chia seeds
Chapter '13. Level of Undesirable Substances' in the application dossier for notification (http://www.food.gov.uk/multimedia/pdfs/chiaappinvagrop.pdf)

Refined Buglossoides oil
Paragraph 'F.3 External chemical contaminants' and 'Table 9 – Potential external contaminants' of the application dossier for notification (http://www.food.gov.uk/multimedia/pdfs/buglossoides-arvensis-application.pdf).

4.6.2 Microbiological content

In this paragraph the results of the analysis on microbiological content should be provided. At least four batches of the novel protein and the existing counterpart should be analysed, taking into account, among others, relevant microbes and methods listed in Regulation (EC) No 2073/2005. For further information, see paragraph 4.6 and paragraph 3.4.7. Box 24 provides examples of the microbiological content in the application dossier for notification.

Box 24: Microbiological content in the application dossier for notification of Chia seeds and of refined Buglossoides oil

Chia seeds
Chapter '14. Microbiological Information of the Chia Seed' in the application dossier for notification (http://www.food.gov.uk/multimedia/pdfs/chiaappinvagrop.pdf)

Refined Buglossoides oil
Paragraph 'F.2 Microbiology' and 'Table 12 – Microbiological tests' of the application dossier for notification (http://www.food.gov.uk/multimedia/pdfs/buglossoides-arvensis-application.pdf).

4.6.3 Toxicity and safety studies

In this paragraph the results of the analysis on toxicity and allergenicity should be provided. No toxicological tests will be needed, if full substantial equivalence can be established based on compositional comparison. For further information, see paragraph 4.6 and paragraph 3.4.8. Box 25 provides examples of the toxicological content in the application dossier for notification.

Box 25: Toxicological content in the application dossiers for notification of Chia seeds and of refined Buglossoides oil

Chia seeds
'Chapter 15. Allergy' of the application dossier for notification (http://www.food.gov.uk/multimedia/pdfs/chiaappinvagrop.pdf).

Refined Buglossoides oil
Paragraph 'F.1 Inherent Substances' and 'Table 10 – Dioxins and dioxin-like PCBs' and 'Table 11 - Polycyclic aromatic hydrocarbons (PAHs)' of the application dossier for notification

4.6.4 Quality and Hygiene system

Describe the Quality Management Systems (e.g. HACCP, GMP, ISO, GlobalGAP) you propose to use for the novel protein. This should include a description of the HACCP scheme which is used to identify and control microbiological hazards. This HACCP scheme should include the stages of storage and transport. For further information, see paragraph 3.4.2.

4.7 Other relevant data

In the application dossier, the results from a literature survey about any other relevant data on the novel protein can be provided, including the reports of any safety studies.

If necessary, the application dossier for notification should also include a proposal for labelling, to demonstrate that consumers and other users will be adequately informed of the nature of the novel protein, its intended use, and any restrictions that may need to be respected. Requirements for labelling of the novel protein are additional to the general EU requirements on food labelling. Where necessary, labelling of novel protein may mention:

- Characteristics - composition, nutritional value, intended use;
- Materials which may affect the health of some individuals, such as allergy;
- Materials that give rise to ethical concerns.

The application dossier should include details of any monitoring that will be undertaken to provide on-going assurance that the product is of appropriate quality with regard to its composition and the presence of undesirable substances. Box 26 provides examples of the description of the other relevant data for chia seeds and refined Buglossoides oil.

Box 26: Other relevant data in the application dossier for notification of Chia seeds and of refined Buglossoides oil

Chia seeds
Chapter '8 Labelling' and chapter '17. OTHER RELEVANT DATA' of the application dossier for notification (http://www.food.gov.uk/multimedia/pdfs/chiaappinvagrop.pdf).

Refined Buglossoides oil
Chapter 'G Other relevant data' of the application dossier for notification (http://www.food.gov.uk/multimedia/pdfs/buglossoides-arvensis-application.pdf).

4.8 Evaluation and conclusion by the applicant

The applicant has to evaluate all the information provided in the former chapters and conclude on the substantial equivalence of the novel protein with the existing counterpart. The evaluation and the conclusion drawn can only be based on information presented in the application dossier. Box 27 provides examples of the conclusion in the application dossier for notification.

Box 27: Conclusion in the application dossier for notification of Chia seeds and of refined Buglossoides oil

Chia seeds
Chapter '16. CONCLUSION' of the application dossier for notification (http://www.food.gov.uk/multimedia/pdfs/chiaappinvagrop.pdf).

Refined Buglossoides oil
Chapter 'A.1 Basis of application' of the application dossier for notification (http://www.food.gov.uk/multimedia/pdfs/buglossoides-arvensis-application.pdf).

4.9 References and appendices

The applicant has to list all references in the text in a reference list at the end of the main text in the application dossier.

To improve readability of the main text in the application dossier, it is advised to put the most important information in the main text and present detailed data in tables and figures in appendices. Box 28 provides examples of the references and appendices for chia seeds and refined Buglossoides oil.

Finalise a notification dossier by adding a summary.

Box 28: References and appendices in the application dossier for notification of Chia seeds and of refined Buglossoides oil

Chia seeds
Chapter '18. REFERENCES' and chapter '19. APPENDIX' of the application dossier for notification (http://www.food.gov.uk/multimedia/pdfs/chiaappinvagrop.pdf).

