TECHNICAL REPORT

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Outcome of a public consultation on the draft guidance on the preparation and presentation of an application for authorisation of a novel food in the context of Regulation (EU) 2015/2283

European Food Safety Authority

Abstract

The European Food Safety Authority (EFSA) carried out a public consultation to receive input from the scientific community and all interested parties on the draft guidance on the preparation and presentation of an application for authorisation of a Novel Food, prepared by the EFSA Panel on Dietetic Products, Nutrition and Allergies (NDA Panel) and endorsed by the Panel for public consultation at its Plenary meeting on 1 February 2016. The written public consultation for this document was open from 18 February 2016 to 21 April 2016. EFSA received 193 comments from 25 interested parties. As part of EFSA's public consultation, a stakeholders' meeting was held in Brussels on 11 April 2016. EFSA and its NDA Panel wish to thank all stakeholders for their contributions. The current report summarises the outcome of the public consultation, and includes a brief summary of the comments received and how the comments were addressed. The NDA Panel prepared an updated version of the guidance taking into account the comments received. The guidance was discussed and adopted at the NDA Plenary meeting on 21 September 2016, and is published in the EFSA Journal.

Keywords: guidance, novel foods, traditional foods, authorisation, safety, public consultation

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1. Introduction

1.1. Background as provided by the European Commission

On 25 November 2015, the European Parliament and the Council adopted the Regulation of the European Parliament and of the Council on novel foods[1].

The Regulation requires that all applications for the authorisation of novel foods shall be submitted to the Commission who may then request a risk assessment from the European Food Safety Authority (EFSA). In assessing the safety of novel foods, EFSA shall, where appropriate, consider the following:

1) whether the novel food concerned is as safe as food from a comparable food category already existing on the market within the Union;
2) whether the composition of the novel food and the conditions of its use do not pose a safety risk to human health in the Union;
3) a novel food, which is intended to replace another food, does not differ from that food in such a way that its normal consumption would be nutritionally disadvantageous for the consumer.

The Regulation also introduces a special procedure for safety assessment for traditional foods from third countries, based on a history of safe food use. In this case, a notification for the placing on the market of a traditional food from a third country is sent to the Commission who forwards it to all the Member States and EFSA. A Member State or EFSA may submit duly reasoned safety objections on the placing on the market of the notified food. In this latter case, the applicant may transform the notification into an application, for which a safety evaluation will be requested from EFSA. In assessing the safety of these types of novel foods, EFSA shall, where appropriate, consider the following:

1) whether the history of safe food use in a third country is substantiated by reliable data submitted by the applicant;
2) whether the composition of the food and the conditions of its use do not pose a safety risk to human health in the Union;
3) where the traditional food from the third country is intended to replace another food, whether it does not differ from that food in such a way that its normal consumption would be nutritionally disadvantageous for the consumer.

The Commission shall adopt implementing rules on administrative and scientific requirements for the preparation and the presentation of the applications for novel foods, as well as for the notifications and applications for traditional foods from third countries for the scientific assessment, respectively in accordance with Article 13 and Article 20 of the Regulation. These implementing measures need to be complemented with scientific and technical guidance regarding the information that needs to be submitted by the applicants. In this context, the current Commission Recommendation 97/618/EC[2], which is in place for the additional safety assessment of the novel food applications under the current rules (Regulation (EC) No 258/97[3]), should serve as the basis for updating the guidance on preparation and presentation of applications for novel foods.

1.2. Terms of Reference as provided by the European Commission

In accordance with Article 29 of Regulation (EC) No 178/2002, the European Commission asks the European Food Safety Authority to update and develop scientific and technical guidance for the preparation and presentation of applications for authorisation of novel foods, and to develop scientific and technical guidance for notifications and applications for authorisation of Traditional Foods from third countries.

[1] Regulation (EU) 2015/2283 of the European Parliament and of the Council on novel foods, amending Regulation (EU)
[2] OJ L 253, 16.9.1997, p. 1.
[3] OJ L 43, 14.2.1997, p. 1.

1.3. Consideration

Upon a request from the European Commission, the EFSA NDA Panel developed a draft guidance document on the preparation and presentation of an application for authorisation of a novel food. In line with EFSA's policy on openness and transparency, and in order for EFSA to receive comments on its work from the scientific community and stakeholders, EFSA engages in public consultations on key issues. Accordingly, the draft guidance was published on EFSA's website for comments (18 February 2016 to 21 April 2016) (see Appendix A) and a stakeholders' meeting was held in Brussels on 11 April 2016[4]. The NDA Panel prepared an updated version of the guidance, taking into account the comments received. The updated guidance was discussed and adopted at the NDA Plenary meeting on 21 September 2016, and is published in the EFSA Journal (EFSA NDA Panel, 2016a). EFSA is committed to publishing the comments received during the public consultation, as well as a report on the outcome of the consultation.

2. Screening and evaluation of comments received

2.1. Comments received

EFSA received 193 written comments from 25 interested parties, including universities, national and international risk assessment bodies, expert societies, consumer organisations, Member States' competent authorities, the food industry and food industry associations.

Comments related to policy or risk management aspects were considered to be outside the scope of the consultation, and are not addressed in this report.

Table 1: List of organisations submitting comments

Organisation	Country
AESGP - the Association of the European Self-Medication Industry	BE
Analyze & realize GmbH	DE
CASP	CZ
Committee "Novel Foods and New Technologies" of the Codex Alimentarius Austriacus Commission	AT
ELC - Federation of European Specialty Food Ingredients Industries	BE
Eurogroup for Animals	BE
Federal Food Safety and Veterinary Office	CH
Federal Public Service of Health, Food Chain Safety and Environment	BE
Food Law Consult	BE
Food Safety Authority of Ireland	IE
Food Supplements Europe	BE
FDE - FoodDrinkEurope	BE
Intertek Scientific &Regulatory Consultancy	UK
IPIFF	BE
Mead Johnson Nutrition	US
Mission of Chile to the European Union	CL
National Food Agency	SE
Nutraveris	BE
Pen & Tec Consulting	CH
Schuttelaar & Partners	BE
Secretaría de Economía (Secretariat of Economy of a non-EU country)	MX
Snow Pony Ltd	UK
SYNPA - Association de producteurs et de distributeurs d'ingrédiens alimentaires de spécialité	FR
TNO/COST Action ImpARAS	NL
UK Advisory Committee on Novel Foods and Processes	UK

AT: Austria; BE: Belgium; CH: Switzerland; CL: Chile; CZ: Czech Republic; DE: Germany; FR: France; IE: Ireland; MX: Mexico; NL: Netherlands; SE: Sweden; UK: United Kingdom; US: United States.

[4] https://www.efsa.europa.eu/en/events/event/160411

All written comments received are listed in Appendices B and C.

A summary of the comments received is given below.

2.2. General comments

2.2.1. Comments related to risk management

EFSA would like to highlight that the following comments (1 to 8) are considered to be related to risk management rather than to risk assessment. These comments are not further discussed in the present report as they are not part of EFSA's remit, and thus they were not taken into account when updating the draft guidance.

Comments received:

1. Clarifications were required about the criteria that will be applied to classify a food/ingredient as a novel food/ingredient. For instance, whether a food with a low proportion of a new ingredient would be considered a novel food.
2. The "grey area" between food and medicinal products or narcotics was pointed out. Botanical or animal extracts used as ingredients were taken as potential examples. It was suggested to clarify that Novel Foods/ingredients should not have pharmacological, psychotropic or addictive properties. Reference was made to "narcotic or psychotropic substances within the meaning of the United Nations Single Convention on Narcotic Drugs, 1961, and the United Nations Convention on Psychotropic Substances, 1971". Concern was expressed that the list of narcotics is not always up to date and regulates only comparatively potent psychoactive substances.
3. "Grey areas" in regulation around botanical/plant extracts in food supplements and foods were pointed out. A call for setting criteria (e.g. purity criteria, level of dilution) to define botanical/plant preparation vs. isolated substances was made.
4. There was a request to clarify the scientific basis for setting a limit of 25 years in relation to the history of safe use. Criteria to assess a significant degree of human consumption were also required.
5. The draft guidance defines an 'application' as a stand-alone dossier. It was noted that novel foods/ingredients may be the outcome of a joint-research program between several entities or may be used by an end user manufacturer under specific conditions. EFSA should consider the opportunity for a partner to submit additional information.
6. It was stated that it is very important to harmonise the criteria set in the section related to Description/identity of the novel food with the Union List when it is drawn up for existing products. There should be harmonisation of approach so that new approvals fit into the new list.
7. There was a proposal to include information on foreseeable misuse of the product, the proposed labelling, risk management measures proposed by the applicant and any measures needed to restrict the product to the target population.
8. With respect to precautions and restrictions of use, it was stated that labelling is an effective risk management measure and that applicants should be allowed to propose specific wording in the application. There were also comments that past post-market monitoring has been a useful tool to consider the long term effects of innovations in food; it was proposed to require applicants to include any plans for post-market monitoring.

2.2.2. Generic comments

Comments received

9. A definition of "whole food" was required. It was suggested to use the definition proposed by EFSA's Scientific Committee (EFSA SC, 2011c).

10. It was noted that Commission Recommendation 97/618/EC links the novel food categories with their specific data requirements in simplified format (tables and decision trees), which was viewed as user-friendly by applicants. It was suggested to introduce similar tools in the present guidance.

11. Reference was made to the possibility to submit an application in case the notification for a traditional food from a third country has failed (Article 16 of Regulation (EU) 2015/2283).

12. Several comments concerned the confidential treatment of data. In particular, it was stated that information on the production process may be commercially sensitive and should be subject to confidential treatment. The importance of a proper communication between the applicant and EFSA on which portions of the dossier are considered confidential was stressed. Reference was made to the EFSA guidance on food additives (EFSA ANS Panel, 2012) which allows applicants to provide a non-confidential description of the manufacturing process, when they intend to maintain the entire process confidential.

13. Clarification was sought on EFSA's approach (e.g. quantitative or qualitative) to determining the necessity of the data for the purposes of establishing data protection (Article 26 (2)(c) of Regulation (EU) 2015/2283). It was proposed that provisions on data protection included in the guidance for nutrition and health claims be used as a model. It was requested to clarify that "at the time the first application was made" (Article 26 (2) (a), (b)) corresponds to the submission date to the Commission (not when it has been accepted by EFSA's Apdesk). It was also noted that some novel foods are protected with intellectual property rights and that patents usually outline the production process. A reference to pending patents was suggested.

14. Further guidance was requested with respect to the submission of parallel applications for the authorisations of a novel food and a health claim (Article 28 of Regulation (EU) 2015/2283) as the two dossiers may contain redundant information (e.g. administrative part, description of the food).

15. The view was expressed that the guidance should make a clear distinction between principles and best practice on the one hand, and information that must be submitted on the other. A flexible approach is needed given the many different types of food and food ingredients that are assessed under the framework. It was considered important to ensure that core information / issues are considered and that applicants are thoughtful about the appropriate scientific testing for their product. Explanations should be provided where an applicant considers information or data is not necessary.

16. It was recommended to involve the experts working on the EFSA compendium in the evaluation of botanicals.

17. In case a food is produced from a genetically modified organism, there was a request to clarify that it falls within the scope of Regulation (EU) 2015/2283 and not the GMM regulation (i.e. absence of GMM & rDNA).

18. It was stated that toxicity studies will most probably be too expensive for small and medium enterprises and concerns with respect to unfair competition were expressed.

19. Clarification was requested on whether all data need to be submitted in English and, in particular, whether information in other official languages of the EU needs to be translated.

Panel consideration of comments received:

Ad9. The Panel agrees. A footnote was added to "whole food" which refers to the Scientific Committee guidance on conducting repeated-dose 90-day oral toxicity studies in rodents on whole food/feed (EFSA SC, 2011c).

Ad10. The Panel considers that simplified decision trees, although sometimes useful, can be only of exemplary nature, but cannot be comprehensive and cover the broad spectrum of Novel Foods.

Ad11. The reference to Article 16 of the Regulation in the section "Scope" was added. See EFSA guidance on the preparation and presentation of the notification and application for authorisation of traditional foods (EFSA NDA Panel, 2016b).

Ad12. A short paragraph (section 2.3.2) was added in the section "production process" which asks for a non-confidential summary on the production process.

Ad13. In case of a favourable Opinion and following the provisions of the novel food Regulation, the Panel has to consider whether the data claimed as proprietary by the applicant were needed to reach the conclusion (i.e. on the safety of the novel food under the proposed conditions of use). The Panel's considerations of the claimed proprietary data also take into account the quality, quantity and type of other (non-proprietary) data available (including both data in favour and not in favour) that are pertinent to the safety of the novel food. It should be noted that the decision on granting the protection of proprietary data (e.g. linked to requirements for data exclusivity) under Articles 26 and/or 28 of Regulation (EU) 2015/2283 falls under the responsibility of the European Commission when authorising the novel foods.

Ad14. Applicants are free to submit the same data in parallel submissions on the same food, as long as they are pertinent for the respective applications. However, it is noted that while novel food applications shall be submitted through the European Commission, a request for a claim relating to a novel food for which a request for authorisation has been submitted shall be made separately via a Member State and in accordance with the provisions of Regulation (EC) No 1924/2006. It is beyond the scope of this guidance to address this issue further.

Ad15. The Panel agrees with this view. The Panel considers that these issues are addressed by general principle No 6 (including changing "should" to "must" regarding the absolute requirements), general principal No 7 and general principle No 9.

Ad16. The Panel notes that experts of the EFSA Working Group on Botanicals were consulted during the public consultation phase, and that their comments are reflected in changes in several sections of the guidance (including the sections on the description of the novel food, production process, compositional data, and specifications). The guidance also makes reference to the EFSA guidance on the safety assessment of botanicals and botanical preparations (EFSA SC, 2009).

Ad17. For foods produced with genetically modified microorganisms (GMMs), applicants were referred to the requirements as laid down by the EFSA guidance on the risk assessment of GMMs and their products intended for food and feed use (EFSA GMO Panel, 2011).

Ad18. The Panel applies the same scientific principle for the safety assessment of novel foods, irrespective of the size of applying companies.

Ad19. The Panel notes that the Commission shall adopt implementing rules on administrative (including the language requirement) and scientific requirements for the preparation and the presentation of the applications for novel foods, as well as for the notifications and applications for traditional foods from third countries for the scientific assessment, respectively, in accordance with Article 13 and Article 20 of the Regulation. These implementing measures need to be complemented with scientific and technical guidance regarding the information that needs to be submitted by the applicants.

2.3. Nature of specific comments

2.3.1. General principles

Comments received:

20. With respect to the structure of the application (lines 249-257), some commenters recommended that all sections should be covered and addressed in an application. Where sections are not considered relevant, this should be explained and justified by the applicant. Other comments requested further guidance on the type of justifications that would be acceptable.

21. It was suggested to indicate that relevant information on substances or mixtures that are used for applications other than food (cosmetics, chemicals, pharma) should be sourced and provided, in particular vertebrate studies, to avoid duplication of animal testing (Recital 32 of Regulation (EU) No 2015/2283).

Panel consideration of comments received:

Ad20. The Panel considers that general principles No 6 together with No 9 address this issue.

Ad21. The Panel agrees that all studies which are pertinent to the safety of the novel food should be provided. The Panel notes that both section 2.9 (nutritional information) and section 2.10 (toxicology) indicate to make use of already existing pertinent studies.

2.3.2. Organisation and content of the application

Comments received:

22. It was recommended that the applicant provides a summary of the application which includes the pertinent sections; thus, to replace "Introduction" with "Summary of application".

Panel consideration of comments received:

Ad22. The Panel notes that any application shall be accompanied by a summary, as per Article 10 of the Regulation. This will be taken up by the Commission when adopting implementing rules (see Ad19). Thus, the Panel considers that requesting another summary as part of the application itself would be redundant.

2.3.3. Description of the novel food

Comments received:

23. Reference to the "nature of the novel food" was considered to introduce a new – and potentially confusing – concept. It was suggested to avoid introducing this term or to define it.

24. Several comments pointed out that the "categories" proposed in the guidance do not correspond to the regulatory categories of novel foods as outlined in Regulation (EU) No 2015/2283 (Article 3(2)(a)). Comments were made that "chemical substances" or "polymers" were not part of the legal definition, while the categories 'vitamins, minerals and other substances' or 'food that was only used in food supplements' were missing. A comment was also made that the category of novel foods falling under new or intentionally modified molecular structure seemed to be limited to polymerization only. It was proposed to clarify that those novel foods falling in a regulatory category which are not explicitly listed in the guidance should be assigned to the relevant "category(ies)". The suggestion was also made to include a comparison table between the categories of novel foods listed in the Regulation and the categories in the guidance, similar to Table 1 of the SCF opinion (SCF, 1996). In addition, it was requested whether the novel food/ingredient should be categorised according to the regulatory categories in the application dossier.

25. In relation to chemical substances, it was proposed that the primary, secondary and tertiary structure of molecules and the size, shape, distribution and crystal form of the particles should also be requested. It was stated that information on isomeric form may be relevant. It was asked whether applications on chemical substances without identification number or pending identification number are acceptable.

26. In relation to polymers, it was proposed that the primary, secondary and tertiary structure of molecules should also be requested. It was suggested to clarify the meaning of "polymers" (e.g. whether it includes protein (polymer of amino acids), DNA or RNA (polymer of nucleic

acids). Further guidance on the expression of particle size (e.g. minimum, average, range) was requested.

27. In relation to foods from microorganisms, fungi or algae, the importance of specifying the strain was highlighted. Further guidance on the methods which can be used for the genetic characterization of organisms (i.e. 16S rDNA sequence?) was requested. It was suggested to delete "Origin and history of the organism" as a bullet point in this section as it is covered under section 5.1. History of the source.

28. In relation to foods of mineral origin, it was proposed that the shape, distribution and crystal form of the particles should also be requested. It was requested to specify which methods can be used to determine particle size. It was proposed that additional information, such as the isomeric structure or ligands, could also be requested. Clarification was required on whether the information requested should be provided for the mineral source, the inorganic food product, or both.

29. In relation to food of plant origin, it was proposed to include possible extracts (aqueous or solvent) of the various parts.

30. In relation to food of animal origin, it was proposed to include possible extracts (aqueous or solvent) of the various parts. It was proposed to reformulate the heading as follows: "information to be provided on the animals etc., used in or to produce food...". It was proposed to indicate that this section covers insects.

31. In relation to foods from cell culture or tissue culture derived from animals, plants, fungi or algae, it was suggested to clarify that this section refers to *in vitro* cultures. It was suggested to replace the term "multicellular" by "eukaryotic" (e.g. yeasts are single cell eukaryotes) and the term "mushrooms" by "fungi". It was proposed to mention the growth medium, as it may impact the safety assessment.

32. Clarifications of the difference between *"food consisting of, isolated from or produced from microorganisms"* and *"food isolated from or produced from cell cultures derived from micro-organisms."* was requested. It was noted that a novel food derived from microorganisms through fermentation or propagation could fall into both these categories.

33. There was a comment that if a comparative safety approach is taken, each section should compare these parameters to the existing food that it will replace in the diet.

Panel consideration of comments received:

Ad23. The suggestion was taken on board and the text was amended accordingly (the term "nature" of the novel food was deleted).

Ad24. The introduction of this section was extended to point out that the proposed classification is based on scientific considerations (chemistry, production process, source) and is not meant to reflect the regulatory categories which are outlined in Article 3(2)a of the Regulation.

Ad25. The paragraph on chemical substances refers only to low molecular weight substances. The primary, secondary and tertiary structures are related mainly to proteins. For proteins, the characterisation of the secondary and tertiary structures is not required in order to assess safety or nutritional aspects. Chemical substances without CAS or other identification number or pending identification number are not excluded. However, if available, they should be provided.

Ad26. The paragraph on polymers is related to polymers of synthetic origin. Also in this case, the secondary and tertiary structures are not required and thus not asked for in the guidance. The Panel considers that particle size and distribution (as requested in the guidance in addition to the shape), is sufficient information regarding the size of the polymers.

Ad27. The Panel largely agrees on this comment. Guidance on the identification and characterisation of foods from microorganisms, fungi or algae was extended, referring to internationally accepted molecular methods, and reference is provided to indicate that the approach for the

demonstration of the identity of bacteria and yeasts should follow the EFSA guidance on Health Claims (EFSA NDA, 2016c). "History" of the organism has been deleted in section 2.

Ad28. The section on foods of mineral origin has been completed to require information on the shape, crystal form and distribution of the particles. The methods used to determine particle size are up to the applicant. Additional information, such as the isomeric structure or ligands, is not requested. The information requested in section 2.2. concerns the novel food, not its source. Information on the starting material should be provided in section 2.3 (production process).

Ad29. This information should be provided as part of section 2.3 (production process) where the method (including extraction) and extraction solvents should be described.

Ad30. See Ad29. The Panel acknowledges that insects are widely consumed in many third countries and confirms that section 2.2.4 is the appropriate section for providing a detailed description of the food if it consists of, is isolated from, or is produced from insects. However, the Panel considers that it is not necessary to single out one specific class of animal in this section of the guidance.

Ad31. The Panel notes that cell and tissue cultures are "*in vitro*", and that adding this term would be superfluous. Information related to unicellular organisms (including yeasts) should be provided under section 2.2.3. Section 2.2.7 outlines information required in relation to cultures of multicellular origin specifically, which is why this term belongs there. The Panel agrees with the comment on the relevance of the growth medium (growth medium, culture conditions) but considers that this should be addressed in section 2.3 (production process).