Refined Buglossoides oil
Chapter 'References' on p24 and the appendices starting on p28 of the application dossier for notification (http://www.food.gov.uk/multimedia/pdfs/buglossoides-arvensis-application.pdf).

Annex 1 Overview of competent authorities in EU members states

EU Member State	Insti-tution[a]	Name	Link to the novel food page information
Austria		Österreichische Agentur für Gesundheit und Ernährungssicherheit GmbH (AGES)	http://www.ages.at/ages/ernaehrungssicherheit/neuartige-lebensmittel
		Bundesministerium für Gesundheit (BMG)	http://www.bmg.gv.at/home/Schwerpunkte/VerbraucherInnengesundheit/Lebensmittel/Neuartige_Lebensmittel/
Belgium		Department for Foods, Animal Foods and Other Consumption Products (DG for Animals, Plants and Foodstuffs)	http://www.health.belgium.be/eportal/foodsafety/foodstuffs/novelfoods/%3Ffodnlang%3Dnl
		Hoge Gezondheidsraad	
		Federal public Service – Health, Food Chain Safety and Environment (FSP-HFCSE)	
		Conseil Supérieur de la Santé (CSS)	
Denmark		Danish Veterinary and Food Administration	http://www.foedevarestyrelsen.dk/english/Aboutus/Organization/Head_Office/Pages/default.aspx
		Ministeriet for Fødevarer, Landbrug og Fiskeri (MfFLoF)	
Finland		Coordination authority in Finland is Food Safety Authority Evira (Evira)	http://www.evira.fi/portal/en/food/manufacture+and+sales/novel+foods/novel+food+applications/
		Novel Food Board (NFB)	
France		French Agency for Food, Environmental and Occupational Health & Safety (ANSES)	http://www.anses.fr/en/content/novel-foods-and-food-ingredients
		Direction Générale de la Concurrence, de la consummation et de la répression des Fraudes (DGCCRF)	
		Agence française de sécurité sanitaire des alimentes (AFFSA)	
Germany		Bundesinstitut für Risikobewertung / Federal Institute for Risk Assessment (BfR)	http://www.bfr.bund.de/de/novel_foods-215.html
		Bundesinstitut für gesundheitlichen Verbrachersschutz und Veterinärmedizin (BgVV)	
		Bundesamt für Verbrachersschutz und Lebensmittelsicherheit (BVL)	
Ireland		Food Safety Authority of Ireland (FSAI)	http://www.fsai.ie/science_health/novel_food_applications/safety_assessments.html
Netherlands	AU	Ministerie van Volksgezondheid, Welzijn en Sport (VWS)/ Ministry of Public Health, Welfare and Sport	
	AB	The Medicines Evaluation Board (CBG MEB)	http://www.cbg-meb.nl/CBG/en/novel-foods/actueel/default.htm
Poland		Instytut Roślin I Przetworów Zielarkich (IRPZ)	
		Instytut Żywności I Żywienia (IZIZ)	
		Państwowa Inspekcja Sanitarna	http://gis.gov.pl/dep/?lang=en&dep=14&id=29
Spain		Agencia Española de Seguridad Alimentaria y Nutrición. Ministry of Agriculture, Fisheries and Food. D.G IA y (AESAN)	http://www.aesan.msc.es/en/AESAN/web/cadena_alimentaria/subseccion/nuevos_alimentos_nuevos_ingredientes.shtml
Sweden		National Food Administration (NFA)	
United Kingdom		Advisory Committee on Novel Foods and Processes (ACNFP)	http://acnfp.food.gov.uk/assess/
		Food Safety Agency (FSA)	

[a] AU = Authority, AB = Assessment body, and AB+AU = Authority + Assessment body

[b] (BNV) Bureau Nieuwe Voedingsmiddelen or Novel Food Unit is part of CBG-MED

Annex 2 Fees to be paid to authority for assessment Novel Food

EU Member State	Authority	Authorisation	Notification
Belgium (1998)	DG for Animals, Plants and Foodstuffs / Superior Health Council	€3,718.50	€1,239.50
Germany (…)	BfR	€2,556 and €5,113.	€2,556 - €5,113
Netherlands (2008)	CBG MEB	€25,838	€2,086
Finland	EVIRA / NFB	Evira: €2,463 for processing dossier Novel Food Board: €2,700 – €25,000 (assessment: depending on the complexity and work to be done)	Evira: €985 for processing dossier Novel Food Board: €700. Total: €1,685
United Kingdom (2013)	ACNFP	€4,650 (£4,000)	€2,005 (£1,725)

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LEI Wageningen UR carries out socio-economic research and is the strategic partner for governments and the business community in the field of sustainable economic development within the domain of food and the living environment. LEI is part of Wageningen UR (University and Research centre), forming the Social Sciences Group together with the Department of Social Sciences and Wageningen UR Centre for Development Innovation.

The mission of Wageningen UR (University & Research centre) is 'To explore the potential of nature to improve the quality of life'. Within Wageningen UR, nine specialised research institutes of the DLO Foundation have joined forces with Wageningen University to help answer the most important questions in the domain of healthy food and living environment. With approximately 30 locations, 6,000 members of staff and 9,000 students, Wageningen UR is one of the leading organisations in its domain worldwide. The integral approach to problems and the cooperation between the various disciplines are at the heart of the unique Wageningen Approach.

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