Ad32. Such clarification is not needed because the later mentioned category *("food isolated from or produced from cell cultures derived from micro-organisms")* does not exist in the guidance. Both cases are covered by section 2.2.3 on "foods consisting of, isolated from or produced from microorganisms, fungi or algae".

Ad33. Pertinent references and information on existing foods on the market can be used and included in the application to support the safety of the submitted Novel Food, e.g. on closely related species.

2.3.4. Production process

Comments received:

34. In the sentence "The description should be detailed enough to allow conclusions to be drawn regarding the impact of the process on the safety and nutritional value of the Novel Food." (lines 369-371), it was suggested to specify "nutritional value, including bioavailability".

35. It was proposed to add "and cell culture or tissue culture from plants and animals" in line 390 and replace "microalgae" by "algae" in analogy to class "Foods consisting of, isolated from or produced from (…) algae".

36. The relevance of providing the reaction conditions was questioned, considering that Novel Food authorizations would, by default, be generic. Products which meet the specifications included in the Union list could legally be marketed, even if the manufacturing process differs slightly. It was also argued that this information would not typically impact "on potential by-products, impurities or contaminants that could raise safety concerns".

37. Similar to the above comment, the view was expressed that the emphasis should not be on the exact methods used to rear and process insects – as these may vary amongst producers – but whether different methods may result in a different final product in terms of its safety and nutritional value. It was suggested that the requirements outlined in this section should apply "if relevant to the properties of the Novel Food".

38. For Novel Foods derived from plants, it was proposed that the extraction solvent and ratios to whole plant should also be specified. It was suggested to harmonise the approach with EMA's monographs on herbal ingredients.

39. It was proposed to require information on housing and slaughter conditions for farmed animals (line 388).

40. It was proposed that information about the breeding practices used for animal production and the propagating practices used for plant production should be requested.

41. It was noted that the reference to the EFSA Guidance on safety assessment of botanicals and botanical preparations (EFSA SC, 2009) was relevant to all uses of plants and plant preparations (e.g. meal replacements, soups, powdered drink mixes, sports products); thus, the emphasis on food supplements was deemed unjustified.

42. Additional guidance on information requirements for novel foods produced by fermentation processes using micro-organisms was requested. It was asked whether information according to the guidance for the risk assessment of genetically modified micro-organisms and their derived products intended for food and feed use (EFSA GMO Panel, 2011) should be provided.

Panel consideration of comments received:

Ad34. The Panel notes that both aspects are addressed in later sections (section 2.8 "ADME" and section 2.9 "Nutritional information").

Ad35. The guidance was amended as suggested.

Ad36. The Panel considers that detailed information, including reaction conditions, on the production process should be provided.

Ad37. See response to Ad36.

Ad38. The ratio between the extraction solvent and the material was added.

Ad39. The guidance was amended to add propagating practice for plant production and the breeding, rearing, feeding and farming conditions for farmed animals or the hunting, catching or collecting and killing of wild living animals.

Ad40. See Ad39.

Ad41. The Panel agrees with the comment and the emphasis on food supplements was deleted.

Ad42. Section 2.3 (production process) requests a detailed description of the production process, including fermentation. Regarding Novel Foods obtained from genetically modified microorganisms, see Ad17.

2.3.5. Compositional data

Comments received:

43. It was suggested to reformulate the sentence line 396 as follows: "physico-chemical and biochemical properties and microbiological characterisation of the novel food".

44. Challenges related to the provision of analytical data on five independently manufactured batches were noted, in particular for products in an early stage of development or subject to seasonal constraints. References were made to specific sectors (e.g. medicines, chemicals) where data on three representative batches are considered sufficient. There were comments that the emphasis should be on the batches being representative of the variations seen in the production of the product, rather than increasing the number of batches from three to five. A question was raised on whether batches are consecutive or whether it does not matter. Clarification was sought on whether the batches should be analysed simultaneously or whether the analyses can be performed separately by the same laboratory with the same validated methods. There was also a comment that data on "pilot plant" batches should be acceptable and that manufacturers are responsible for ensuring that the novel food/ingredient produced on a commercial scale meets the proposed specifications.

45. With respect to the requirement that "when several production processes are proposed, [analytical] data should be provided for each given process", it was proposed to clarify that

this would only apply in case different processes would lead to differing properties of the Novel Food.

46. It was noted that the guidance refers to AOAC, ACS and European pharmacopeia methods. The position of EFSA regarding Asian pharmacopeia (e.g. Chinese, Japanese or Korean pharmacopeia) was requested.

47. In the general requirements, it was suggested to specify that analyses of heavy metals (Pb, Hg, Cd and As) are required and, depending on the type of food, also data on mycotoxins, PCBs/dioxins and pesticides.

48. In relation to single substances and simple mixtures, it was suggested to specify *"solubility data in water and other media that are representative of the defined use"* (line 425). Clarification on the way to express minimum purity value was requested and whether information on minor components, such as their identity or quantity, should be provided. It was noted that the mass balance for these ingredients may not necessarily sum up to 100%, due to many factors (e.g. analytical variability). Reference was made to some monographs for pure vitamins and minerals (such as JECFA or FCC), where the purity is listed as a range. Thus, it was suggested to remove the word "complete" before "mass balance". It was also requested to specify the techniques that can be used for the assessment of particle size, shape and distribution. There was a comment that requirements for liquid preparations (e.g. data on vapour pressure, specific weight and viscosity) should also be specified.

49. Challenges related to the provision of analytical data on botanicals were highlighted, including often the lack of validated methods, accredited laboratories and reference substances.

50. It was noted that total carbohydrate content of foods is often calculated by difference (i.e. the amounts of other constituents (protein, fat, water, alcohol, ash) are subtracted from the total weight of the food), rather than analysed directly. "Carbohydrate" estimated in this fashion may contain unidentified substances. It was proposed that solely analytical data should be considered for the mass balance, or that the meaning of "carbohydrate" in this context should be specified.

51. It was considered that the indication that the amount of unidentified constituents should be "as low as possible" was ambiguous (line 438). It was advised to rather indicate a figure and leave room for case-by-case deviation where justified.

52. It was proposed to combine the text referring to proximate composition of whole foods (lines 435-436) with the paragraph covering other nutritional constituents (lines 442-443) (e.g. fatty acids, sugars, dietary fibre). There was a suggestion to present the data in a tabular form with reference to detailed analytical documentation (as annexes). It was also suggested to combine it with Specifications.

53. It was noted that any food which contains protein could be considered a "potential allergen" (line 446). It was suggested to rather use the term "known allergens".

Panel consideration of comments received:

Ad43. The text was changed as proposed.

Ad44. The Panel notes that the purpose of batch testing is to show that the compositional data of a novel food produced with the described production process can meet the proposed specifications. The Panel is aware that the results from neither three nor five batches can provide reassurance that the specifications are constantly met once the novel food is on the market. However, the Panel considers that five batches will provide more suitable information on the range and variability of compositional parameters of the novel food. If less than five batches are tested, the applicant should provide a rationale. Batches can also be consecutive if the raw materials used for the production of the batches were obtained independently (e.g. sourced at different time points, different provider or different geographical source). The guidance does not request that the analyses of the batches are performed at the same time. Batches from pilot scale production are acceptable provided that they are representative.

Ad45. If several production processes are applied, the applicant should provide the details of each applied production process and propose specifications on the basis of compositional data of the Novel Food derived from all these production processes.

Ad46. The mentioning of AOAC, ACS, EP is exemplary ("e.g.") and not exhaustive.

Ad47. The guidance requests that information on the identities and quantities of impurities or by-products, residues and chemical and microbiological contaminants is provided. This may include heavy metals, mycotoxins, PCBs/dioxins and pesticides, and these examples have been added to the text. The Panel notes that Novel Foods must comply with existing EU regulations which include also heavy metals, mycotoxins, PCBs/dioxins and pesticides.

Ad48. The Panel considers "solubility in water and common solvents" (as stated in the guidance) to be more useful to characterise the substance. The method to determine the minimum purity, particle size, shape, etc. depends on the type of substance and must be chosen by the applicant. "Viscosity" for liquid preparations was added. "Complete" before "mass balance" was deleted as proposed.

Ad49. The Panel notes the challenges related to the provision of analytical data on botanicals. Experts of the EFSA Working Group on Botanicals were consulted during the public consultation phase and their comments are reflected in changes in several chapters of the guidance (including the chapters on the description of the traditional food, production process, compositional data, specifications and toxicology). The guidance now also makes reference to the EFSA guidance on the safety assessment of botanicals and botanical preparations (EFSA SC, 2009).

Ad50. The Panel notes that for the main constituents qualitative and quantitative characterisation should be performed at least via sum parameters as stated in the guidance. Generally a mere calculation of the content of components is not accepted.

Ad51. The Panel considers that no generally applicable figure can be given in the guidance for a maximum amount of unidentified constituents. As suggested by the commenter, this is to be defined case-by-case in relation to safety considerations and/or technological constraints.

Ad52. The Panel considers that the two paragraphs mentioned should not be combined because they relate to different analytical requirements (sum parameters *versus* specific analyses).

Ad53. The sentence was revised and now refers to the source of the Novel Food.

2.3.6. Stability

Comments received:

54. Challenges and constraints related to the assessment of the stability of a novel food ingredient in the final products were described, considering that not all uses can be anticipated. Views were expressed that the assessment of the stability of a novel ingredient in final products should be the responsibility of the end user and should be tested as part of the final product development phase. For instance, in case interested parties wish to use a novel ingredient in a food category for which it is not yet authorised, they could submit an "extension application", including stability data specific for the novel final product. Some commenters acknowledged that ingredient manufacturers could provide data on stability in model systems representative for their primary intended uses.

55. It was requested that stability data on three batches be considered sufficient, in line with other sectors (e.g. medicines, food supplements).

56. There was a request to clarify the length and conditions of stability studies and whether stability studies performed in accelerated conditions (higher temperature and humidity) are acceptable.

57. It was suggested that the sentence "under normal conditions of storage" be specified as "normal storage and use by end consumers", to ensure that the effects of storage throughout the food chain and normal use by consumers are considered.

58. It was highlighted that the oxidative stability of lipids in products rich in fat, particularly unsaturated fat, needs to be addressed, and that this should be mentioned in the guidance. Reference was made to the Belgian Superior Health Council scientific advice on the oxidative stability of oils.

59. It was proposed to request applicants to specify the ingredients added to the novel food to stabilise it in storage or in use (e.g. tocopherols).

60. It was noted that interaction or migration of molecules from the packaging, especially if it is made of a plastic polymer, could add further information on the safety of the food.

Panel consideration of comments received:

Ad54. In case interested parties wish to use a novel ingredient in a food category for which it is not authorised yet, Regulation (EU) 2015/2283 foresees the possibility to apply for an extension of use. The Panel agrees on the possibility of a model-based approach as an alternative to testing stability in real foods. This option has been added to the text.

Ad55. See Ad44.

Ad56. The duration of the stability testing may depend on the proposed uses, type of novel food and the end of shelf-life proposed by the applicant. Testing under accelerated conditions is acceptable and has been added to the guidance as an option.

Ad57. The Panel considers that the data provided in this section should address stability over shelf-life of the product.

Ad58. The Panel acknowledges the particular susceptibility of lipids to oxidation/degradation. However, the Panel refrains from providing a specific example.

Ad59. The Panel agrees that this is a relevant element of the stability assessment, and the text has been amended accordingly.

Ad60. The Panel considers that this comment is not specific for novel foods, and thus it is out of the scope of this guidance.

2.3.7. Specifications

Comments received:

61. It was proposed to add the size range of the particles.

62. It was proposed to list probable parameters in the case of biological novel foods as opposed to simple chemicals (e.g. protein, fat, carbohydrate (sugars), ash, trace elements).

63. It was proposed to add the term "relevant" before contaminants (line 482), to reflect that not all known contaminants are required to be covered in the specifications.

64. Guidance was requested on the number of batches required for testing to specification as well as all contaminants.

65. In relation to specific criteria for microbiological testing, it was suggested to refer to the general guidance on this topic on the Commission website.

Panel consideration of comments received:

Ad61., Ad62., Ad63. Considering the wide range and complexity of different types of Novel Foods, the Panel cannot provide a comprehensive list of parameters to be included in the specifications.

Ad64. See Ad44.

Ad65. The Panel is aware of existing regulations in place with regards to microbiological limits (among others such as contaminants). For this guidance, the Panel considers that it is not needed to refer to specific requirements laid down by legislation other than by Regulation (EU) 2015/2283.

2.3.8. History of use of the Novel Food and of its source

Comments received:

66. Concerning the "history of the source", the first sentence of the section was found unclear. In case a food is produced with a genetically modified source (e.g. micro-organism, fungi or algae), clarification was sought on whether EFSA guidance for GMM should be followed; it was recommended to cite EFSA guidance for GMM where relevant.

67. It was proposed to cross-reference in that section that information about the potential to have consumed the novel ingredient in other foods and the impact on the dietary intakes are considered under section 2.7.

68. The relevance of the section on the "history of use of the novel food" was questioned.

69. Clarification was requested on the extent to which history of use may be appreciated as an indicator of toxicological/allergenic safety in the assessment, i.e. the conditions under which this type of information could be used to demonstrate safety.

70. The relevance of providing information on non-food uses was questioned when such uses do not lead to exposure through the oral route or when they result in small internal exposure. It was proposed to restrict the requirement for information on non-food uses to those leading to an ingestion of the product or significant internal exposure.

71. Concerns were expressed that "searching for studies with specific and typical components of the novel food and for studies with similar foods from the same or other closely related sources" would broaden the information required which seems not to be relevant.

72. Clarification was requested on the type of documentation that can be submitted in support of the history of use of a novel food or its source (i.e. commercial products databases, official records of approvals by authorities, scientifically published data, government reports, any information/reports indicating a history of use, recipe books, history of cuisine); flexibility was requested.

Panel consideration of comments received:

Ad66. See Ad17.

Ad67. The Panel agrees with this suggestion and the proposed cross-reference has been made.

Ad68. In some case there is a history of use which may provide information about reported adverse effects, conditions of use, precautions or other potentially relevant information. The relevance may vary across different types of novel foods.

Ad69. The appreciation of whether the history of use provides evidence for safety is the object of the assessment by the Panel. This is to be considered case-by-case on the basis of available information.

Ad70. The Panel agrees that in general data on oral exposure are of most relevance. However, also data from studies using other routes of exposure may provide information on possible adverse effects, mechanisms, and interactions with other substances.

Ad71. The Panel considers that studies with specific and safety-relevant components of the novel food and studies with similar foods from the same or other closely related sources may provide relevant information.

Ad72. The Panel considers that the guidance is sufficiently flexible. The types of documents are not limited to peer-reviewed scientific publications, although it is considered that anecdotal and

grey literature are usually of lower relevance. The weighing of the evidence is carried out case-by-case.

2.3.9. Proposed uses and use levels and anticipated intake

Comments received:

73. It was proposed to specify "the proposed maximum amounts in final product(s), *if used as ingredient*".

74. It was suggested to combine sections 2.7.2 Proposed uses and use levels and 2.7.3 Anticipated intake of the novel food.

75. Specific guidance was requested on the proposed maximum amounts to be specified in case of final product(s) marketed as powder or concentrate which are intended to be consumed as reconstituted following manufacturers' instructions. It was requested that the applicant be allowed to propose a maximum amount in the product as consumed.

76. There were comments that the Food Additives Intake Model (FAIM) tool is not a suitable tool for assessing the exposure to a novel food/ingredient. Concerns were expressed that the specific food categories contained in FAIM were tailored to food additives and may not suit the intended uses of novel foods/ingredients. The example of infant formulae was taken. It was also argued that the consumption patterns/conditions of food additives differ from those of novel foods/ingredients: indirect and chronic consumption for food additives vs. deliberate and occasional consumption for novel foods/ingredients (e.g. insect-based product, functional foods). Concerns were expressed that the use of the FAIM tool would lead to large overestimations. The view was expressed that Tier 1 should be based on the EFSA Comprehensive Database and Tier 2 should be the based on individual data from national food consumptions surveys.

77. There was a comment that in the case a novel food is intended for consumption by infants, an ad hoc assessment should be performed, which considers the worst case scenario of exposure. The guidance should indicate this.

78. Regarding default body weights, it was suggested to refer to EFSA Scientific Committee guidance on selected default values (EFSA SC, 2012).

79. It was suggested to add a footnote in line 523 with a reference to Annex II Part D of Regulation (EC) No 1333/2008 – list of food categories.

80. There was a suggestion to reformulate sub-heading 2.7.4 as "Combined intake from novel food and other sources".

81. Several comments questioned the consideration of non-dietary sources (e.g. cosmetics, pharmaceuticals) in the exposure assessment. It was noted that pharmaceuticals/medicines legislation is separate and inconsistent with food legislation in most EU Member States. It was also stated that if cosmetics are to be considered then the whole area of environmental exposure should also be included, which would become unworkable and unfair to the food industry. Some commenters proposed to restrict the assessment to those uses which lead to exposure via the oral route or to significant "internal exposure".

82. With respect to the combined intake from multiple sources, clarification was requested on the extent to which the pre-existing source(s) and the Novel Food should be equivalent (e.g. for a novel source of protein, what pre-existing sources of protein should be considered). Specific rules were also requested about the summation of the values from different uses. The assumption that a 95th percentile consumer of foods would also consume maximum dose supplements on the same day, every day, was considered unrealistic; the use of the mean values from food use was proposed. It was proposed that EFSA prepares a guide to understanding intakes.

83. It was noted that a Novel Food may be intended to replace an existing source or to be an additional source. Clarification on whether these two situations may translate into specific data requirements or considerations in the assessment was requested.

84. There was a comment that food supplements are legally defined as foodstuffs and should be addressed as any other food; thus, it was proposed not to single out food supplements in lines 522 and 534.

85. It was noted that some undesirable substances (such as naturally occurring contaminants like mycotoxins or heavy metals) may be present at concentrations that vary from lot to lot. Reference was made to probabilistic approaches that have been previously supported by EFSA (EFSA PPR Panel, 2012).

Panel consideration of comments received:

Ad73. The text was changed to "The proposed maximum amounts in product(s) as consumed".

Ad74. For the sake of clarity, the Panel has kept these two subsections separated as they concern different issues.

Ad75. The applicant should specify the proposed maximum amounts in product(s) *as consumed*, and this is now clarified in the text.

Ad76. The Panel agrees with this comment. The emphasis on the FAIM tool in the guidance was reduced. The FAIM tool and the published excel sheets of the EFSA Comprehensive Food Consumption Database are both based on the same summary statistics. Therefore both could serve as Tier 1 options.

Ad77. The Panel considers that this section on the anticipated intake and the provided references to existing EFSA Guidance on exposure fully cover also the intake assessment for infants. The Panel notes that also for the intake assessment for infants, high percentiles (e.g. at least 95th) rather than worst case scenarios are used for assessing high intakes.

Ad78. The Panel agrees and a reference to the EFSA guidance on default values (EFSA SC, 2012) was added.

Ad79. A footnote was added with the indication that applicants should preferably use the latest version of the EFSA food classification system (FoodEx) (EFSA, 2011).

Ad80. The Panel agrees and the subsection title 2.7.4 of the guidance was amended as proposed.

Ad81. The Panel notes that some products are classified as a food in one Member State and as a medicine in another Member State. In some cases, particularly where it concerns contaminants, environmental exposure may also be of relevance. Whether exposure other than from foods may be relevant should be considered on a case-by-case basis. The guidance provides this flexibility.

Ad82. Comments were taken into account. The guidance now clarifies that for total intakes, intakes from the novel food and from the background should be considered, and on a case-by-case basis intakes from other sources.

Ad83. Section 2.7.3 was extended with a consideration on when a novel food is intended to replace another food already existing on the market.

Ad84. The Panel acknowledges that the same principles apply to "Food supplements" and other foodstuffs, and the term was deleted.

Ad85. Variations in the content of undesirable substances should be addressed in the specifications. The intake estimate for such substances and related safety assessment should be based on the proposed maximum level. The Panel considers that methods for assessing exposure to undesirable substances are adequately covered in the guidance.

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

Comments received:

86. It was suggested to refer to "kinetics" rather than "toxicokinetics" since this should also cover general aspects of nutrient metabolism.)

87. Concern was expressed that the sentence "toxicokinetic data are critical for (…) the selection of appropriate animal models" may imply that animal models have to be used.

88. It was proposed to also refer to in vitro methods in the sentence "they constitute an important element of the risk assessment to account for differences between experimental animals and humans" (reference was made to the scientific committee opinion on nanotechnologies (EFSA SC, 2011b).

89. For novel food from microorganisms, fungi, algae, plants, animals, cell and tissue cultures, clarification was sought on whether one marker would be sufficient to evaluated ADME or whether several markers are required. Challenges related to the assessment of ADME for plants and other complex organisms were highlighted.

90. Novel Foods may be prepared in nano form to aid dispersal before dissolving or swelling or agglomeration. This point especially applies, one would assume, to mineral forms. If they are salts they will dissolve in most cases.

Panel consideration of comments received:

Ad86. The Panel agrees with this comment and the text was amended accordingly.

Ad87. The sentence referred to was deleted and applicants were referred to the approach outlined by the EFSA guidance for food additive evaluations (EFSA ANS Panel, 2012).

Ad88. The Panel agrees that this could be specified and "*in vitro* studies" has been added to the sentence as proposed.

Ad89. The Panel considers that the type (single substance or complex mixture) rather than source of the novel food is relevant for the consideration of the approach to be taken to investigate ADME. For complex mixtures, the guidance refers to the EFSA guidance for food additive evaluations (EFSA ANS Panel, 2012) which recommends focusing on toxicologically relevant constituents.

Ad90. ADME studies should be conducted with the Novel Foods in the formulation in which it is intended to be consumed. For the requirements related to engineered nanomaterials, the guidance refers to the EFSA SC Opinion on engineered nanomaterials in food and feed which is currently under review by EFSA (EFSA-Q-2016-00281[5]).

2.3.11. Nutritional information

Comments received:

91. It was suggested to find a more suitable heading for this section.

92. There was a comment that aspects of bioavailability should be covered.

93. Several comments pointed out the challenges related to the assessment of the influences of production, storage and further processing, handling and cooking on the nutrient composition of the novel food, considering that not all uses can be anticipated. It was noted that end users would be responsible for the nutritional information on their product. There was also a comment that the requirements regarding the effect of cooking are unclear, and that it is outside of scope.

94. It was proposed that the request for data on anti-nutritional factors and possible interactions with nutrients be limited to novel foods that are intended to modify bioavailability or are known to contain physiologically relevant amounts of the respective compounds. The difficulty in demonstrating that the *in-vitro* inhibitory activity of a food/ingredient is of physiological relevance was highlighted. It was stated that physiologically relevant effects of this type

[5] http://registerofquestions.efsa.europa.eu/roqFrontend/questionLoader?question=EFSA-Q-2016-00281

would most likely be revealed by 90-days oral toxicity studies. It was proposed that, in case such compounds are present in the novel food/ingredient, an appropriate margin of safety may protect consumers.

95. In regard to the nutritional information, we read that information on the "anti-nutritional factors" needs to be provided. More explanation? Because as an example the "modification of bioavailability" is given. We see more molecules, like lysosomes or phytosomes. These are combinations of active ingredients dispersed into lecithin. This would increase the bioavailability of the botanical or other substances. If a combination of 2 different substances would change the bioavailability wouldn't EFSA miss this in its evaluation of the ingredient (e.g. phytosomes, increased bioavailability)?

96. It was proposed to indicate that new animal testing should be kept to the minimum and should not be carried out when alternative validated methods and recognized risk assessment models are available.

Panel consideration of comments received:

Ad91. The Panel is aware that the heading "Nutritional information" is rather broad, but uses this term in analogy to the heading "Toxicological information" (section 2.9). The scope of this section is specified in the first and following paragraphs of this section in the guidance.

Ad92. The Panel agrees that this aspect could be specified, and the text was amended accordingly.

Ad93. This second paragraph under the heading "Nutritional Information" primarily relates to potential influences of the production process and storage on the content and supply of nutrients or anti-nutrients. Information on the potential nutritional impact from cooking may be of relevance, where the intended uses include cooking. Cooking may also be important to reduce or inactivate anti-nutritional substances or toxins. The text was extended to clarify when the effect of cooking should be considered and addressed.

Ad94. The request for data on anti-nutritional factors and possible interactions with nutrients refers only to those instances where there is indication of the presence of such substances in a Novel Food (e.g. based on the composition or nature of the novel food, ADME data, animal data or literature).

Ad95. The Panel understands that this comment relates to safety concerns that might arise from the increased bioavailability of a substance. This has been taken into account in the revised sentence by referring also to factors other than anti-nutritional factors that might impact absorption and bioavailability (either decreasing or increasing). If a combination is "novel", bioavailability should be addressed (see section 2.8 ADME of the guidance).

Ad96. Animal testing is normally not required for the evaluation of the nutritional impact of the novel food. As outlined at the end of this section, only in specific cases, data from investigations *in vitro* and/or in animal models and/or human studies may be needed to address the interaction of the novel food with the diet and nutrients. The Panel notes general principle No 12 which stresses that unnecessary use of animals should be avoided.

2.3.12. Toxicological information

Comments received:

97. It was noted that the guidance outlines that the need for toxicity studies is dependent on the specific characteristics of the novel food. Therefore, it was proposed to start the section with the criteria to be considered in order to make decisions on whether and which toxicity studies are necessary (lines 668-681).

98. It was suggested to re-introduce into the guidance the three scenarios set out in section 3.7 of Commission Recommendation 97/618/EC and section XIII of the SCF guidance (SCF, 1996).

It takes substantial equivalence as the first tier for the toxicological approach. This approach was considered to be similar to the exemption from exhaustive safety assessment applied to strains of micro-organisms that are on the QPS list. It was noted that substantial equivalence of the end product would also be an important factor for applications relating to novel food processes. Further guidance on how substantial equivalence can reduce the need for toxicological and other testing was requested.

99. Currently a tiered approach to toxicological risk assessment is used, starting with a 28 day study which informs whether further testing is required. The NDA Panel supports the tiered approach suggested in the guidance but therefore it is questionable why a 90-day sub chronic toxicity study should become the standard tool for assessing toxicological risks.

100. With respect to the representativeness of the test product used in the toxicity studies, it was noted that the scale up from the pilot to the manufacturing plant may trigger some variations in the ingredient composition. It was requested to consider compounds which, although slightly different in composition, are manufactured with the same production process, as representative materials.

101. In lines 663-665, the following reformulation was suggested: "If this is not the case, a rationale should be provided to substantiate why the material used for the toxicological studies is not representative of the novel food and appropriate for safety assessment."

102. Emphasis was requested that alternative approaches to animal testing should be the preferred options.

103. It was noted that tolerability data may be relevant for novel foods (e.g. when they are macro-ingredients such as saccharides) and should be mentioned, both in relation to animal and human data. Reference was made to the EFSA guidance on food additives (EFSA ANS Panel, 2012).

104. Further guidance was required on the tests that are recommended to assess the genotoxicity of novel foods. It was requested to specify the requirements rather than referring to horizontal guidance documents. Guidance was also sought on the approach to follow when such tests are not feasible (e.g. adequate concentration cannot be reached due to precipitation).

105. With respect to 90-day subchronic toxicity studies, scientific uncertainty with respect to their necessity was pointed out and the importance of case-by-case decisions was re-iterated, with reference to EFSA guidance on GMOs. It was requested to re-iterate in this section that "decisions on whether tests are necessary need to be considered in light of the data already available". Besides, further guidance was requested on the instances in which *in vitro* or *in silico* studies can be used instead of 90-day rodent tests.

106. It was advised that appropriate animal models that address differences in the safety profile for neonatal animals compared to adults should be used to characterise safety for infants and young children. It was stated that the neonatal pig is a well-established model for studying infant formula nutrient interactions and has also been identified as an appropriate model for safety testing of substances in infant formula. It was noted that JECFA accepted the neonatal piglet model to assess the safety of additives (i.e. carrageenan, OSA-Modified Starch and pectin) for use in infant (0-12 weeks of age) formula.

107. Line 746: Extended One-Generation Toxicity Study (OECD 443) not 2 generation testing (OECD 416) as with other EU regulatory requirements.

108. In the light of the EFSA Scientific Committee opinion on the risk profile of insects (EFSA SC, 2015) which indicates that insects carry no additional biological or chemical risks compared to other sources of proteins under the condition that insects are fed on vegetal substrates and processed under good hygiene conditions, it was asked whether fulfilling these conditions would exempt the applicant from toxicological analyses.

109. The need for a full safety assessment (e.g. testing for intrinsic or acquired antimicrobial resistance) in case a microorganism serves solely as production vehicle and is not present in the final food was questioned. It was suggested to also mention yeasts in the sentence "a

wide variety of bacterial and fungal species are used in food and feed production (…)' (line 755) and to replace 'viable bacteria' by 'viable microorganism' (line 757).

110. In relation to engineered nanomaterials, it was suggested to refer to the outcome of the OECD survey on the approaches to develop or use concepts of grouping, equivalence and read-across based on physical-chemical properties of nanomaterials (OECD, 2016). It was also suggested to require applicants to provide justification for the appropriateness of the methods used to assess nanomaterials, in order to reflect Article 10(4) of Regulation (EU) 2015/2283.

111. There was a comment that the requirements outlined in the Guidance are similar to those applied to medicines. The applicability of these standards to foods was questioned.

Panel consideration of comments received:

Ad97. The suggestion was not followed and the sequence of first paragraphs remained unchanged.

Ad98. Regulation (EU) 2015/2283 does not refer to the concept of "substantial equivalence" as authorisations are intended to be generic. However, the Panel notes that such data, if pertinent to the Novel Food, should be provided.

Ad99. The guidance refers to the ANS guidance (EFSA ANS Panel, 2012) and considers that a subchronic toxicity study should normally be submitted as it is more relevant. This is in line with the ANS guidance which states that *"Within Tier 1, a subchronic toxicity study should normally be conducted for a period of at least 90 days (OECD TG 408) in rodents, modified to include assessment of some additional parameters described in the more recent guideline on repeated-dose 28-day oral toxicity study in rodents (OECD 407)".*

Ad100. The Panel considers that the representativeness of the test material is sufficiently addressed in the Guidance.

Ad101. The Panel stresses the need that the test material used for the toxicological testing should be representative of the novel food.

Ad102. Avoidance of unnecessary animal testing is addressed by general principle No 12.

Ad103. The guidance states that "Other studies that may be relevant include immunotoxicity, hypersensitivity and food intolerance, studies on neurotoxicity, endocrine activity and modes of action."

Ad104. It is not the purpose of the guidance and it is also not feasible to provide specific guidance for all possible types of novel foods. Where horizontal guidance prepared by the Scientific Committee exists, it should be considered (as stated in general principal No 1). The Panel notes the considerations provided in the section on "top dose" of the EFSA Genotoxicity guidance (EFSA SC, 2011a).

Ad105. The Panel considers that this comment is addressed in the guidance by the general principles, and in the considerations provided in the section on toxicological information.

Ad106. Appropriate animal models should be used as noted in the guidance.

Ad107. The Panel considers that both tests are acceptable.

Ad108. The Panel notes that the considerations and conclusions made in the EFSA risk profile of insects cannot be used as an a priori exemption from providing toxicological data.

Ad109. The Panel considers that it depends on the type of product and the used microorganism whether a full assessment of the microorganism/fungi is needed. The proposed change ("microorganism" instead of bacteria) was applied.

Ad110. The Panel refers to the existing EFSA guidance on engineered nanomaterials (EFSA SC, 2011b) and notes that the EFSA Scientific Committee has received a new mandate (EFSA-Q-2016-00281) from the European Commission to provide guidance on the human and animal risk assessment of the application of nanoscience and nanotechnologies in agro/food/feed.

Ad111. The Panel notes that the risk assessment of novel foods may indeed share some common principles with that of medicines. The Panel considers that the guidance takes into account that conventional metabolism and kinetic studies may not be feasible for all components in a mixture or may not be needed at all depending on the available information (e.g. composition, production process, source, proposed uses, data from the literature).

2.3.13. Allergenicity

Comments received:

112. It was requested to delete the term "glyco" (from glycoproteins).

113. Further guidance was requested concerning the methods to be used to analyse the protein content and whether it should aim at identifying a certain protein, all proteins individually or total protein content.

114. Clarification was requested on the term "protein fractions".

115. The sentence "The default assumption for Novel Foods containing proteins is that such Novel Foods have allergenic potential." was understood to imply that all proteins have the same allergenic properties. It was proposed to reformulate. The commenter suggested to state that "All novel food containing proteins *may* have allergenic potential."]

116. Reference to Directive 2000/13/EC, which was repealed by Regulation No 1169/2011, was questioned. In addition, paragraph 11 of Article 6 of that Directive could not be found.

117. It was proposed that the information on the history of safe use outside the EU could also be used in relation to allergenicity.

118. Further guidance on how to address the allergenicity of insects was requested, in particular in relation to cross-reactivity issues (e.g. allergies to other arthropods such as arachnids, crustaceans, mariapods). Clarification was sought on how the NDA Panel would implement the Scientific Committee recommendation that future insect-food products should "indicate presence of the insect protein and the possible allergenicity or cross reactivity on the label of the product" (EFSA SC, 2015).

119. With respect to the assessment of the risk of cross-reactivity of individuals sensitised to known food allergens, a tiered approach was proposed. In addition to the factors listed in section 10.1, it was noted that consideration of this risk where needed should include the botanical relatedness of plants, fruits and vegetables. Where risks are identified it may be appropriate to undertake immunological assays in line with the latest clinical knowledge and practice. A human study would be the final tier if concerns were identified and should be subject to ethical approval.

120. A question was asked regarding the extent to which cross-allergenicity needs to be proved for closely related novel foods. E.g. is the proof of cross-allergenicity for a few species of insects sufficient to prove it for all insect-based Novel Foods or should the composition of all specific species be shown?

121. Clarifications were sought on the criteria that are applied by the Panel to conclude that an allergic reaction is unlikely. The 'EFSA guidance on the preparation and presentation of applications pursuant to Article 6 Paragraph 11 of Directive 2000/13/EC' indicates the studies that can be presented but information on how they will be reviewed is lacking.

122. There were comments that the issue of de novo sensitization requires further consideration in the guidance. Reference was made to the work of the impARAS network (www.imparas.eu). A comment was also made that de novo sensitization is difficult to predict and may be better addressed with risk management activities such as post market monitoring.

Panel consideration of comments received:

Ad112. "glyco" was deleted from glycoproteins.

Ad113. As a minimum, the dossier should provide information on the total amount of protein, information on the used validated method, and information on the LOD/LOQ if no protein was detected. Guidance for the protein analysis is provided in sections 2.4 and 10.1, and in the opinion of the EFSA NDA Panel (2014).

Ad114. The term "protein fraction" was changed to "peptides".

Ad115. The proposal was not followed.

Ad116. The reference to paragraph 11 of Article 6 concerns the second amendment (Directive 2003/89/EC) of Directive 2000/13/EC.

Ad117. Available information on (cross)allergenicity or the absence of reported allergic reactions as part of the history of a novel food should be provided and should be based on a comprehensive literature search as outlined in the guidance.

Ad118. The Panel considers that the information to be provided for insect proteins should follow as outlined in the guidance, and that the assessment of insect proteins follows the same principles as for other novel proteins.

Ad119. The "taxonomic relationship" of the source of the novel food was added. As outlined in the guidance, the Panel takes the default assumption that novel foods containing proteins have allergenic potential. If an applicant wishes to demonstrate that the Novel Food is unlikely to trigger adverse reactions in sensitive individuals under the proposed conditions of use, they should follow the approach outlined in the guidance on the preparation and presentation of applications pursuant to Article 6 Paragraph 11 of Directive 2000/13/EC, as amended (EFSA NDA Panel, 2013).

Ad120. Cross-allergenicity of the novel food should be considered on a case-by-case basis, e.g. where there is evidence for allergenicity reported for related species.

Ad121. Guidance is given by referring to the approach outlined in the EFSA guidance on the preparation and presentation of applications pursuant to Article 6 Paragraph 11 of Directive 2000/13/EC, as amended (EFSA NDA Panel, 2013). The assessment by the NDA Panel will follow the same criteria as applied in its opinions on such applications.

Ad122. The Panel is aware of the limited ability to predict *de novo* sensitizing activity of proteins. The guidance suggests considering potential allergenicity on the basis of the novel food composition, particularly its protein(s), its source (including taxonomic relationships), the production process, and available experimental and human data. This includes both *de novo* sensitization and cross-reactivity. The comment on post-market monitoring is beyond EFSA's remit.

2.3.14. Concluding remarks

Comments received:

123. In the sentence "where potential health hazards have been identified (e.g. on the basis of the composition of the Novel Food, its production process, its history of use, results from animal or human studies)", it was suggested to also mention *in vitro* studies.

Panel consideration of comments received:

Ad123. The Panel notes that the list in brackets is illustrative (and non-comprehensive).

2.3.15. Editorial comments

Comments received:

124. line 212: replace "point (f) of this paragraph" by "point (f)) of Article 3, paragraph 2 of Regulation (EU) 2015/2283".

125. line 265: format "4" in superscript (footnote) and delete the words 'experimental and other' to align to the title of Directive 2010/63/EU. *("duplication of animal testing should be avoided, where possible.")*

126. line 281: should read "organisation and content of the *application*"

127. line 294: remove extra '.'

128. line 350: replace part by part(s)

129. line 389: remove the word 'living' as it is repetition.

130. line 628: wrong citation; replace EFSA, 2010b by EFSA 2011a.

Panel consideration of comments received:

Ad124. - Ad130. All editorial comments were accepted and respective changes were applied in the guidance.

References

EFSA (European Food Safety Authority), 2011. Evaluation of the FoodEx, the food classification system applied to the development of the EFSA Comprehensive European Food Consumption Database. EFSA Journal 2011;9(3):1970, 27 pp. doi:10.2903/j.efsa.2011.1970

EFSA ANS Panel (EFSA Panel on Food Additives and Nutrient Sources added to food), 2012. Guidance for submission for food additive evaluations. EFSA Journal 2012;10(7):2760, 60 pp. doi:10.2903/j.efsa.2012.2760

EFSA GMO Panel (EFSA Panel on Genetically Modified Organisms), 2011. Scientific Opinion on guidance on the risk assessment of genetically modified microorganisms and their products intended for food and feed use. EFSA Journal 2011;9(6):2193, 54 pp. doi:10.2903/j.efsa.2011.2193

EFSA NDA Panel (EFSA Panel on Dietetic Products, Nutrition and Allergies), 2013. Guidance on the preparation and presentation of applications pursuant to Article 6 Paragraph 11 of Directive 2000/13/EC, as amended. EFSA Journal 2013;11(10):3417, 17 pp. doi:10.2903/j.efsa.2013.3417

EFSA NDA Panel (EFSA Panel on Dietetic Products, Nutrition and Allergies), 2014. Scientific Opinion on the evaluation of allergenic foods and food ingredients for labelling purposes. EFSA Journal 2014;12(11):3894, 286 pp. doi:10.2903/j.efsa.2014.3894

EFSA NDA Panel (EFSA Panel on Dietetic Products, Nutrition and Allergies), 2016a. Guidance on the preparation and presentation of an application for authorisation of a novel food in the context of Regulation (EU) 2015/2283. EFSA Journal 2016;14(11):4594, 24 pp. doi:10.2903/j.efsa.2016.4594

EFSA NDA Panel (EFSA Panel on Dietetic Products, Nutrition and Allergies), 2016b. Guidance on the preparation and presentation of the notification and application for authorisation of traditional foods from third countries in the context of Regulation (EU) 2015/2283. EFSA Journal 2016;14(11):4590, 16 pp. doi:10.2903/j.efsa.2016.4590

EFSA NDA Panel (EFSA Panel on Dietetic Products, Nutrition and Allergies), 2016c. General scientific guidance for stakeholders on health claim applications. EFSA Journal 2016;14(1):4367, 38 pp. doi:10.2903/j.efsa.2016.4367

EFSA SC (EFSA Scientific Committee), 2009. Guidance on Safety assessment of botanicals and botanical preparations intended for use as ingredients in food supplements. EFSA Journal 2009;7(9):1249, 19 pp. doi:10.2093/j.efsa.2009.1249

EFSA SC (EFSA Scientific Committee), 2011a. Scientific opinion on genotoxicity testing strategies applicable to food and feed safety assessment. EFSA Journal 2011;9(9):2379, 69 pp. doi:10.2903/j.efsa.2011.2379

EFSA SC (EFSA Scientific Committee), 2011b. Guidance on the risk assessment of the application of nanoscience and nanotechnologies in the food and feed chain. EFSA Journal 2011;9(5):2140, 36 pp. doi:10.2903/j.efsa.2011.2140

EFSA SC (EFSA Scientific Committee), 2011c. Guidance on conducting repeated-dose 90-day oral toxicity study in rodents on whole food/feed. EFSA Journal 2011;9(12):2438, 21 pp. doi:10.2903/j.efsa.2011.2438

EFSA SC (EFSA Scientific Committee), 2012. Guidance on selected default values to be used by the EFSA Scientific Committee, Scientific Panels and Units in the absence of actual measured data. EFSA Journal 2012;10(3):2579, 32 pp. doi:10.2903/j.efsa.2012.2579

EFSA SC (EFSA Scientific Committee), 2015. Risk profile related to production and consumption of insects as food and feed. EFSA Journal 2015;13(10):4257, 60 pp. doi:10.2903/j.efsa.2015.4257

EFSA Panel on Plant Protection Products and their Residues (PPR), 2012. Guidance on the Use of Probabilistic Methodology for Modelling Dietary Exposure to Pesticide Residues. EFSA Journal 2012;10(10):2839, 95 pp. doi:10.2903/j.efsa.2012.2839

Abbreviations

ACS	American Chemical Society
ADME	Absorption, distribution, metabolism, excretion
AOAC	Association of Analytical Communities
CAS	Chemical Abstracts Service
FAIM	Food Additive Intake Model
FCC	Food Chemical Codex
GMM	Genetically modified microorganism
GMO	Genetically modified organism
GMP	Good Manufacturing Practice
JECFA	Joint (FAO/WHO) Expert Committee on Food Additives
LOD	Limit of detection
LOQ	Limit of quantification
OECD	Organisation for Economic Co-operation and Development
rDNA	recombinant Deoxyribonucleic Acid

Appendix A – Explanatory text for the public consultation on the draft guidance on the preparation and presentation of the application for authorisation of a Novel Food

EFSA has launched an open consultation on its draft guidance on the preparation and presentation of the application for authorisation of a Novel Food. This document aims to provide guidance on the data needed to carry out the safety assessments of Novel Foods. It assists applicants in the presentation of applications in a structured format.

In line with EFSA's policy on openness and transparency and in order for EFSA to receive comments from the scientific community and stakeholders, EFSA has launched a public consultation on the draft document developed by the NDA Panel of EFSA.

Interested parties are invited to submit written comments **by 21 April 2016**. Please use the electronic template provided to submit comments and refer to the line and page numbers. Please note that after 2 hours your working session will expire and comments submitted after that time will not be recorded and transmitted. If you would like to submit additional data to support your comments or files send an email to: NDA.PublicConsult.62@efsa.europa.eu. Please note that comments will not be considered if they:

- are submitted after the closing date of the public consultation;
- are not related to the contents of the document;
- contain complaints against institutions, personal accusations, irrelevant or offensive statements or material;
- are related to policy or risk management aspects, which are out of the scope of EFSA's activity.

EFSA will assess all comments from interested parties which are submitted in line with the criteria above. The comments will be further considered by the relevant EFSA Panel and taken into consideration if found to be relevant.

All comments submitted will be published. Comments submitted by individuals in a personal capacity will be presented anonymously. Comments submitted formally on behalf of an organisation will appear with the name of the organisation.

Submit comments (deadline: 21 April 2016)

Appendix B – Full list of comments submitted by means of the electronic form on the EFSA website

Chapter text	Organisation	Comment text
GENERIC COMMENTS	ELC - Federation of European Specialty Food Ingredients Industries	ELC very much welcomes the work undertaken so far by the EFSA Panel on Dietetic Products, Nutrition and Allergies, which represents a significant and important improvement on Commission Recommendation 97/618/EC. We believe that further reflection on the points raised by ELC will help bring greater clarity to the Guidance.
GENERIC COMMENTS	ELC - Federation of European Specialty Food Ingredients Industries	Line 274: We think that EFSA's approach (e.g. quantitative or qualitative?) to determining the necessity of the data for the purposes of establishing data protection needs to be explained further.
GENERIC COMMENTS	Eurogroup for Animals	Definitions: Include the definition on 'whole foods'. It is mentioned on line 730. Suggestion: "'whole food" refers to a product to be consumed by humans which is composed of a multitude (up to thousands) of individual substances. Whole food range from plant based products such as maize or potatoes to more refined products such as fruit juices or flour, to foods consisting of microorganisms as well as animal-derived food products such as meat and milk.' from EFSA Scientific Committee; 2011. EFSA guidance on conducting repeated-dose 90-day oral toxicity study in rodents on whole food/feed. EFSA Journal 2011;9(12):2438 General Principles: 257/258 - Include an extra bullet pt : Information on Foods which contain substances or mixtures that are used for other applications than food (cosmetics, chemicals, pharma) which are relevant to the data requirements for Novel foods should be sourced and provided, in particular vertebrate studies, to avoid duplication of animal testing according to Rec 32 of Regulation 2015/2283. Line 265: In accordance with Directive 2010/63/EU... Remove the '4' and replace it as a superscropt for the footnote. Also delete the words' experimental and other' as the Directive 2010/63/EU's title is ' on the protection of animals used for scientific purposes'. Line 267: include in the wording: '...replaced, reduced or refined and duplication of animal testing should be avoided, where possible'. This text is in line with Recital 32 of Reg 2015/2283 Organisation and content of the notification: Line 294; remove extra '.' 2. Production Process Line 388 - 390: change the wording to '...;the breeding, rearing, feeding, housing, farming conditions and slaughter for farmed animals...'. Also remove the word 'living (L389) as it is repetition. 7. Absorption, distribution, metabolism and excretion (ADME)

Chapter text	Organisation	Comment text
		Line 604: with reference to 'animal models' makes it appear an animal model has to be used. It would be best to change the wording to ' ..selection of the appropriate model' or '...the selection of the appropriate (animal or non-animal) model. Line 606: suggested change of wording to include: ' ...differences between in vitro methods, experimental animals and humans' (even for nano the scientific committee guidance (L875 - 877) includes in vitro methods) Line 628: Is there an error in the Reference given here. The document referenced EFSA SC guidance on RA of the application of nanoscience and nanotechnologies is not EFSA, 2010b as stated here, but rather EFSA 2011a 9.3 Subchronic toxicity Line 719: Include wording: 'Decisions on whether tests are necessary need to be considered in light of the data already available. Comment on 90 day study requirement: There is prevailing sceintific uncertainty with regard to the determination of the necessity of the 90 day feeding trials. EFSA has previously called for case-by-case decisions. (references: Contrary to the announced mandatory requirement for 90-day rodent feeding studies, all guidance documents of the European Food Safety Authority (EFSA) relating to the risk assessmentof GM food and feed advise consideration of the performance of such studies under specific circumstances, determined on a case-by-case basis. EFSA (2011) Guidance for RA of food and feed from GM plants. EFSA Journal 9, 2150 + EFSA (2012) Guidance on the RA of food and feed from GM animals. EFSA Journal 10, 2501 + U.G Sauer & K.A Reid ATLA 40, 183–1 + FP7 GRACE Line 746: EOGRT (OECD 443) not 2 generation testing (OECD 416) as with other EU regulatory requirements. Line 781: reference OECD nano read-across http://www.oecd.org/officialdocuments/publicdisplaydocumentpdf/?cote=env/jm/mono(2016)3&doclanguage=en Line 831: include - ' ...results from in vitro, animal and human studies'

Chapter text	Organisation	Comment text
GENERIC COMMENTS	Federal Food Safety and Veterinary Office	Although medicinal products and narcotics do not fall under the definition of "food", the distinction between food and these products often poses problems in practise. We would welcome a paragraph clarifying that Novel Food products should not have pharmacological, psychotropic or addictive properties and outlining how to deal with risk assessments of borderline cases. There are e.g. new products consisting of substances that commonly occur at low levels in botanical or animal components of the diet, which are extracted and re-introduced at much higher levels (sometimes even as pure substances) in specific products. The dose may be equal or lower to the dose commonly used in oral medicinal products. Concerning narcotics, we are aware that "narcotic or psychotropic substances within the meaning of the United Nations Single Convention on Narcotic Drugs, 1961, and the United Nations Convention on Psychotropic Substances, 1971" are excluded as Novel Food. However the list of narcotics is not always up to date and regulates only comparatively potent psychoactive substances.
GENERIC COMMENTS	Food Safety Authority of Ireland	The draft EFSA Guidance provides a lot of information (generic and specific) on the preparation of a novel food application dossier. Commission Recommendation 97/618/EC is and was a well used reference for the preparation of novel food application dossiers under Regulation 258/97. Commission Recommendation97/618/EC directly links the novel food categories with various data requirements in simplified format (Tables and decision trees) towards the end of the document, and this has always been viewed as very user-friendly by applicants. However, this simplified format is absent from the current draft EFSA Guidance and as all of the information is already provided in text form, it should not prove too difficult to synopsise and simplify it in Table or Decision Tree format, similar to that in Commission Recommendation 97/618/EC.
GENERIC COMMENTS	Food Safety Authority of Ireland	This is a good concise document and with some refinement will make it generally easy for applicants to put application dossiers together.
GENERIC COMMENTS	Food Supplements Europe	Food Supplements Europe welcomes the work EFSA undertakes to provide guidance for applications on novel foods. The guidance is comprehensible and helpful, with a clear layout and references to many other EFSA guidance documents for various specific areas. Focus on food supplements Food supplements are legally defined as foodstuffs. In a number of parts of the guidance, food supplements are singled out, whereas the requirements are valid for all novel foods and not specifically for food supplements. To avoid confusion, we would suggest that the guidance should remain general, covering all novel foods, irrespective of the matrix they are intended to be used in.

Chapter text	Organisation	Comment text
GENERIC COMMENTS	Food Supplements Europe	General Principles: Line 276: Even with regard to safety/human health, it may still be possible and appropriate to retain some aspects of the confidential data as confidential. Organisation and content of the notification (should read application?) Line 294: Do all data need to be submitted in English? Does data in non-EU languages need to be translated prior to submission? Does information in other official languages of the EU need to be officially translated? Introduction Line 297: The draft guidance introduces the concept of the "nature of the Novel Food". This wording, not used in the Regulation is a bit confusing especially in the light of the legal definition included in the Regulation. This guidance should be a tool to help operators preparing their submissions and should therefore avoid introducing new concepts. In order to be consistent with the rest of the draft guidance, we propose to slightly amend this sentence as follows: " The Novel Food should be briefly described in an introductory paragraph, including the source, the main aspects of the production process and typical compositional features. Its purpose and intended use should be described."
GENERIC COMMENTS	Intertek Scientifi &Regulatory Consultancy	276 There are no provisions here for how submissions covered under Article 26 - Authorisation procedure in case of data protection. The guidance for nutrition and health claims does include such provisions and can be used as a model. Article 26 says: (a) the newly developed scientific evidence or scientific data was designated as proprietary by the initial applicant at the time the first application was made; (b) the initial applicant had exclusive right of reference to the proprietary scientific evidence or scientific data at the time the first application was made; and This legally means not when it has been accepted by EFSA's Apps desk as application but before. I.e. at the point it is actually given to the Commission. This needs to be very clear in the dossier since many applicants will subsequently publish data, so that timing is critical.
GENERIC COMMENTS	Mead Johnson Nutrition	Although Regulation (EU) 2015/2283 foresees the opportunity to bundle a Novel Food to a Health Claim application, the Draft Guidance does not provide any direction in this respect. In particular, without clear direction provided in the Guidance, the applicants would have to submit 2 dossiers with likely redundant information (e.g., administrative part, description of the food etc…).

Chapter text	Organisation	Comment text
GENERIC COMMENTS	Mead Johnson Nutrition	185-220: The Draft Guidance elaborates the categories of novel foods found in Regulation (EU) 2015/2283. While we do not expect EFSA to interpret statutory provisions, some guidance is welcome as to distinguish different categories of novel foods. In particular, EFSA should clarify the difference between "food consisting of, isolated from or produced from microorganisms" and "food isolated from or produced from cell cultures derived from micro-organisms." As an example, a novel food derived from microorganisms through fermentation or propagation could fall into both the categories.
GENERIC COMMENTS	Mead Johnson Nutrition	233-234: The Draft Guidance defines an 'application' as a stand-alone dossier. Industry experience teaches that a Novel Food may be the outcome of a joint-research program between two or more entities. In this case, while one food business may be responsible for the submission, some confidential information (e.g., trade and industry secrets) may stay with the partner-developer of the Novel Food. On the other hand, when a novel food is used as an ingredient in another matrix, like in the case of a finished product, stability data are likely generated by the recipient of the novel food instead of the manufacturer. EFSA should consider the opportunity for the partner to submit additional information. 265-269: Mead Johnson Nutrition is committed to the highest standards of safety and recognizes the importance of safety data extrapolated from animal models. Nonetheless, Mead Johnson Nutrition believes that the reduction of the number of animal studies is a commendable goal both from an ethical and economic perspective, which in turn may help to reduce the cost of food innovation. To this aim, EFSA should be open to consider relevant data obtained with different animal models required by other authorities for similar submission (e.g., FDA GRAS submission). 276-280: While the European Commission will have to take appropriate measures to protect confidential information under article 23 of the Regulation, it is important for the applicant to properly communicate to EFSA which portions of the dossier are considered confidential. This is the same approach followed by other authorities outside the EU for novel food submission (e.g., Food Standard Authority Australia New Zealand).
GENERIC COMMENTS	Mission of Chile to the European Union	How do you manage the EU that the dossier submitted respecting confidentiality and protecting intellectual property?

Chapter text	Organisation	Comment text
GENERIC COMMENTS	National Food Agency	The National Food Agency welcomes the proposed guidance document. The document covers the most aspects and considerations necessary for a comprehensive assessment. A few comments and suggestions are given for consideration. p. 9. General principles Paragraph: "The structure of the application..": line 249-257; It is unclear what sections in the application is mandatory, all sections should be addressed. We recommend that all sections should be covered and addressed in an application. If some are not considered relevant, this should be explained and justified by the applicant (as stated in the following para). p. 10. Structure of Part 1 Introduction: We recommend that the applicant provide a Summary of the application which includes the pertinent sections indicated here, thus to replace "Introduction" with "Summary of application".
GENERIC COMMENTS	Pen & Tec Consulting	Line 212: Instead of referring to "point (f) of this paragraph" suggest to refer to "point (f)) of Article 3, paragraph 2 of Regulation (EU) 2015/2283" so that it is clear applicants need to check the NF Regulation & not this EFSA guidance document if they want to check point f.
GENERIC COMMENTS	Schuttelaar & Partners	Even though it is mentioned (lines 249-257) that, when justification is given, not all sections need to be covered in each application dossier, more guidance could be given (either here or throughout the document) on which kind of justifications would be acceptable. In other words: what are the conditions under which EFSA could envisage that an applicant does not need to cover all sections?
GENERIC COMMENTS	Secretaría de Economía	Se estima necesario identificar cuál es el periodo de tiempo que la evidencia científica ha determinado para evaluar el efecto a la salud derivado del consumo de nuevos alimentos. Asimismo, se requiere conocer el indicador o parámetro que se empleará para medir el grado significativo del consumo humano de un nuevo alimento.

Chapter text	Organisation	Comment text
GENERIC COMMENTS	SYNPA	Line 274: Regulation 2015/2283, Article 26 (c) provides that only where the novel food could not have been assessed and authorised by EFSA, data protection may apply. The second criterion is currently missing in the Guidance and should be included for consistency. We think that EFSA's approach (e.g. quantitative or qualitative?) to determining the necessity of the data for the purposes of establishing data protection needs to be explained further. Line 297: The draft guidance introduces the concept of the "nature of the Novel Food". This wording, not used in the Regulation is a bit confusing especially in the light of the legal definition included in the Regulation. This guidance should be a tool to help operators preparing their submissions and should therefore avoid introducing new concepts. In order to be consistent with the rest of the draft guidance, we propose to slightly amend this sentence as follows: "The Novel Food should be briefly described in an introductory paragraph, including the source, the main aspects of the production process and typical compositional features. Its purpose and intended use should be described."
GENERIC COMMENTS	UK Advisory Committee on Novel Foods and Processes	The primary role of the Advisory Committee on Novel Foods and Process (ACNFP) is the safety assessment of any novel food or process submitted in the UK for approval or notification under the Novel Foods Regulations (EC) No. 258/97. The Committee also carefully reviews the Opinions on applications submitted to other member states. The ACNFP welcomes these Guidance documents form EFSA and in general found them very helpful. The view of the Committee is that, in the guidance there should be a clear distinction between principles and best practice on the one hand, and information that must be submitted on the other. A flexible approach is needed given the many different types of food and food ingredients that are assessed under the framework. The Committee suggests that it is important to ensure that core information / issues are considered and that applicants are thoughtful about the appropriate scientific testing for their product. Explanations should be provided where an applicant considers information or data is not necessary.
1. Description of the Novel Food	Committee "Novel Foods and New Technologies" of the Codex Alimentarius Austriacus Commission	add a footnote stating that not explicitly listed categories of Novel Foods corresponding to the definition should be assigned to categories listed under 1.1. – 1.8.

Chapter text	Organisation	Comment text
1. Description of the Novel Food	ELC - Federation of European Specialty Food Ingredients Industries	Line 297: The draft guidance introduces the concept of the "nature of the Novel Food". This wording, not used in the Regulation is a bit confusing especially in the light of the legal definition included in the Regulation. This guidance should be a tool to help operators preparing their submissions and should therefore avoid introducing new concepts. In order to be consistent with the rest of the draft guidance, we propose to slightly amend this sentence as follows: "The Novel Food should be briefly described in an introductory paragraph, including the source, the main aspects of the production process and typical compositional features. Its purpose and intended use should be described."
1. Description of the Novel Food	ELC - Federation of European Specialty Food Ingredients Industries	We would like to draw attention to the fact that the draft guidance describes the Novel Food in a different way than the categories listed in the Regulation. While we acknowledge the scientific point of view and rationale, we find this confusing as the novel food has to be assigned to one (or several) category(ies) according to the legal definition. For example, categories 1.1 Chemical substances and 1.2 Polymers are not part of the legal definition. By contrast, the legal category "vitamins, minerals and other substances" is not included in the draft EFSA guidance.
1. Description of the Novel Food	Federal Public Service of Health, Food Chain Safety and Environment	Section 1 : The category '(ix) vitamins, minerals and other substances' is missing
1. Description of the Novel Food	Food Safety Authority of Ireland	Under the heading "Description of the Novel Food" I don't see any reference to the NF categories outlined in Article 3.2 of Regulation (EU) 2015/2283. I would have thought the NF should be categorised in the application dossier?
1. Description of the Novel Food	Food Supplements Europe	Line 300 and chapter 1 on description of the novel food: we would like to draw attention to the fact that the draft guidance describes the Novel Food in a different way than the categories listed in the Regulation. While we acknowledge the scientific point of view and rationale, we find this confusing as the novel food has to be assigned to one (or several) category(ies) according to the legal definition. For example, categories 1.1. Chemical substances and 1.2 Polymers are not part of the legal definition. On the opposite, the legal category "vitamins, minerals and other substances" is not included in the draft EFSA guidance.

Chapter text	Organisation	Comment text
1. Description of the Novel Food	FoodDrinkEurope	Introduction Line 297: The draft guidance introduces the concept of the "nature of the Novel Food". This wording, not used in the Regulation is a bit confusing especially in the light of the legal definition included in the Regulation. This guidance should be a tool to help operators preparing their submissions and should therefore avoid introducing new concepts. In order to be consistent with the rest of the draft guidance, we propose to slightly amend this sentence as follows: " The nature of the Novel Food should be summarized in an introductory paragraph, including the source, the main aspects of the production process and typical compositional features. Its purpose and intended use should be described." We suggest rewording of sentence 2 starting with "This guidance...." The Novel Food should be briefly described in an introductory paragraph, including the source, the main aspects of the production process and typical compositional features. Its purpose and intended use should be described." Line 300 and chapter 1 on description of the novel food: We would like to draw the attention to the fact that the draft guidance describes the Novel Food in a different way than the categories listed in the Regulation. While we acknowledge the scientific point of view and rationale, we find this confusing as the novel food has to be assigned to one (or several) category (ies) according to the legal definition. Line 310-314 seems to imply that the category of novel foods falling under new or intentionally modified molecular structure is limited to polymerization only. On the opposite, the legal category "vitamins, minerals and other substances" is not included in the draft EFSA guidance.
1. Description of the Novel Food	Intertek Scientifi &Regulatory Consultancy	300 Under Section 1 Description it is very important to harmonise these criteria with the Union List when it is drawn up for existing products. There should be harmonisation of approach so that new approvals fit comfortably into the new list. The specification is very important. Again a general comment for this section would be that if a comparative safety approach is taken then each section should compare these parameters to the existing food that it will replace in the diet.

Chapter text	Organisation	Comment text
1. Description of the Novel Food	Mead Johnson Nutrition	296-299 EFSA consistently utilizes the expression 'nature' without defining the meaning of it. Some clarification around this terminology is welcomed. Many novel foods are protected with IP rights and patents usually outline the production process of a novel food. A reference to pending patents would be pertinent in this section. 303- 361: While the Guidance further specify a new category (i.e., polymers) within the ones defined in Article 3(2) of Regulation (EU) 2015/2283, vitamins, minerals and other substances used in accordance with Directive 2002/46/EC, Regulation (EC) No 1925/2006 or Regulation (EU) No 609/2013 (num. X) are missing. The Guidance should include a comparison table between the types of Novel Foods listed in the Regulation and the categories listed in Part 1 as it was the case with the classes of Novel Foods in Commission Recommendation 97/618/EC (see Table 1).
1. Description of the Novel Food	Pen & Tec Consulting	Line 300: 2 categories are missing: vitamin/minerals & food that was only used in food supplements. If EFSA already knows which basic information is required to describe these novel food ingredients we suggest to include these as point 1.9 & 1.10, or create a general section for "other" ingredients & include general requirements.
1. Description of the Novel Food	SYNPA	Line 300 : We would like to point it out that the draft guidance describes the Novel Food in a different way than the categories listed in the Regulation. While we acknowledge the scientific point of view and rationale, we find this confusing as the novel food has to be assigned to one (or several) category(ies) according to the legal definition. For example, categories 1.1 Chemical substances and 1.2 Polymers are not part of the legal definition. By contrast, the legal category "vitamins, minerals and other substances" is not included in the draft EFSA guidance.
1.1. Chemical substances	Federal Public Service of Health, Food Chain Safety and Environment	Section 1.1 : add "primary, secondary and tertiary structure of molecules" Section 1.1 : add "size, shape, distribution and crystal form of the particles"
1.1. Chemical substances	Food Law Consult	According to the EU definition, a food supplement should contain concentrated sources of ingredients. This applies also for botanicals. There are however no purity criteria for botanicals. In other words from which point on are we still talking about plant preparations? E.g. Bach flowers preparations are not considered novel and allowed in food supplements in BE. These are extremely diluted preparations.(do not consider plant prep anymore) So one could say, there's no safety issue even for plants preparations from plants which are considered toxic at higher levels. I've asked the BE authorities which would be the lowest level of dilution that would be accepted.

Chapter text	Organisation	Comment text
1.1. Chemical substances	Food Law Consult	While on the other side I've seen highly concentrated preparations (berberine, EGCG, curcumine,…), which are mostly not traditionally used but are sometimes considered not to be novel, for example because of the marketing of 1 product at 1 dose for a specific use in 1 country. There should be purity criteria for botanicals. From which point on are we still considering the ingredients a botanical preparation and not a isolated substance
1.1. Chemical substances	Food Supplements Europe	Line 307: Information on isomeric form may be relevant.
1.1. Chemical substances	Nutraveris	L305 For Novel food related to chemical substances, is any identification number mandatory, or can EFSA accept application without identification number or pending identification number?
1.2. Polymers	Federal Public Service of Health, Food Chain Safety and Environment	Section 1.2: add "primary, secondary and tertiary structure of molecules"
1.2. Polymers	Food Safety Authority of Ireland	Possibly more clarity needed on what exactly a polymer constitutes for this purpose. For example a peptide or protein is a polymer of amino acids. DNA or RNA is a polymer of nucleic acids. I am presuming neither of these examples are considered appropriate under this heading here as I thought it referred to sugars, carbohydrates etc?
1.2. Polymers	Food Supplements Europe	Line 315: How does particle size need to be expressed? Minimum, average, range...?
1.3. Foods consisting of, isolated from or produced from microorganisms, fungi or algae	Intertek Scientifi &Regulatory Consultancy	318 Strain is very important to be included here and in the Union List to avoid confusion in the market.
1.3. Foods consisting of, isolated from or produced from microorganisms, fungi or algae	Nutraveris	L321 The genetic characterization of unicellular organisms is essential to characterize the Novel Food consisting of, isolated from or produced from microorganisms. However, various methods can be used for this genetic characterization. EFSA should therefore indicate which methods can be used for the genetic characterization of organisms (i.e. 16S rDNA sequence?).
1.3. Foods consisting of, isolated from or produced from microorganisms, fungi or algae	Pen & Tec Consulting	Line 322: Suggest to delete since this is already covered in Section 5.1.
1.4. Food consisting of, isolated from or produced from material of mineral origin	Committee "Novel Foods and New Technologies" of the Codex Alimentarius Austriacus Commission	add in line 333 "particle size, shape and distribution" in analogy to 1.2
1.4. Food consisting of, isolated from or produced	Federal Public Service of Health, Food Chain Safety	Section 1.4: Line 333 – add "shape, distribution and crystal form of the particles"

Chapter text	Organisation	Comment text
from material of mineral origin	and Environment	
1.4. Food consisting of, isolated from or produced from material of mineral origin	Food Safety Authority of Ireland	Is it appropriate to ask for other information like isomeric structure or ligands etc?
1.4. Food consisting of, isolated from or produced from material of mineral origin	Food Supplements Europe	Line 324: Should the information below be provided for the mineral source, the inorganic food product, or both?
1.4. Food consisting of, isolated from or produced from material of mineral origin	FoodDrinkEurope	Lines 333: There is lack of consistence where particle size is mentioned. For example under section 1.2 line 315 includes particle size, shape and distributions whereas line 333 only mentions particle size.
1.4. Food consisting of, isolated from or produced from material of mineral origin	Intertek Scientifi &Regulatory Consultancy	141 Where a Traditional Food from Third Country notification has been turned down, resulting in a full application it would seem prudent to start the new application by presenting/Annexes the failed notification and the basis for its failure as a starting point?
1.4. Food consisting of, isolated from or produced from material of mineral origin	Nutraveris	L333 Particle size is a criterion for the characterization of Novel food consisting of, isolated from or produced from material of mineral origin. Particle size can be assessed through various methods. EFSA should indicated which methods can be used to determine particle size.
1.5. Food consisting of, isolated from or produced from plants or their parts	Food Safety Authority of Ireland	While specific parts of plants are mentioned here, it should also include possible extracts (aqueous or solvent) of the various parts.
1.6. Food consisting of, isolated from or produced from animals or their parts	Food Safety Authority of Ireland	The same point as for 1.5. Extracts should also be considered.
1.6. Food consisting of, isolated from or produced from animals or their parts	Food Supplements Europe	Line 344: The heading is inaccurate: should refer to "information to be provided on the animals etc., used in or to produce food...". Also, when referring to animals, as indicated in the Regulation, this covers insects as well. Perhaps this should be more clearly stated in the EFSA guidance.
1.6. Food consisting of, isolated from or produced from animals or their parts	National Food Agency	1.6, p. 11, last bullet point: Part(s) used.

Chapter text	Organisation	Comment text
1.7. Foods consisting of, isolated from or produced from cell culture or tissue culture derived from animals, plants, fungi or algae	Food Safety Authority of Ireland	I think the first sentence in this section should refer to in vitro cultures for clarity. Instead of "multicellular" it should be "eukaryotic" as there are single cell eukaryotes such as yeasts. In the examples in brackets, the word "mushrooms" should be replaced with "fungii" There should be a mention of growth medium also as the content may have an impact on the safety assessment.
2. Production process	AESGP	While a detailed description of the process is required to allow conclusions to be drawn regarding the impact of the process on the safety and nutritional value of the Novel Foods, no further information is provided on the information required for Novel Foods produced by fermentation processes using micro-organisms. We note that other EFSA guidance (notably 2009 'Guidance of EFSA prepared by the Scientific Panel of Food Contact Material, Enzymes, Flavourings and Processing Aids on the Submission of a Dossier on Food Enzymes') further specify the information required on the micro-organism including when such micro-organism has been genetically modified. EFSA is kindly asked to provide clarification on the following: • What information would be required for Novel Foods produced by fermentation processes using micro-organisms? • Should additional information be provided according to the `Guidance Document of the Scientific Panel on Genetically Modified Organisms for the Risk Assessment of Genetically Modified Micro-organisms and their Derived Products Intended for Food and Feed Use` (EFSA, 2011)?
2. Production process	Committee "Novel Foods and New Technologies" of the Codex Alimentarius Austriacus Commission	add in line 390 "and cell culture or tissue culture from plants and animals" and replace "microalgae" by "algae" in analogy to category "Foods consisting of, isolated from or produced from cell culture or tissue culture derived from animals, plants, fungi or algae"
2. Production process	ELC - Federation of European Specialty Food Ingredients Industries	Lines 379-382: Information on reaction conditions needs to be included in the dossier. Those details may be part of company know-how. We wonder about the relevance of such information when the Novel Food authorization would, by default, be generic. Such a level of detail cannot be included in the Union list and a competitive product will be legal on the market as long as it meets the specifications included in the Union list i.e. the manufacturing process may differ slightly. In addition, we believe that if this detailed information is required, it should be eligible for confidentiality status.

Chapter text	Organisation	Comment text
2. Production process	Eurogroup for Animals	Definitions: Include the definition on 'whole foods'. It is mentioned on line 730. Suggestion: "'whole food" refers to a product to be consumed by humans which is composed of a multitude (up to thousands) of individual substances. Whole food range from plant based products such as maize or potatoes to more refined products such as fruit juices or flour, to foods consisting of microorganisms as well as animal-derived food products such as meat and milk.' from EFSA Scientific Committee; 2011. EFSA guidance on conducting repeated-dose 90-day oral toxicity study in rodents on whole food/feed. EFSA Journal 2011;9(12):2438 General Principles: 257/258 - Include an extra bullet pt : Information on Foods which contain substances or mixtures that are used for other applications than food (cosmetics, chemicals, pharma) which are relevant to the data requirements for Novel foods should be sourced and provided, in particular vertebrate studies, to avoid duplication of animal testing according to Rec 32 of Regulation 2015/2283. Line 265: In accordance with Directive 2010/63/EU... Remove the '4' and replace it as a superscropt for the footnote. Also delete the words' experimental and other' as the Directive 2010/63/EU's title is ' on the protection of animals used for scientific purposes'. Line 267: include in the wording: '...replaced, reduced or refined and duplication of animal testing should be avoided, where possible'. This text is in line with Recital 32 of Reg 2015/2283 Organisation and content of the notification: Line 294; remove extra '.' 2. Production Process Line 388 - 390: change the wording to '...;the breeding, rearing, feeding, housing, farming conditions and slaughter for farmed animals...'. Also remove the word 'living (L389) as it is repetition. 7. Absorption, distribution, metabolism and excretion (ADME) Line 604: with reference to 'animal models' makes it appear an animal model has to be used. It would be best to change the wording to ' ..selection of the appropriate model' or '...the selection of the appropriate (animal or non-animal) model. Line 606: suggested change of wording to include: ' ...differences between in vitro methods, experimental animals and humans' (even for nano the scientific committee guidance (L875 - 877) includes in vitro methods) Line 628: Is there an error in the Reference given here. The document referenced EFSA SC guidance on RA of the application of nanoscience and nanotechnologies is not EFSA, 2010b as stated here, but rather EFSA 2011a 9.3 Subchronic toxicity

Chapter text	Organisation	Comment text
		Line 719: Include wording: 'Decisions on whether tests are necessary need to be considered in light of the data already available. Comment on 90 day study requirement: There is prevailing sceintific uncertainty with regard to the determination of the necessity of the 90 day feeding trials. EFSA has previously called for case-by-case decisions. (references: Contrary to the announced mandatory requirement for 90-day rodent feeding studies, all guidance documents of the European Food Safety Authority (EFSA) relating to the risk assessmentof GM food and feed advise consideration of the performance of such studies under specific circumstances, determined on a case-by-case basis. EFSA (2011) Guidance for RA of food and feed from GM plants. EFSA Journal 9, 2150 + EFSA (2012) Guidance on the RA of food and feed from GM animals. EFSA Journal 10, 2501 + U.G Sauer & K.A Reid ATLA 40, 183–1 + FP7 GRACE Line 746: EOGRT (OECD 443) not 2 generation testing (OECD 416) as with other EU regulatory requirements. Line 781: reference OECD nano read-across http://www.oecd.org/officialdocuments/publicdisplaydocumentpdf/?cote=env/jm/mono(2016)3&doclanguage=en Line 831: include - ' ...results from in vitro, animal and human studies'
2. Production process	Federal Public Service of Health, Food Chain Safety and Environment	Section 2: Line 390 – specify that information about the breeding practices used for animal production and the propagating practices used for plant production must be given
2. Production process	Food Supplements Europe	Lines 375-382: information on reaction conditions needs to be included in the dossier. Those details may be part of the company know-how. We believe that this detailed information, if included, should be eligible to confidentiality status. In addition, we wonder about the relevance of such information when the Novel Food authorization would, by default, be generic. Such level of detail cannot be included in an authorization decision and a competitive product will be legal on the market as long as it's compliant with the specifications. However, the manufacturing process may differ [slightly]. Line 392: There is no reason to refer specifically to food supplements as the use of novel plant and plant preparations in other types of foods (e.g. meal replacements, soups, powdered drink mixes, sports products etc.) is covered in the same way by the legislation. We would suggest to indicate that this information is relevant to all uses of plants and plant preparations.

Chapter text	Organisation	Comment text
2. Production process	FoodDrinkEurope	Lines 375-382: Information on reaction conditions needs to be included in the dossier. Those details may be part of the company know-how, and are also covered by the measures implemented for production control and quality assurance referenced in the previous paragraph (Lines 375-378). We believe that these detailed information (for example the operational limits and key parameters referenced in line 376 and reaction conditions referenced in line 380), if included, should be eligible to confidentiality status. In addition, we wonder the relevance of such information when the Novel Food authorization would, by default, be generic. Suh level of details cannot be included in an authorization decision and a competitive product will be legal on the market as long as it's compliant with the specifications. However, the manufacturing process may differ [slightly]. Additionally, this level of detail does not appear to address the objectives stated in lines 371-372 that it "should specifically focus on potential by-products, impurities or contaminants that could raise safety concerns", as this type of information would not typically impact this.
2. Production process	Intertek Scientifi &Regulatory Consultancy	385 Extraction solvent and ratios to whole plant should also be specified here. Please look at the EMA's monographs on herbal ingredients and harmonise approach as far as possible. Thios will alow direct comparisons between products used for medicinal and for food use where applicable.
2. Production process	IPIFF	The ways in which insects producers raise their produce (e.g. substrates used, ways of automating processes) vary from one producer to another. Given that authorisations shall be 'generic' and that common applications are encouraged by the European Commission, such a focus on production processes seems to make the process of common applications, as well as the benefiting of generic applications, unnecessarily complex. In our opinion, the essential question is not what exact methods are used to rear and process insects, but whether the different ways of rearing and processing insects result in a different final produce in terms of its safety and nutritional value. IPIFF therefore suggests to add a condition along the lines of "if relevant to the properties of the Novel Food" to this section.
2. Production process	Mead Johnson Nutrition	367-393: The Draft Guidance requires the applicant to describe the production process in a very detailed way. While it is not yet clear what information will be disclosed under Article 10(2) of the Novel Food Regulation, it is of paramount importance for food business operators that commercial interests, including IP rights, are protected in line with Regulation (EC) No 1049/2001. Even in the absence of data protection, this is essential to reward investments and, hence, to foster innovation. As an example, the EFSA 'Guidance for submission for food additive evaluation' allows the applicants to provide a non-confidential description of the manufacturing process, when they intend to maintain the entire process confidential.
2. Production process	National Food Agency	p. 12, 1st para: add ", incl. bioavailability", after nutritional value.

Chapter text	Organisation	Comment text
2. Production process	SYNPA	Lines 379-382: Information on reaction conditions needs to be included in the dossier. Those details may be part of company know-how. We wonder about the relevance of such information when the Novel Food authorization would, by default, be generic. Such a level of detail cannot be included in the Union list and a competitive product will be legal on the market as long as it meets the specifications included in the Union list i.e. the manufacturing process may differ slightly. In addition, we believe that if this detailed information is required, it should be eligible for confidentiality status.
2. Production process	UK Advisory Committee on Novel Foods and Processes	From line 378: The Committee supported the requirement to provide a production process flow diagram with the control points indicated as this had often been found to be valuable in its assessments of novel foods
3. Compositional data	CASP	As previously commented Draft guidance on the preparation and presentation of a notification for authorisation of Traditional Foods from third countries SENT TO EFSA ON APR 7TH,2016, 11:00 CET and ACCEPTED the requirement of "at least five representative batches" in lines 408-409:"The analytical information should preferably be provided on at least five representative batches of the Novel Food that have been independently produced (i.e. with independent batches of raw materials)"goes even above the pharma requirements for stability studies of medicines, where normally the stability studies are performed with 3 production batches. We therefore believe that analytical data on 3 representative batches should be sufficient because also for NEW medicinal substances only 3 batches are prescribed : NOTE FOR GUIDANCE ON STABILITY TESTING: STABILITY TESTING OF NEW DRUG SUBSTANCES AND PRODUCTS(CPMP/ICH/2736/99) - this clearly shows how more strict the unsubstantiated approach of EFSA draft guidance in this sense is. The burden for food industry innovation is surpassing the innovation expenses in pharma industry where at submission also only pilot batches are acceptable with production batches stability promise. Also the last IADSA brochure "Stability Testing for the Shelf Life Determination of Food Supplements" is anchoring in Chapter 7.3 Product samples 3 batches: "Ideally, the analyses should be on samples from three consecutive batches"(© IADSA 2016).
3. Compositional data	Committee "Novel Foods and New Technologies" of the Codex Alimentarius Austriacus Commission	add in line 396 "physico-chemical and biochemical properties and microbiological characterization of the Novel Food."

Chapter text	Organisation	Comment text
3. Compositional data	ELC - Federation of European Specialty Food Ingredients Industries	Lines 408-412: EFSA is requesting analytical information on at least 5 representative batches that are independently produced. When a product is in development phase, it might be difficult to fulfil this requirement. We believe that analytical data on 3 representative batches should be sufficient unless there is too much variation between batches. This is in line with the requirements for active pharmaceutical ingredients for which data should be submitted on 3 batches (ICH guideline Q1A(R2) and EMEA CPMP/QWP/122/02). "Pilot plant" size of the batches should be acceptable. This size of batch can fulfil the aim of demonstrating the reproducibility of batches with analytical data within the specification. Upscaling to large size commercial batches with analytical data within the specification would then be the responsibility of the manufacturer.
3. Compositional data	Food Safety Authority of Ireland	In line 408 it mentions data from at least five representative batches. I was of the impression that three would be sufficient?
3. Compositional data	Food Supplements Europe	Lines 408-412: EFSA is requesting analytical information on at least 5 representative batches that are independently produced. When a product is in the development phase, it might be difficult to fulfill this requirement. We believe that analytical data on 3 representative batches should be sufficient unless there are wide variations between batches. This is in line with the requirements for active pharmaceutical ingredients for which data should be submitted on 3 batches (ICH guideline Q1A(R2) and EMEA CPMP/QWP/122/02). We therefore believe that 5 batches should not be the standard requirement. If the applicant can demonstrate that the process/product composition is well controlled and that there is little variability, 3 batches should be sufficient.
3. Compositional data	FoodDrinkEurope	Lines 408-412: EFSA is requesting analytical information on at least 5 representative batches that are independently produced. When a product is in development phase, it might be difficult to fulfill this requirement. We believe that analytical data on 3 representative batches should be sufficient unless there are too much variations between batches. This is in line with the requirements for active pharmaceutical ingredients for which data should be submitted on 3 batches (ICH guideline Q1A(R2) and EMEA CPMP/QWP/122/02).
3. Compositional data	Intertek Scientifi &Regulatory Consultancy	408 You first mention here about 5 batches. However this should also be the criteria for testing to specification as well as all contaminants etc. Are 3 batches sufficient? Often prior to approval it is not easy to produce 5 full scale batches and EFSA has accepted 3 in a number of past applications Does it matter whether they are consecutive or non— consecutive?

Chapter text	Organisation	Comment text
3. Compositional data	IPIFF	EFSA states that "when several production processes are proposed, such data should be provided for each given process". This data should come from five representative batches of the Novel Food. It is not clear here what constitutes a single "production process": would producers using a variety of substrates and processing methods need to provide such data (based on 5 representative samples) for each of these processes, even if there is no reason to believe the data on composition will differ in each of these cases? IPIFF therefore suggests to add a condition along the lines of "if such a different production process leads to differing properties of the Novel Food" to this section.
3. Compositional data	Mead Johnson Nutrition	408-412: The Draft Guidance requires the applicant to provide data on 5 different batches of the final product. This means that a food business operator will have to produce five batches, submit stability data as part of the dossier and wait for the final approval, which likely will happen after the expiration date of the product. It appears that this approach will lead to increased food waste in contrast with recent policies enacted by the EU to reduce this phenomenon (i.e., 'Stop food waste'). Providing stability data on a fewer number of batches (e.g., 3) would be more reasonable considering that, as requested by the Guidance, novel food manufacturers must have quality control schemes in place.
3. Compositional data	Mission of Chile to the European Union	Whereas a food or ingredients can be classified as Novel Food, is there a limit on the proportion of food ingredient where as Novel Food ingredient is excluded? For example. Food salmon with pepper; if the chili is in low proportions xx% of the food, chili should not be applied as Novel Food.
3. Compositional data	Nutraveris	L400-402 Validated methods should be used for the analyses of composition data. EFSA indicates that AOAC, ACS and European pharmacopeia methods can be used for these analyzes. What is the position of EFSA regarding Asian pharmacopeia, such as for instance Chinese, Japanese or Korean pharmacopeia?
3. Compositional data	Nutraveris	L408 EFSA indicates that analytical information should be provided on at least five representative batches produced independently. EFSA should clarify whether the five batches should be analyzed simultaneously or if analyzes can be performed separately, for instance at the end of each batch production, by the same laboratory with the same validated methods.
3. Compositional data	SYNPA	Lines 408-412: EFSA is requesting analytical information on at least 5 representative batches that are independently produced. When a product is in development phase, it might be difficult to fulfil this requirement. We believe that analytical data on 3 representative batches should be sufficient unless there is too much variation between batches. This is in line with the requirements for active pharmaceutical ingredients for which data should be submitted on 3 batches (ICH guideline Q1A(R2) and EMEA CPMP/QWP/122/02).

Chapter text	Organisation	Comment text
3. Compositional data	UK Advisory Committee on Novel Foods and Processes	p13 – from line 408: The Committee notes the proposal to change the number of representative batches required to be analysed from the currently accepted standard of three, to five. This change does not appear to have been well-explained or justified. The Committee considers that an emphasis on the batches being representative of the variations seen in the production of the product is more important than increasing the number of batches.
3.1. General requirements	analyze & realize GmbH	Lines 408-409 Although the requirement to provide analytical data on 5 independently manufactured batches can be understood, it will be a substantial challenge for products in an early stage of development, and especially for botanical products with seasonal harvests. Applicants should be allowed to deviate from this requirement if the rationale is plausibly explained and they can substantiated that the evaluated products are representative for the marketed products.
3.1. General requirements	Pen & Tec Consulting	Line 414-415: Suggest to specify that analysis of heavy metals (Pb, Hg, Cd) & Ar are required, and depending on the type of food also data on mycotoxins, PCBs/dioxins & pesticides.
3.2. Single substances and simple mixtures thereof	Food Supplements Europe	Line 425: Should better read: Solubility data in water and other media that are representative of the defined use. Line 427: How should this be expressed? Should there be information on other minor components, such as their identity or quantity?
3.2. Single substances and simple mixtures thereof	FoodDrinkEurope	Lines 428-430: The draft guidance indicates that a complete mass balance should be elaborated for single substances and simple mixtures thereof. We would recommend changing the language to remove the word "complete". While it is true that for these types of ingredients that mass balance should be able to be calculated to close to 100%. However, due to many factors (such as analytical variability) the mass balance for these ingredients may not calculate to 100%. This is reflected in monographs for pure vitamins and minerals that are established by recognized international agencies (such as JECFA or FCC), where the purity is often listed as a range. For example the JECFA monograph for magnesium chloride (INS 511) lists purity from 99.0 to 105.0%. By removing the word "complete", this should temper the expectation that mass balance should always calculate to 100% for these ingredients.
3.2. Single substances and simple mixtures thereof	Nutraveris	L426 Regarding single substances and simple mixture, particle size, shape and distribution are required for their characterization. EFSA should clarify which technics can be used for the assessment of particle size, shape and distribution.
3.2. Single substances and simple mixtures thereof	Pen & Tec Consulting	Line 426: Particle size, shape & distribution are only relevant for solid preparations. Suggest to also specify requirements for liquid preparations, e.g: data on vapour pressure, specific weight & viscosity.

Chapter text	Organisation	Comment text
3.3. Complex mixtures and whole foods	analyze & realize GmbH	The carbohydrate content in foods is often derived by subtracting the sum of the contents [%] in fat, protein, sugars, moisture, insoluble fibres and ash from 100 %. Hence, 'carbohydrates' may contain unidentified substances. Only true analytical data should be considerd for the mass balance, or the meaning of 'carbohydrate' in this context should be specified.
3.3. Complex mixtures and whole foods	Food Safety Authority of Ireland	Line 438 ends with "as low as possible". This sort of ambiguity leads to trouble eventually and so it would be advisable to put a figure on here leaving room for case by case deviation where justified. Line 446 refers to "potential allergens". Unfortunately every food with a protein content could be considered a "potential allergen". Maybe better wording here would be "known allergens"?
3.3. Complex mixtures and whole foods	National Food Agency	p. 13, last para: text referring to proximate composition of whole foods could be combined with the 2nd para on p. 14, covering other nutritional constituents that are relevant, including e.g. fatty acids, sugars, dietary fibre etc. Could be presented in a tabular form with reference to detailed analytical documentation (as annexes). Perhaps also combine with 4. Specifications.
3.4. Stability	analyze & realize GmbH	The rationale for this requirement is understandable, especially with respect to future generic authorizations of food ingredients. But unless applicants for a novel food ingredient and all their possible current and future B2B customers possibly intended to use this ingredient collaborate on the application, it will be difficult for most applicants to provide stability data on the final products. Factors like formulation, processing and packaging may affect the stability of the novel ingredient in the final products. Those technological details are usually not or only partially known to ingredient manufacturers. Future technological progress or changing market interest cannot be anticipated at the time of the application. On the other side, manufacturers of final products are usually reluctant to development and implement products with ingredients that are not yet authorized. It can be expected that ingredient manufacturers provide data for the stability of novel ingredients in model systems representative for their primary intended uses. If a manufacturer of final products wants to use a novel ingredient in a category, for which it is not yet authorized, he may apply for an application extension and provide stability data specific for the novel final product.

Chapter text	Organisation	Comment text
3.4. Stability	CASP	We have evaluated the requirements of Chapter 3. Compositional data that have the lines 361-364: 361 Compositional data and their variability should support the setting of specifications which is 362 representative of the product to be marketed (Section 5). The analytical information should preferably 363 be provided on at least five representative batches of the Traditional Food that have been 364 independently produced (i.e. with independent batches of raw materials). and came to opinion that line 363 are establishing inappropriate burden to applicants especially from SME, because the requirement of analytical information from at least five representative batches is unjustified and is transposing to next Sub-Chapter 3.1. Stability the adoption of the same demand for 5 stability batches for the design of stability studies to be submitted. It is to be noted that this goes even above the pharma requirements for stability studies of medicines, where normally the stability studies are performed with 3 production batches. Also the last IADSA brochure "Stability Testing for the Shelf Life Determination of Food Supplements" is anchoring in Chapter 7.3 Product samples 3 batches: "Ideally, the analyses should be on samples from three consecutive batches"(© IADSA 2016). Finally the valid Scientific Committee on Food GUIDANCE ON SUBMISSIONS FOR SAFETY EVALUATION OF SOURCES OF NUTRIENTS OR OF OTHER INGREDIENTS PROPOSED FOR USE IN THE MANUFACTURE OF FOODS SCF/CS/ADD/NUT/21 Final 12 July 2001 is not requiring such wide documentation of batch stability at all and any precautionary measures to assess the safety of the Novel Food by EFSA under the proposed conditions of use during the authorization procedure should be appropriate to level of risk of traditional foods from third countries, based on a history of safe food use.

Chapter text	Organisation	Comment text
3.4. Stability	ELC - Federation of European Specialty Food Ingredients Industries	Lines 466-468: The draft guidance request to investigate the stability in finished products when the novel food is an ingredient added to other foods. We fully agree that the behaviour of the novel food in finished products should be assessed. However, an ingredient manufacturer cannot test each and every recipe of the targeted finished products. The final food producer needs to check the stability of the novel food as part of the product development phase.
3.4. Stability	Federal Public Service of Health, Food Chain Safety and Environment	Based on our experience of previous applications, no sufficient consideration is given in the dossiers on the oxidative stability of lipids in products rich in fat, particularly unsaturated fat. The Belgian Superior Health Council has elaborated an extensive scientific advice on the oxidative stability of oils, (unfortunately is only available in French http://health.belgium.be/internet2Prd/groups/public/@public/@shc/documents/ie2divers/19067528_fr.pdf and Dutch http://health.belgium.be/internet2Prd/groups/public/@public/@shc/documents/ie2divers/19067528.pdf). Therefore, we recommend the addition of the following sentence (or similar) in section 3.4 STABILITY, at the end of line 465: "For Novel Food rich in unsaturated fat, particular attention should be given to lipid oxidation."
3.4. Stability	Food Law Consult	For evaluation of botanicals the experts working on the EFSA compendium should be involved (e.g. Robert Anton, Ulla Beckman Sundh, Luc Delmulle, Maria Teresa Nogueira, Kirsten Pilegaard, Mauro Serafini) Analytical data is often a real problem. Validated methods don't exist. Labs are not accredited. Reference substances are not available or really expensive. Total extracts of botanicals could be allowed.
3.4. Stability	Food Safety Authority of Ireland	It would be good to know what if anything the applicant adds to the NF to stabilise it in storage or in use, e.g. tocopherols
3.4. Stability	Food Supplements Europe	Lines 466-468: the draft guidance requests to investigate the stability in finished products when the novel food is an ingredient added to other foods. We fully agree that the behavior of the novel food in finished products should be assessed. However, an ingredient manufacturer cannot test each and every recipe of the targeted finished products. The final food producer needs to check the stability of the novel food as part of the product development phase.
3.4. Stability	FoodDrinkEurope	Lines 466-468: The draft guidance request to investigate the stability in finished products when the novel food is an ingredient added to other foods. We fully agree that the behavior of the novel food in finished products should be assessed. However, an ingredient manufacturer cannot test each and every recipe of the targeted finished products. The final food producer needs to check the stability of the novel food as part of the product development phase.

Chapter text	Organisation	Comment text
3.4. Stability	FoodDrinkEurope	Lines 481-483: As indicated in lines 470-472, the specification should cover relevant parameters. Not all contaminants are relevant for all ingredients, therefore we would recommend adding the word "relevant" before contaminants on line 482 to ensure consistency in this section that specifications are not needed for all known contaminants, but rather specifications are needed only for relevant contaminants.
3.4. Stability	Nutraveris	L454-455 Stability study are mandatory to demonstrate the lack of change of the novel food during storage and the absence of any hazard that may arise during storage. EFSA should however clarify the length and the conditions of stability studies. In case of absence of stability studies performed in standard conditions, are stability studies performed in accelerated conditions (higher temperature and humidity) acceptable for EFSA?
3.4. Stability	Schuttelaar & Partners	In case the Novel Food is used as an ingredient, the stability of the processed foods must be investigated. Please note that even within one particular food category, various production processes may be used which might affect the stability of the final product. To what extent is it important for the applicant to be aware of all production processes employed by the final food business operators on its Novel Food ingredient? Would it be sufficient to demonstrate the stability of the Novel Food ingredient under "normal conditions of storage" (line 461-462) and indicate that, under "normal processing methods", the stability of the Novel Food ingredient is not threatened?
3.4. Stability	SYNPA	Lines 466-468: The draft guidance request to investigate the stability in finished products when the novel food is an ingredient added to other foods. We fully agree that the behaviour of the novel food in finished products should be assessed. However, an ingredient manufacturer cannot test each and every recipe of the targeted finished products. The final food producer needs to check the stability of the novel food as part of the product development phase.
3.4. Stability	UK Advisory Committee on Novel Foods and Processes	p14 – From line 353: Currently the approach to stability testing is to test the novel ingredient under a number of storage conditions but not the intended end uses. The Committee questioned whether it was intended for stability data to be required in the full range of uses proposed or just the ones where it could be predicted that stability might be affected. A proportionate approach that does not over-burden applicants undertaking stability testing over a number of years would be preferable. p14 - In line 462 of the EFSA document it would be better that "normal storage" clearly meant "normal storage and use by end consumers". This is to ensure the effects of storage throughout the food chain and normal use by consumers are considered
4. Specifications	Federal Public Service of Health, Food Chain Safety and Environment	Section 4, lines 478 to 483: the specification should include size range of the particles

Chapter text	Organisation	Comment text
4. Specifications	Food Safety Authority of Ireland	Under this section it would be useful to list probable parameters in the case of biological novel foods as opposed to simple chemicals: For example - Protein, Fat, Carbohydrate (sugars), Ash, trace elements etc.
4. Specifications	Food Supplements Europe	Lines 482: We would suggest including the word "relevant" in this sentence before contaminants as indicated earlier in this paragraph, not all contaminants are relevant for all ingredients and it is indicated that a rational for the parameters selected should be provided.
4. Specifications	Intertek Scientifi &Regulatory Consultancy	469 You do not mention here about 5 batches. However this should also be the criteria for testing to specification as well as all contaminants etc. Are 3 batches sufficient? Often prior to approval it is not easy to produce 5 full scale batches and EFSA has accepted 3 in a number of past applications Does it matter whether they are consecutive or non— consecutive?
4. Specifications	Intertek Scientifi &Regulatory Consultancy	482 The guidance is weak on specific criteria for microbiological testing. It could cite the general guidance somewhere in this link from Commission website http://ec.europa.eu/food/food/biosafety/salmonella/microbio_en.htm?
5. History of use of the Novel Food and of its source	IPIFF	Here we have two questions: - It is not entirely clear what the relation is between section 5 and other sections from the guidance document. To what extent will EFSA appreciate a history of use as an indicator of toxicological/allergenic safety? - What types of data will EFSA consider? Is this merely scientifically published data and government reports or also more broadly information/reports indicating a history of use?
5.1. History of the source	Mead Johnson Nutrition	486-491: The Draft Guidance advises the applicant to provide data on the history of use of the source organism, if it is the case. The Draft Guidance should indicate what type of data may be used to establish a history of use (e.g., commercial products databases, official records of approvals by authorities, etc…).
5.1. History of the source	National Food Agency	The first sentence is unclear.
5.1. History of the source	Pen & Tec Consulting	In the case that a food is produced from a micro-organism, fungi or algae the source could also be genetically modified. In this case, we assume additional testing is required following EFSA guidance for GMM. In addition, it should be clear that the food falls within the scope of the NF Regulation & not the GMM regulation (i.e. absence of GMM & rDNA). No reference is made to the EFSA GMM guidance - recommend to include this in the relevant parts (i.e. Section 3, Section 5.1 & Section 9.6.2 in case the micro-organism is QPS but also GMM).
5.1. History of the source	Schuttelaar & Partners	Please clarify the relationship between the data provided in section 5 and the demonstration of safety of the Novel Food. Especially in cases where the source product has a widespread history of safe use, this might indicate a lack of chemical or toxicological risks. To what extent does EFSA follow this line of reasoning and under what conditions is such an argument valid?

Chapter text	Organisation	Comment text
5.1. History of the source	UK Advisory Committee on Novel Foods and Processes	P15 – It would be useful to cross-reference in the history of use section of the guidance that information about the potential to have consumed the novel ingredient in other foods and the impact on the dietary intakes are considered under section 6.3.
5.2. History of use of the Novel Food	ELC - Federation of European Specialty Food Ingredients Industries	Line 496: The draft guidance requests to include, as part of the history of use, the non-food use. We wonder the relevance of such information when the non-food use does not lead to the ingestion of the Novel food (e.g. injected product). We therefore suggest to restrict the non-food use to the ones leading to an ingestion of the product.
5.2. History of use of the Novel Food	Food Supplements Europe	Line 496: the draft guidance requests to include, as part of the history of use, the non-food use. We wonder the relevance of such information when the non food use does not lead to the ingestion of the Novel food (e.g. injected product). We therefore suggest restricting the non food use to the ones leading to an ingestion of the product, including where ingestion may occur as a secondary means of exposure.
5.2. History of use of the Novel Food	FoodDrinkEurope	Line 496: The draft guidance requests to include, as part of the history of use, the non-food use. We wonder the relevance of such information, as in the majority of cases exposure through nonfood u would result in comparatively small internal exposure to the Novel food (meaning what is absorbed into circulation). We therefore suggest to indicate that applicants should consider "relevant-non-food uses", in order to provide more guidance that consideration of exposure should be limited to either those that result in ingestion of the ingredient or significant exposure through a non-oral route. Lines 500-503: would broaden the information required which seems not to be relevant.
5.2. History of use of the Novel Food	Mead Johnson Nutrition	Authorities outside the EU (e.g., Health Canada) allow novel food manufacturers to support the history of use also with non-scientific evidences (e.g., recipe books, history of cuisine, etc...). The Guidance document should provide flexibility with regards to the documentation that can be submitted. 496-499: The Draft Guidance also mentions the non-food applications as part of the history of use of the novel food. While cosmetic applications may provide some insights on the safety of the ingredient and its allergenicity, it appears that data on oral intake provide more significant information for the intended use. The Guidance should acknowledge this factor.
5.2. History of use of the Novel Food	Mission of Chile to the European Union	By wich criteria have been set 25 years as a limit on the income of Novel Food? It should clearly establish the scientific basis for that time. If the food has entered the year 2000 and has a proven consumer without adverse health effects Europe or other markets history, this data is more relevant than time
5.2. History of use of the	National Food Agency	Relevant here?

Chapter text	Organisation	Comment text
Novel Food		
5.2. History of use of the Novel Food	SYNPA	Line 496: The draft guidance requests to include, as part of the history of use, the non-food use. We wonder the relevance of such information when the non-food use does not lead to the ingestion of the Novel food (e.g. injected product). We therefore suggest to restrict the non-food use to the ones leading to an ingestion of the product.
6. Proposed uses and use levels and anticipated intake	UK Advisory Committee on Novel Foods and Processes	P 15 – It is very beneficial that there is a clearer requirement to state the purpose of adding a novel food or ingredient to the food chain. It is an issue that the Committee have struggled with in the past. The purpose or intention behind use of a novel food sets the context of understanding the food safety risks of most relevance and the potential consumer exposure if authorised. This can also be informative in assessing whether a food meets the criteria under the regulation not to be misleading or nutritionally disadvantageous.
6.2. Proposed uses and use levels	AESGP	Line 525 EFSA is kindly requested to clarify the proposed maximum amounts to be specified in case of final product(s) marketed as powder or as concentrates and intended to be consumed as reconstituted following manufacturers' instructions.
6.2. Proposed uses and use levels	Committee "Novel Foods and New Technologies" of the Codex Alimentarius Austriacus Commission	add a footnote in line 523 with a reference to Annex II Part D of Regulation (EG) N°. 1333/2008 – list of food categories
6.2. Proposed uses and use levels	Food Supplements Europe	Line 522: A novel food is not used as food supplement, but as ingredient in any food, including food supplements. When used as an ingredient, this covers food supplements as well as any other type of food not explicitly mentioned. As such this is covered by the second bullet in line 523. We suggest deleting "food supplement" here, as it is not correct.
6.2. Proposed uses and use levels	Mead Johnson Nutrition	525: The proposed maximum amount in the final product should take into account also the reconstitution factor like in the case of infant and follow-on formulas. The applicant should be allowed to propose a maximum amount in the product as consumed.
6.2. Proposed uses and use levels	National Food Agency	The proposed maximum amounts in final product(s), if used as ingredient. Section could be combined with section 6.3.
6.2. Proposed uses and use levels	UK Advisory Committee on Novel Foods and Processes	p15 - The Committee suggests that three additional points should be added to 6.2; the foreseeable misuse of the product, the proposed labelling / risk management measures proposed by the applicant and any measures needed to restrict the product to the target population. While some of these points are not required for the risk assessment, the dossier is an important document for the assessment process and has a wider function.
6.3. Anticipated intake of the Novel Food	Food Supplements Europe	Line 534: There is no need to single out food supplements as this applies to all types of foods.

Chapter text	Organisation	Comment text
6.3. Anticipated intake of the Novel Food	Intertek Scientifi &Regulatory Consultancy	538-548 The FAIM tool is not, in our view, a suitable tool for assessing the exposure to a novel food/ingredient. The FAIM tool is an exposure assessment tool which was specifically developed to support the calculation of food additive exposure estimates and to harmonise the submission of the related data by industry. The food classification system has been specifically developed to consider the applications of food additives, and the relevant functionality of these food improvement agents. It is not considered that these food categories would ever truly be relevant for the applications of novel foods/ ingredients, which are typically functional ingredients, which are used in specific foods with specific labels. The food uses are not akin to the applications of specific food additive categories (e.g. antioxidants, thickeners) whereby indirect consumption may be significant and must be considered in the exposure assessment model. In addition, as described in the 'FAIM – Instructions for use' document as circulated by the FIP unit in September 2012, the level of detail available on foods in the FoodEx nomenclature did not always match the exact description of the food item as identified in Regulation (EU) No 1129/2011 (with some item descriptions being identified to be too precise, or others which were not distinguishable), as a result, some food groups could not be presented in the FAIM template. Although it is important that the screening tool considers the maximum exposure level of the entire population, we feel that on the basis of the points above, the FAIM tool is not suited for this specific purpose. As such, we believe that the guidance should be amended so that Tier 1 is clearly identified as the EFSA Comprehensive Database. The food categories available in this database, particularly in the more recent release considering the more refined categories (i.e. Level 3 and 4). We agree with the approach of including the reference to calculations based on individual data from national food consumptions surveys as Tier 2, as required. In the case of novel foods intended for consumption by infants, we consider that an ad hoc assessment should be performed, which considers the worst case scenario of exposure. The guidance should be amended to indicate this. Reference here should be given to EFSA's latest opinion Guidance on selected default values to be used by the EFSA Scientific Committee, Scientific Panels and Units in the absence of actual measured dat. Here default bodyweights for example are given for different population groups. http://www.efsa.europa.eu/en/efsajournal/pub/2579
6.3. Anticipated intake of the Novel Food	IPIFF	We are somewhat worried that using the principles of the FAIM tool as intake assessment will widely overestimate the anticipated intake of the Novel Food. For the example of e.g. cricket-meal there will be various food categories which can include this Novel Food ingredient. However, each of these applications will merely exist as a small-scale 'alternative' to pre-existing products (e.g. alternative energy bar, alternative burger, etc.). This means that even a person who is a high-level consumer of one of these food categories will only rarely eat a product which includes insects. Most consumers will occasionally eat one insect-product without consuming any other. This seems to be difficult to capture using (the principles of) the FAIM tool.

Chapter text	Organisation	Comment text
6.3. Anticipated intake of the Novel Food	Mead Johnson Nutrition	538-548: The Draft Guidance recommends the use of the EFSA Food Additive Intake Model (FAIM) tool for establishing the anticipate intake of the Novel Food. The model does not capture infant formulae as these products are considered sole source of nutrition. The Draft Guidance should also consider this case.
6.4. Combined intake from multiple sources	ELC - Federation of European Specialty Food Ingredients Industries	Lines 577-582: For the assessment of intake, the draft guidance requests the inclusion of intake from other uses. In line with our comments on line 496, we believe that only non-food use leading to ingestion of the novel food should be taken into account.
6.4. Combined intake from multiple sources	Food Safety Authority of Ireland	Lines 584 and 585 mention potential intake of a novel ingredient from consumer products including cosmetics and pharmaceuticals. This has never been considered for novel food exposure up to now and should not because pharmaceuticals/medicines legislation is separate and inconsistent with food legislation in most EU Member States. If an ingredient is a medicine (pharmaceutical) then it cannot automatically be a food also. In the case of cosmetics, they are not ingested per se and so only exposure via the oral route can be considered for a novel food assessment. If cosmetics are considered for exposure then the whole area of environmental exposure should also be included and it becomes unworkable and even unfair to the food industry.
6.4. Combined intake from multiple sources	Food Supplements Europe	Lines 577-582: for the assessment of the intake, the draft guidance requests to include the intake from other uses. In line with our comments on line 496, we believe that only other uses that lead to the intentional ingestion of the novel food should be taken into account.
6.4. Combined intake from multiple sources	FoodDrinkEurope	Lines 577-582: For the assessment of the intake, the draft guidance requests to include the intake from other uses. In line with our comments on line 496, we believe that only relevant nonfood exposure leading to significant internal exposure to the novel food should be taken into account. Lines 584-586: When considering exposure from potential non-dietary sources, it is important to consider internal exposure, and thus allow for adjustment factors when the non-dietary exposures to ingredients are less bioavailable than oral exposure. For example, when considering dermal exposure to a food ingredient through a non-food source, applicants should be able to reduce calculated exposure if there is sufficient rationale that the ingredient is not bioavailable through that exposure route.

Chapter text	Organisation	Comment text
6.4. Combined intake from multiple sources	Intertek Scientifi &Regulatory Consultancy	579 Whilst we agree with the section, we believe EFSA should have clear rules about the summation of the values from different uses. For example it is very unrealistic to assume a 95th percentile consumer of foods (eg 5 maximum servings a day) would also consume maxuimum dose supplements on the same day, every day. Using the mean values from food use would be more realistic. We also propose that EFSA prepares basic guide to understanding intakes for the member state competent authorities, to avoid over-regulation and unnecessary warning labels etc.
6.4. Combined intake from multiple sources	IPIFF	Where pre-existing intake of the Novel Food should be provided, it is somewhat unclear to what extent the food which has a pre-existing intake should be exactly equivalent to the Novel Food. For example, to what extend is the generic protein intake relevant when applying for the authorisation of a novel source of proteins?
6.4. Combined intake from multiple sources	National Food Agency	6.4. proposed new wording for heading: "Combined intake from novel food and other sources"
6.4. Combined intake from multiple sources	Schuttelaar & Partners	To what extent do foods closely related to the Novel Food that is applied for need to be taken into consideration when outlining the existing intake of the Novel Food? Is only the exact product as outlined in section 4 relevant or also closely related products? (e.g. protein concentrate when applying for a protein isolate or animal protein when applying for a vegetable protein)
6.4. Combined intake from multiple sources	Schuttelaar & Partners	To what extend does it matter whether a Novel Food will replace an existing intake of the Novel Food or be an additional source thereof? Are different arguments in each of these situations necessary to demonstrate safety and/or the lack of a disadvantage to the consumer?
6.4. Combined intake from multiple sources	SYNPA	Lines 577-582: For the assessment of intake, the draft guidance requests the inclusion of intake from other uses. In line with our comments on line 496, we believe that only non-food use leading to ingestion of the novel food should be taken into account.

Chapter text	Organisation	Comment text
6.5. Estimate of exposure to undesirable substances	FoodDrinkEurope	Lines 588-594: We agree that exposure estimates to undesirable substances should also follow a similar approach as the intake estimate of the Novel Food, such as considering anticipated exposure for average and high (typically 95th percentile) consumers. Additionally, if applicants have information pertaining to the range in concentrations that the undesirable substance are present in the Novel Food, they should be able to consider this in their assessments of these substances. The concentration of the Novel Food that consumers are exposed to can be tightly controlled by food manufacturers through quality processes and procedures, which makes the exposure assessment relatively simple. However, some undesirable substances (such as naturally occurring contaminants like mycotoxins or heavy metals that could be present in some foods) will be present at concentrations that vary somewhat from lot-to-lot of the Novel Food. If there is significant data available on the occurrence of these substances in the Novel Food, applicants should be able to use this data when conducting their exposure assessment. Probabilistic approaches that utilize this type of information have been supported previously by EFSA, such as in the EFSA Guidance on the Use of Probabilistic Methodology for Modelling Dietary Exposure to Pesticide Residues.
6.6. Precautions and restrictions of use	Mead Johnson Nutrition	596-599: As labeling is an effective risk management measure, the applicant should be allowed to propose specific wording in the application.
6.6. Precautions and restrictions of use	UK Advisory Committee on Novel Foods and Processes	p17 – The Committee commented that in the past post-market monitoring has been a useful tool to consider the long term effects of new innovations in food entering the EU market. In this section it would be beneficial for applicants to be asked to include any plans for post-market monitoring.

Chapter text	Organisation	Comment text
7. Absorption, distribution, metabolism, and excretion (ADME)	Eurogroup for Animals	Definitions: Include the definition on 'whole foods'. It is mentioned on line 730. Suggestion: "'whole food" refers to a product to be consumed by humans which is composed of a multitude (up to thousands) of individual substances. Whole food range from plant based products such as maize or potatoes to more refined products such as fruit juices or flour, to foods consisting of microorganisms as well as animal-derived food products such as meat and milk.' from EFSA Scientific Committee; 2011. EFSA guidance on conducting repeated-dose 90-day oral toxicity study in rodents on whole food/feed. EFSA Journal 2011;9(12):2438 General Principles: 257/258 - Include an extra bullet pt : Information on Foods which contain substances or mixtures that are used for other applications than food (cosmetics, chemicals, pharma) which are relevant to the data requirements for Novel foods should be sourced and provided, in particular vertebrate studies, to avoid duplication of animal testing according to Rec 32 of Regulation 2015/2283. Line 265: In accordance with Directive 2010/63/EU... Remove the '4' and replace it as a superscropt for the footnote. Also delete the words' experimental and other' as the Directive 2010/63/EU's title is ' on the protection of animals used for scientific purposes'. Line 267: include in the wording: '...replaced, reduced or refined and duplication of animal testing should be avoided, where possible'. This text is in line with Recital 32 of Reg 2015/2283 Organisation and content of the notification: Line 294; remove extra '.' 2. Production Process Line 388 - 390: change the wording to '...;the breeding, rearing, feeding, housing, farming conditions and slaughter for farmed animals...'. Also remove the word 'living (L389) as it is repetition. 7. Absorption, distribution, metabolism and excretion (ADME) Line 604: with reference to 'animal models' makes it appear an animal model has to be used. It would be best to change the wording to ' ..selection of the appropriate model' or '...the selection of the appropriate (animal or non-animal) model. Line 606: suggested change of wording to include: ' ...differences between in vitro methods, experimental animals and humans' (even for nano the scientific committee guidance (L875 - 877) includes in vitro methods) Line 628: Is there an error in the Reference given here. The document referenced EFSA SC guidance on RA of the application of nanoscience and nanotechnologies is not EFSA, 2010b as stated here, but rather EFSA 2011a 9.3 Subchronic toxicity

Chapter text	Organisation	Comment text
		Line 719: Include wording: 'Decisions on whether tests are necessary need to be considered in light of the data already available. Comment on 90 day study requirement: There is prevailing sceintific uncertainty with regard to the determination of the necessity of the 90 day feeding trials. EFSA has previously called for case-by-case decisions. (references: Contrary to the announced mandatory requirement for 90-day rodent feeding studies, all guidance documents of the European Food Safety Authority (EFSA) relating to the risk assessmentof GM food and feed advise consideration of the performance of such studies under specific circumstances, determined on a case-by-case basis. EFSA (2011) Guidance for RA of food and feed from GM plants. EFSA Journal 9, 2150 + EFSA (2012) Guidance on the RA of food and feed from GM animals. EFSA Journal 10, 2501 + U.G Sauer & K.A Reid ATLA 40, 183–1 + FP7 GRACE Line 746: EOGRT (OECD 443) not 2 generation testing (OECD 416) as with other EU regulatory requirements. Line 781: reference OECD nano read-across http://www.oecd.org/officialdocuments/publicdisplaydocumentpdf/?cote=env/jm/mono(2016)3&doclanguage=en Line 831: include - ' ...results from in vitro, animal and human studies'

Chapter text	Organisation	Comment text
7. Absorption, distribution, metabolism, and excretion (ADME)	Intertek Scientifi &Regulatory Consultancy	625 We would recommend an explanation in here that is is nano as consumed that is important for this risk assessment. Many people do not understand this point. For example they may be prepared in nano form top aid dispersal before dissolving or swelling or agglomeration. This point especially applies, one would assume, to mineral forms. If they are salts they will dissolve in most cases.
7. Absorption, distribution, metabolism, and excretion (ADME)	National Food Agency	"Toxico" could be deleted and only "kinetics" used, since this should also cover general aspects of nutrient metabolism, as mentioned.
7. Absorption, distribution, metabolism, and excretion (ADME)	Nutraveris	L614-621 ADME data can be obtained for simple compounds. However, for novel food made from plants, ADME data is difficult, or impossible, to obtain. EFSA should clarify the ADME data required for novel food consisting of, isolated from or produced from microorganisms, fungi or algae, plants and their parts, or from animals and their parts, or from cell culture and tissue culture. Is one marker per organism sufficient to evaluate ADME (with the most relevant marker) or do other markers need to be assessed? Moreover, EFSA should take into account the difficulty in assessing ADME data when working on plants and other complex organisms.
8. Nutritional information	analyze & realize GmbH	Line 634/635: As much as such information is desirable, it will be challenging to provide it, especially for food ingredients (see our comments in section 3.4). Line 636/637: This request should be limited to novel foods that are dedicated to suppressing absorption or modifying bioavailability, or are known to contain physiologically relevant amounts of the respective compounds. For most novel foods or novel food ingredients, an assessment of possible anti-nutritional factors in the novel food beyond the toxicological evaluation would require extensive animal and human studies. Several health claim applications demonstrated how difficult it is to prove that the in-vitro inhibitory activity of a food/ingredient is of physiological relevance. Physiologically relevant inhibition of absorption or decreased bioavailability of nutrients due to interaction with the novel food will most likely be revealed by the 90-days oral toxicity study. If such compounds are present in the novel food/ingredient, an appropriate margin of safety may protect consumers.
8. Nutritional information	Committee "Novel Foods and New Technologies" of the Codex Alimentarius Austriacus Commission	replace „Nutritional Information" by a more suitable chapter heading
8. Nutritional information	ELC - Federation of European Specialty Food Ingredients Industries	Line 635: The draft guidance requests detail of the nutritional information relating to the Novel Food, "taking into account influences of […] further processing, handling and cooking". When the novel food is an ingredient added to other foods the ingredient manufacturer cannot test each and every recipe of the targeted finished products. The final food producer needs to check the nutritional information on his product.

Chapter text	Organisation	Comment text
8. Nutritional information	Food Law Consult	Line 630: In regard to the nutritional information, we read that info on the "anti-nutritional factors" needs to be provided. More explanation? Because as an example the "modification of bioavailability" is given. We see more molecules, like lysosomes or phytosomes. These are combinations of active ingredients dispersed into lecithin. This would increase the bioavailability of the botanical or other substances. If a combination of 2 different substances would change the bioavailability wouldn't EFSA miss this in its evaluation of the ingredient? (e.g. phytosomes, increased bioavailability)
8. Nutritional information	Food Supplements Europe	Line 651: In line with avoiding unnecessary animal testing, it would be good to indicate here that new animal testing should be kept to the minimum and should not be carried out when alternative validated methods and recognized risk assessment models are available. Here and also in the following section (lines 659-681), it should be clearly emphasized that alternative approaches to animal testing for the filling of toxicological data gaps should be the preferred options and should be encouraged in place of animal testing.
8. Nutritional information	National Food Agency	Aspects of bioavailability should be covered. It is unclear what information the applicant should include with respect to "cooking". Suggest to delete and only mention "processing" possibly handling as well. Changes during cooking is outside the scope.
8. Nutritional information	SYNPA	Line 635: The draft guidance requests detail of the nutritional information relating to the Novel Food, "taking into account influences of […] further processing, handling and cooking". When the novel food is an ingredient added to other foods the ingredient manufacturer cannot test each and every recipe of the targeted finished products. The final food producer needs to check the nutritional information on his product.

Chapter text	Organisation	Comment text
9. Toxicological information	Eurogroup for Animals	Definitions: Include the definition on 'whole foods'. It is mentioned on line 730. Suggestion: "'whole food" refers to a product to be consumed by humans which is composed of a multitude (up to thousands) of individual substances. Whole food range from plant based products such as maize or potatoes to more refined products such as fruit juices or flour, to foods consisting of microorganisms as well as animal-derived food products such as meat and milk.' from EFSA Scientific Committee; 2011. EFSA guidance on conducting repeated-dose 90-day oral toxicity study in rodents on whole food/feed. EFSA Journal 2011;9(12):2438 General Principles: 257/258 - Include an extra bullet pt : Information on Foods which contain substances or mixtures that are used for other applications than food (cosmetics, chemicals, pharma) which are relevant to the data requirements for Novel foods should be sourced and provided, in particular vertebrate studies, to avoid duplication of animal testing according to Rec 32 of Regulation 2015/2283. Line 265: In accordance with Directive 2010/63/EU... Remove the '4' and replace it as a superscropt for the footnote. Also delete the words' experimental and other' as the Directive 2010/63/EU's title is ' on the protection of animals used for scientific purposes'. Line 267: include in the wording: '...replaced, reduced or refined and duplication of animal testing should be avoided, where possible'. This text is in line with Recital 32 of Reg 2015/2283 Organisation and content of the notification: Line 294; remove extra '.' 2. Production Process Line 388 - 390: change the wording to '...;the breeding, rearing, feeding, housing, farming conditions and slaughter for farmed animals...'. Also remove the word 'living (L389) as it is repetition. 7. Absorption, distribution, metabolism and excretion (ADME) Line 604: with reference to 'animal models' makes it appear an animal model has to be used. It would be best to change the wording to ' ..selection of the appropriate model' or '...the selection of the appropriate (animal or non-animal) model. Line 606: suggested change of wording to include: ' ...differences between in vitro methods, experimental animals and humans' (even for nano the scientific committee guidance (L875 - 877) includes in vitro methods) Line 628: Is there an error in the Reference given here. The document referenced EFSA SC guidance on RA of the application of nanoscience and nanotechnologies is not EFSA, 2010b as stated here, but rather EFSA 2011a 9.3 Subchronic toxicity

Chapter text	Organisation	Comment text
		Line 719: Include wording: 'Decisions on whether tests are necessary need to be considered in light of the data already available. Comment on 90 day study requirement: There is prevailing sceintific uncertainty with regard to the determination of the necessity of the 90 day feeding trials. EFSA has previously called for case-by-case decisions. (references: Contrary to the announced mandatory requirement for 90-day rodent feeding studies, all guidance documents of the European Food Safety Authority (EFSA) relating to the risk assessmentof GM food and feed advise consideration of the performance of such studies under specific circumstances, determined on a case-by-case basis. EFSA (2011) Guidance for RA of food and feed from GM plants. EFSA Journal 9, 2150 + EFSA (2012) Guidance on the RA of food and feed from GM animals. EFSA Journal 10, 2501 + U.G Sauer & K.A Reid ATLA 40, 183–1 + FP7 GRACE Line 746: EOGRT (OECD 443) not 2 generation testing (OECD 416) as with other EU regulatory requirements. Line 781: reference OECD nano read-across http://www.oecd.org/officialdocuments/publicdisplaydocumentpdf/?cote=env/jm/mono(2016)3&doclanguage=en Line 831: include - ' ...results from in vitro, animal and human studies'
9. Toxicological information	Food Law Consult	660 – Toxicology Studies will most probably be too expensive for SME's. So big companies are favored. This is market disturbance, unfair competition.
9. Toxicological information	Mission of Chile to the European Union	The documents presented are very similar to a dossier presented for evaluation of a drug (with therapeutic action). Is it understandable that kind of toxic kinetic requirements (which is part of a pharmacokinetic evaluation) in a food? What models should take? Is there a standard for food? Evaluation criteria should be reviewed.
9.1. General considerations	ELC - Federation of European Specialty Food Ingredients Industries	Line 668/9 and section 9.1 Lines 668/9 makes it clear that the need for toxicity studies is dependent on the specific characteristics of the novel food. This fundamental evaluation clearly proceeds questions of how eventual tests should be carried out. Lines 668-681 should therefore logically precede lines 660-67. In addition, this approach is, in our view, more clearly and helpfully articulated in the three scenarios set out section 3.7 of existing Commission Recommendation 97/618/EC. The Panel should consider reintroducing these scenarios into the guidance for clarity.

Chapter text	Organisation	Comment text
9.1. General considerations	Food Safety Authority of Ireland	There may be a typographical error here in line 664. To make sense it should read .....used for the toxicological studies is not representative of the novel food and.....
9.1. General considerations	Food Supplements Europe	Line 659: The comment relating to substantial equivalence as entry point should be reiterated here. Line 668: We very much welcome the statement that the Panel notes that all relevant knowledge on the Novel Food should be considered in order to make decisions on whether and which toxicity studies are necessary. This indicates that not in all cases a full toxicological evaluation is required, which remains in line with the basis of the current 1997 guidance. We believe nevertheless that this could be better clarified. Indeed, as the new novel foods Regulation does no longer have a notification procedure for novel foods that can be demonstrated to be substantially equivalent to existing foods. The new provisions of Regulation 2015/2283 replace the applicant-linked authorisation system with a Union list of approved novel foods. This list is specifically intended to avoid many such foods having to follow the authorisation procedure. However, certain foods may still have to go through the full procedure despite being substantially equivalent to a traditional food with a long history of safe use. It is noted that in the previous guidance by the Scientific Committee for Food, which deals with data requirements applicable to a full novel foods assessment, demonstration of substantial equivalence was taken as the first tier for the toxicological approach. The guidance identified three scenarios in establishing the need for the provision of toxicological data: 1. Substantial equivalence can be established to an accepted traditional food or food ingredient, in which case no further testing is needed; 2. Substantial equivalence can be established except for a single or few specific traits of the NF, in which case any further assessment of safety should focus specifically on these traits; 3. Neither partial nor total substantial equivalence can be established; in this case, the wholesomeness of the whole novel food or macronutrient has to be assessed using an appropriate combined nutritional-toxicological approach. It states that if substantial equivalence to a traditional counterpart cannot be established the wholesomeness assessment has to take into account not only knowledge of the identity, chemical structure and physico-chemical properties of the Novel Food but also aspects such as source, composition, potential intake based on the proposed use in the general diet, the potential exposure of particularly vulnerable population groups, and the likely effects of processing. The greater the predicted dietary exposure the more extensive the required toxicological testing programme will have to be. This is missing now from the proposed guidance and we would strongly recommend that this principle is retained. It is a proportionate approach if to first see to what extent a novel food is substantially equivalent to an existing non-novel food in order to avoid needless sacrifice of laboratory animals, in line with the statements in line 265-269.

Chapter text	Organisation	Comment text
		This would be similar to the exception to undertake an exhaustive safety assessment for strains of micro-organisms that are on the QPS list (lines 762-765). It is noted that substantial equivalence of the end product is also a major important factor for applications relating to novel food processes. Further guidance on how substantial equivalence can reduce the need for toxicological and other testing could be developed by EFSA.
9.1. General considerations	Intertek Scientifi &Regulatory Consultancy	659 There is no mention of tolerability data. This is something that needs discussing specifically for novel foods as many of these ingredients are macoringredients such as saccharides. It is covered under the additives guidance, which is referred to here but probably a special mention is needed as it applies to novel foods more than for additives.
9.1. General considerations	Mead Johnson Nutrition	660-661: Throughout the entire document, but in particular in the toxicological information section, the Draft Guidance reiterates the importance of carrying out safety studies with a representative material of the novel food. It is industry experience that between the R&D and commercialization phase several years may pass, while at the R&D stage some safety studies are already performed. In particular, the scale up from the pilot to the manufacturing plant may trigger some variations in the ingredient composition. With the aim of reducing animal studies, the Guidance should consider as representative materials, compounds which although slightly different in composition, are manufactured with the same production process.
9.1. General considerations	SYNPA	Line 668/9 and section 9.1 Lines 668/9 makes it clear that the need for toxicity studies is dependent on the specific characteristics of the novel food. This fundamental evaluation clearly proceeds questions of how eventual tests should be carried out. Lines 668-681 should therefore logically precede lines 660-67. In addition, this approach is, in our view, more clearly and helpfully articulated in the three scenarios set out section 3.7 of existing Commission Recommendation 97/618/EC. The Panel should consider reintroducing these scenarios into the guidance for clarity.
9.2. Genotoxicity	Nutraveris	L703-708 EFSA indicates that in vitro tests should be performed to assessed genotoxicity. For clarification, EFSA should indicate which test are recommended to assess the genotoxicity of novel foods. Moreover, can EFSA indicate the approach to be followed when such tests are not feasible, as for instance when adequate concentration cannot be reached due to precipitation of the test compound?

Chapter text	Organisation	Comment text
9.2. Genotoxicity	Pen & Tec Consulting	Line 704-705: Instead of referring to all the relevant horizontal guidance documents suggest to include which test EFSA is actually referring to - this will help applicants that are not familiar with preparing EFSA dossiers. For example: "A bacterial reverse mutation test (OECD TG 471) & an in vitro mammalian cell micronucleus test (OECD TG 487) are recommended as a first step. This combination of tests fulfils the basic requirements to cover the three genetic endpoints with the minimum number of tests; the bacterial reverse mutation assay covers gene mutations and the in vitro micronucleus test covers both structural and numerical chromosome aberrations. Follow-up approaches in the event of positive results, recommendations on test types ... are described in detail in the Opinion of the Scientific Committee (EFSA SC, 2011b).
9.3. Subchronic toxicity	Eurogroup for Animals	Definitions: Include the definition on 'whole foods'. It is mentioned on line 730. Suggestion: "'whole food" refers to a product to be consumed by humans which is composed of a multitude (up to thousands) of individual substances. Whole food range from plant based products such as maize or potatoes to more refined products such as fruit juices or flour, to foods consisting of microorganisms as well as animal-derived food products such as meat and milk.' from EFSA Scientific Committee; 2011. EFSA guidance on conducting repeated-dose 90-day oral toxicity study in rodents on whole food/feed. EFSA Journal 2011;9(12):2438 General Principles: 257/258 - Include an extra bullet pt : Information on Foods which contain substances or mixtures that are used for other applications than food (cosmetics, chemicals, pharma) which are relevant to the data requirements for Novel foods should be sourced and provided, in particular vertebrate studies, to avoid duplication of animal testing according to Rec 32 of Regulation 2015/2283. Line 265: In accordance with Directive 2010/63/EU... Remove the '4' and replace it as a superscropt for the footnote. Also delete the words' experimental and other' as the Directive 2010/63/EU's title is ' on the protection of animals used for scientific purposes'. Line 267: include in the wording: '...replaced, reduced or refined and duplication of animal testing should be avoided, where possible'. This text is in line with Recital 32 of Reg 2015/2283 Organisation and content of the notification: Line 294; remove extra '.' 2. Production Process Line 388 - 390: change the wording to '...;the breeding, rearing, feeding, housing, farming conditions and slaughter for farmed animals...'. Also remove the word 'living (L389) as it is repetition. 7. Absorption, distribution, metabolism and excretion (ADME)

Chapter text	Organisation	Comment text
		Line 604: with reference to 'animal models' makes it appear an animal model has to be used. It would be best to change the wording to ' ..selection of the appropriate model' or '...the selection of the appropriate (animal or non-animal) model. Line 606: suggested change of wording to include: ' ...differences between in vitro methods, experimental animals and humans' (even for nano the scientific committee guidance (L875 - 877) includes in vitro methods) Line 628: Is there an error in the Reference given here. The document referenced EFSA SC guidance on RA of the application of nanoscience and nanotechnologies is not EFSA, 2010b as stated here, but rather EFSA 2011a 9.3 Subchronic toxicity Line 719: Include wording: 'Decisions on whether tests are necessary need to be considered in light of the data already available. Comment on 90 day study requirement: There is prevailing sceintific uncertainty with regard to the determination of the necessity of the 90 day feeding trials. EFSA has previously called for case-by-case decisions. (references: Contrary to the announced mandatory requirement for 90-day rodent feeding studies, all guidance documents of the European Food Safety Authority (EFSA) relating to the risk assessmentof GM food and feed advise consideration of the performance of such studies under specific circumstances, determined on a case-by-case basis. EFSA (2011) Guidance for RA of food and feed from GM plants. EFSA Journal 9, 2150 + EFSA (2012) Guidance on the RA of food and feed from GM animals. EFSA Journal 10, 2501 + U.G Sauer & K.A Reid ATLA 40, 183–1 + FP7 GRACE Line 746: EOGRT (OECD 443) not 2 generation testing (OECD 416) as with other EU regulatory requirements. Line 781: reference OECD nano read-across http://www.oecd.org/officialdocuments/publicdisplaydocumentpdf/?cote=env/jm/mono(2016)3&doclanguage=en Line 831: include - ' ...results from in vitro, animal and human studies'
9.3. Subchronic toxicity	IPIFF	It could be clarified to what extend and in which situations in vivo or in silico studies can be used instead of 90 days rodent tests.

Chapter text	Organisation	Comment text
9.3. Subchronic toxicity	Mead Johnson Nutrition	719-729: The Draft Guidance recommends the use of 90 days (OECD TG 408) oral study in rodents modified as to include assessment of the parameters of the repeated-dose 28-day toxicity study in rodents (OECD TG 408). While these models are pertinent for adult population, they may not apply as well to infants and young children populations, whose physiological processes differ from adults in some instances). Appropriate animal models that address differences in the safety profile for neonatal animals compared to adults should be used to best properly characterize safety for infants and young children. The neonatal pig is a well-established model for studying infant formula nutrient interactions (Herfel et al., 2009) and has also been identified as an appropriate model for safety testing of substances in infant formula (Flamm, 2013; IOM, 2004). The piglet serves as an appropriate animal model for assessing safety for the infant based upon: 1) Direct application and relevance pertaining to nutritional requirements, gastrointestinal function, immunological development, and respiratory function in comparison to the juvenile human; 2) Similarity with human infant digestive physiology and nutrient requirements; 3) Similarities in the metabolic functions, intestinal transport times, and characteristics of absorption of nutrients, all of which have made them useful in basic nutritional research (Herfel et al., 2009). JECFA recently accepted the neonatal piglet model to assess the safety of additives (i.e., carrageenan, OSA-Modified Starch and pectin) for use in infant (0-12 weeks of age) formula (Mahadevan, Thorsrud, Brorby, & Ferguson, 2014; Weiner et al., 2015). References Flamm, E. G. (2013). Neonatal animal testing paradigms and their suitability for testing infant formula. Toxicology Mechanisms and Methods, 23(2), 57-67. doi: 10.3109/15376516.2012.725108 Herfel, T. M., Jacobi, S. K., Lin, X., Walker, D. C., Jouni, Z. E., & Odle, J. (2009). Safety evaluation of polydextrose in infant formula using a suckling piglet model. Food and Chemical Toxicology, 47(7), 1530-1537. doi: http://dx.doi.org/10.1016/j.fct.2009.03.039 IOM. (2004). Testing ingredients with preclinical studies. In: Infant Formula: Evaluating the Safety on New Ingredients Infant Formula: Evaluating the Safety of New Ingredients. Washington (DC): The National Academy Press. Mahadevan, B., Thorsrud, B. A., Brorby, G. P., & Ferguson, H. E. (2014). A 3-week dietary safety study of octenyl succinic anhydride (OSA)-modified starch in neonatal farm piglets. Food Chem Toxicol, 72, 83-89. doi:

Chapter text	Organisation	Comment text
		10.1016/j.fct.2014.07.009 Weiner, M. L., Ferguson, H. E., Thorsrud, B. A., Nelson, K. G., Blakemore, W. R., Zeigler, B., . . . Mahadevan, B. (2015). An infant formula toxicity and toxicokinetic feeding study on carrageenan in preweaning piglets with special attention to the immune system and gastrointestinal tract. Food and Chemical Toxicology, 77, 120-131. doi: http://dx.doi.org/10.1016/j.fct.2014.12.022
9.3. Subchronic toxicity	Schuttelaar & Partners	Currently it is not very clear to what in vivo or in silico studies can be used instead of 90 days rodent tests. Does EFSA have specific conditions in mind when such an alternative study would be appropriate?
9.3. Subchronic toxicity	UK Advisory Committee on Novel Foods and Processes	P 19 – Currently a tiered approach to toxicological risk assessment is used, starting with a 28 day study which informs whether further testing is required. The Committee support the tiered approach suggested in the guidance but therefore questioned why a 90 day sub chronic toxicity study should become the standard tool for assessing toxicological risks.

Chapter text	Organisation	Comment text
9.5. Reproductive and developmental toxicity	Eurogroup for Animals	Definitions: Include the definition on 'whole foods'. It is mentioned on line 730. Suggestion: "'whole food" refers to a product to be consumed by humans which is composed of a multitude (up to thousands) of individual substances. Whole food range from plant based products such as maize or potatoes to more refined products such as fruit juices or flour, to foods consisting of microorganisms as well as animal-derived food products such as meat and milk.' from EFSA Scientific Committee; 2011. EFSA guidance on conducting repeated-dose 90-day oral toxicity study in rodents on whole food/feed. EFSA Journal 2011;9(12):2438 General Principles: 257/258 - Include an extra bullet pt : Information on Foods which contain substances or mixtures that are used for other applications than food (cosmetics, chemicals, pharma) which are relevant to the data requirements for Novel foods should be sourced and provided, in particular vertebrate studies, to avoid duplication of animal testing according to Rec 32 of Regulation 2015/2283. Line 265: In accordance with Directive 2010/63/EU... Remove the '4' and replace it as a superscropt for the footnote. Also delete the words' experimental and other' as the Directive 2010/63/EU's title is ' on the protection of animals used for scientific purposes'. Line 267: include in the wording: '...replaced, reduced or refined and duplication of animal testing should be avoided, where possible'. This text is in line with Recital 32 of Reg 2015/2283 Organisation and content of the notification: Line 294; remove extra '.' 2. Production Process Line 388 - 390: change the wording to '...;the breeding, rearing, feeding, housing, farming conditions and slaughter for farmed animals...'. Also remove the word 'living (L389) as it is repetition. 7. Absorption, distribution, metabolism and excretion (ADME) Line 604: with reference to 'animal models' makes it appear an animal model has to be used. It would be best to change the wording to ' ..selection of the appropriate model' or '...the selection of the appropriate (animal or non-animal) model. Line 606: suggested change of wording to include: ' ...differences between in vitro methods, experimental animals and humans' (even for nano the scientific committee guidance (L875 - 877) includes in vitro methods) Line 628: Is there an error in the Reference given here. The document referenced EFSA SC guidance on RA of the application of nanoscience and nanotechnologies is not EFSA, 2010b as stated here, but rather EFSA 2011a 9.3 Subchronic toxicity

Chapter text	Organisation	Comment text
		Line 719: Include wording: 'Decisions on whether tests are necessary need to be considered in light of the data already available. Comment on 90 day study requirement: There is prevailing sceintific uncertainty with regard to the determination of the necessity of the 90 day feeding trials. EFSA has previously called for case-by-case decisions. (references: Contrary to the announced mandatory requirement for 90-day rodent feeding studies, all guidance documents of the European Food Safety Authority (EFSA) relating to the risk assessmentof GM food and feed advise consideration of the performance of such studies under specific circumstances, determined on a case-by-case basis. EFSA (2011) Guidance for RA of food and feed from GM plants. EFSA Journal 9, 2150 + EFSA (2012) Guidance on the RA of food and feed from GM animals. EFSA Journal 10, 2501 + U.G Sauer & K.A Reid ATLA 40, 183–1 + FP7 GRACE Line 746: EOGRT (OECD 443) not 2 generation testing (OECD 416) as with other EU regulatory requirements. Line 781: reference OECD nano read-across http://www.oecd.org/officialdocuments/publicdisplaydocumentpdf/?cote=env/jm/mono(2016)3&doclanguage=en Line 831: include - ' ...results from in vitro, animal and human studies'

Chapter text	Organisation	Comment text
9.6.1. Insects	IPIFF	As indicated in the separately communicated IPIFF document "Insect products as a safe addition to consumer diets", we concluded that the EFSA scientific committee report "Risk profile related to production and consumption of insects as food and feed" indicates that insects carry no additional biological or chemical risks compared to other sources of proteins under the condition that insects are fed on vegetal substrates and processed under good hygiene conditions. To what extent does the EFSA Panel on Dietetic Products, Nutrition and Allergies take over these outcomes? In other words: to what extent does the fact that a producer uses vegetal substrates and complies with additional quality management systems and certification schemes (e.g. ISO 9001 and GMP+) imply that detailed toxicological analysis may not be necessary due to negligible toxicological risks associated with the Novel Food product?
9.6.1. Insects	Snow Pony Ltd	9.6.1 Insects - Procedure for licence needs to be a straight forward process and cost effective for suppliers of edible insects such as ourselves.
9.6.2. Microorganisms	ELC - Federation of European Specialty Food Ingredients Industries	Lines 754-777: ELC agrees that there is a need for a thorough safety assessment of the microorganism when the microorganism is present in the final food. However, in case the microorganism serves only as production vehicle and is not present in the final food we believe that there is no need for a full safety assessment e.g. testing for intrinsic or acquired antimicrobial resistance.
9.6.2. Microorganisms	SYNPA	Lines 754-777: SYNPA agrees that there is a need for a thorough safety assessment of the microorganism when the microorganism is present in the final food. However, in case the microorganism serves only as production vehicle and is not present in the final food we believe that there is no need for a full safety assessment e.g. testing for intrinsic or acquired antimicrobial resistance. Line 755: Synpa suggests to add the term "yeasts" to the following sentence: "A wide variety of bacterial and fungal species are used in food and feed production […] ". Line 757: Synpa suggests to replace the term "viable bacteria" by "viable microorganisms".

Chapter text	Organisation	Comment text
9.6.3. Engineered nanomaterials	Eurogroup for Animals	Definitions: Include the definition on 'whole foods'. It is mentioned on line 730. Suggestion: "'whole food" refers to a product to be consumed by humans which is composed of a multitude (up to thousands) of individual substances. Whole food range from plant based products such as maize or potatoes to more refined products such as fruit juices or flour, to foods consisting of microorganisms as well as animal-derived food products such as meat and milk.' from EFSA Scientific Committee; 2011. EFSA guidance on conducting repeated-dose 90-day oral toxicity study in rodents on whole food/feed. EFSA Journal 2011;9(12):2438 General Principles: 257/258 - Include an extra bullet pt : Information on Foods which contain substances or mixtures that are used for other applications than food (cosmetics, chemicals, pharma) which are relevant to the data requirements for Novel foods should be sourced and provided, in particular vertebrate studies, to avoid duplication of animal testing according to Rec 32 of Regulation 2015/2283. Line 265: In accordance with Directive 2010/63/EU... Remove the '4' and replace it as a superscropt for the footnote. Also delete the words' experimental and other' as the Directive 2010/63/EU's title is ' on the protection of animals used for scientific purposes'. Line 267: include in the wording: '...replaced, reduced or refined and duplication of animal testing should be avoided, where possible'. This text is in line with Recital 32 of Reg 2015/2283 Organisation and content of the notification: Line 294; remove extra '.' 2. Production Process Line 388 - 390: change the wording to '...;the breeding, rearing, feeding, housing, farming conditions and slaughter for farmed animals...'. Also remove the word 'living (L389) as it is repetition. 7. Absorption, distribution, metabolism and excretion (ADME) Line 604: with reference to 'animal models' makes it appear an animal model has to be used. It would be best to change the wording to ' ..selection of the appropriate model' or '...the selection of the appropriate (animal or non-animal) model. Line 606: suggested change of wording to include: ' ...differences between in vitro methods, experimental animals and humans' (even for nano the scientific committee guidance (L875 - 877) includes in vitro methods) Line 628: Is there an error in the Reference given here. The document referenced EFSA SC guidance on RA of the application of nanoscience and nanotechnologies is not EFSA, 2010b as stated here, but rather EFSA 2011a 9.3 Subchronic toxicity

Chapter text	Organisation	Comment text
		Line 719: Include wording: 'Decisions on whether tests are necessary need to be considered in light of the data already available. Comment on 90 day study requirement: There is prevailing sceintific uncertainty with regard to the determination of the necessity of the 90 day feeding trials. EFSA has previously called for case-by-case decisions. (references: Contrary to the announced mandatory requirement for 90-day rodent feeding studies, all guidance documents of the European Food Safety Authority (EFSA) relating to the risk assessmentof GM food and feed advise consideration of the performance of such studies under specific circumstances, determined on a case-by-case basis. EFSA (2011) Guidance for RA of food and feed from GM plants. EFSA Journal 9, 2150 + EFSA (2012) Guidance on the RA of food and feed from GM animals. EFSA Journal 10, 2501 + U.G Sauer & K.A Reid ATLA 40, 183–1 + FP7 GRACE Line 746: EOGRT (OECD 443) not 2 generation testing (OECD 416) as with other EU regulatory requirements. Line 781: reference OECD nano read-across http://www.oecd.org/officialdocuments/publicdisplaydocumentpdf/?cote=env/jm/mono(2016)3&doclanguage=en Line 831: include - ' ...results from in vitro, animal and human studies'

Chapter text	Organisation	Comment text
9.6.3. Engineered nanomaterials	UK Advisory Committee on Novel Foods and Processes	P 20– To reflect the text in the regulation on methodology for Nano-materials, the Committee suggested making reference in the guidance to require applicants to provide justification for the appropriateness of the methods used to assess these materials.
9.7. Human data	Intertek Scientifi &Regulatory Consultancy	783 There is no mention of tolerability data. This is something that needs discussing specifically for novel foods as many of these ingredients are macoringredients such as saccharides. It is covered under the additives guidance, which is referred to here but probably a special mention is needed as it applies to novel foods more than for additives.
9.7. Human data	UK Advisory Committee on Novel Foods and Processes	The Committee supports the suggestion that the presence of pharmacologically active novel ingredients require a higher degree of assessment. The Committee also welcomed the move to ask applicants to rank/ prioritise their evidence so that evidence that most strongly supports the application can be given appropriate scrutiny.
10. Allergenicity	ELC - Federation of European Specialty Food Ingredients Industries	Line 796: The draft guidance introduces the term of "protein fractions" but does not provide any definition (quantity). Could the NDA Panel clarify this term in this guidance?
10. Allergenicity	ELC - Federation of European Specialty Food Ingredients Industries	Line 799: We would like to draw the attention to the sentence – "The default assumption for Novel Foods containing proteins is that such Novel Foods have allergenic potential." – which suggests that all proteins have the same allergenic properties. Assuming that "the multiplicity of the allergenic proteins contained in a whole food, and that different proteins may be differently affected by the same treatment, the impact of food processing on the structural and allergenic properties of allergenic foods/ingredients is difficult to predict" , we propose to amend this sentence as follows: "All novel food containing proteins may have allergenic potential.".
10. Allergenicity	Intertek Scientifi &Regulatory Consultancy	795 Allergenicity. No specific mention here is mentioned for history of safe use outside the EU as support. This in fact may be of equal importace, or even greater in some cases, than analytical data.

Chapter text	Organisation	Comment text
10. Allergenicity	IPIFF	Here we have two comments: - In cases where allergenic risks are limited to those with pre-existing allergies, to what extend can proper labelling mitigate the allergenic risks associated to the Novel Food? In the case of insects, it seems that especially those allergic to other arthropods (e.g. arachnids, crustaceans, mariapods) may be at risks. In its Scientific Opinion "Risk profile related to production and consumption of insects as food and feed", EFSA suggests to, for future insect-food products, "indicate presence of the insect protein and the possible allergenicity or cross reactivity on the label of the product." (p.38). How does the EFSA panel on Dietetic Products, Nutrition and Allergies intend to implement this recommendation? - To what extend does cross-allergenicity need to be proved for closely related Novel Foods? E.g. is the proof of cross-allergenicity for a few species of insects sufficient to prove it for all insect-based Novel Foods or should the composition of all specific species be shown?
10. Allergenicity	Nutraveris	L795-807 The substantiation of the lack of allergenicity can be based on the history of consumption of the novel food outside EU. If data of consumption shows no signs of allergenicity in humans outside EU, are additional analyses listed by EFSA required or is the demonstration of the lack of allergenicity sufficient? When specifications show an absence of protein, can the ingredient be judged to have no allergenic potential?
10. Allergenicity	SYNPA	Line 796: The draft guidance introduces the term of "protein fractions" but does not provide any definition (quantity). Could the NDA Panel clarify this term in this guidance? Line 799: We would like to draw the attention to the sentence – "The default assumption for Novel Foods containing proteins is that such Novel Foods have allergenic potential." – which suggests that all proteins have the same allergenic properties. Assuming that "the multiplicity of the allergenic proteins contained in a whole food, and that different proteins may be differently affected by the same treatment, the impact of food processing on the structural and allergenic properties of allergenic foods/ingredients is difficult to predict" , we propose to amend this sentence as follows: "All novel food containing proteins may have allergenic potential.".

Chapter text	Organisation	Comment text
10. Allergenicity	TNO/COST Action ImpARAS	Comments on behalf of ImpARAS: 796 - please delete glycol, this is not proven 798 - which methods to be used? Identify a certain protein or all proteins individually or total protein content? 808 - These tests are only practicle for an individual protein (like GMO). In case of b=novel proteins we may also have complete products/sources such as insects, which contain thousands of different proteins. As with GMO methods need to be predictive and validated otherwise it is not useful to use. 810 - only useful to test cross-reactivity 813 - what is case of sources? measure all proteins? 814 - This is only possible when METC approval is obtained. May be a problem. 818 - The document 'EFSA Guidance on the preparation and presentation of applications pursuant to Article 6 Paragraph 11 of Directive 2000/13/EC' only states the studies that can be done / reported. However, I was not able to find any criteria on how these data will be reviewed or what type of data/results is needed to underpin the unilekelyness. I.e. when do you have enough data to say this? All suggested tests are based on cross-reactivity. What about de novo sensitization? This might be a greater risk in case of novel protein sources. ImpARAS is a COST Action network investigating the options to assess sensitization (www.imparas.eu). Please also check a recent paper on allergenicity riskassessment of novel proteins: http://www.sciencedirect.com/science/article/pii/S0273230016300605

Chapter text	Organisation	Comment text
10. Allergenicity	UK Advisory Committee on Novel Foods and Processes	p21- The Committee recommended that the allergenicity section of the guidance should reflect the ongoing work by the GM panel on allergenicity. When considering this issue in the UK, a distinction is made between assessing the risk of cross-reactivity for consumers sensitised to known food allergens versus predicting the potential for a new food to become an allergen affecting a significant part of the population with serious reactions. The latter is difficult to predict and may be better addressed with risk management activities such as post market monitoring. For predicting the risk of cross-reactivity of individuals sensitised to known food allergens the Committee has found it useful to apply a tiered approach. In addition to the factors listed in section 10.1 consideration of this risk where needed should include the botanical relatedness of plants, fruits and vegetables. Where risks are identified it may be appropriate to undertake immunological assays in line with the latest clinical knowledge and practice. Section 10.2 would benefit from making clear that a human study would be the final tier if concerns were identified and should be subject to ethical approval.
10.2. Human testing	Food Safety Authority of Ireland	I cannot understand the use of Directive 2000/13/EC which has been repealed by Regulation 1169/2011. I tried to find Article 6, Paragraph 11 of that Directive but there are only 9 points in that Article.
10.2. Human testing	IPIFF	EFSA here refers to Article 6 paragraph 11 of directive 2000/13/EC, as amended. However, when looking this up, it seems that article 6 of Directive 2000/13/EC has only 9 paragraphs. Is there a mistake made here?

Chapter text	Organisation	Comment text
11. Concluding remarks	Eurogroup for Animals	Definitions: Include the definition on 'whole foods'. It is mentioned on line 730. Suggestion: "'whole food" refers to a product to be consumed by humans which is composed of a multitude (up to thousands) of individual substances. Whole food range from plant based products such as maize or potatoes to more refined products such as fruit juices or flour, to foods consisting of microorganisms as well as animal-derived food products such as meat and milk.' from EFSA Scientific Committee; 2011. EFSA guidance on conducting repeated-dose 90-day oral toxicity study in rodents on whole food/feed. EFSA Journal 2011;9(12):2438 General Principles: 257/258 - Include an extra bullet pt : Information on Foods which contain substances or mixtures that are used for other applications than food (cosmetics, chemicals, pharma) which are relevant to the data requirements for Novel foods should be sourced and provided, in particular vertebrate studies, to avoid duplication of animal testing according to Rec 32 of Regulation 2015/2283. Line 265: In accordance with Directive 2010/63/EU... Remove the '4' and replace it as a superscropt for the footnote. Also delete the words' experimental and other' as the Directive 2010/63/EU's title is ' on the protection of animals used for scientific purposes'. Line 267: include in the wording: '...replaced, reduced or refined and duplication of animal testing should be avoided, where possible'. This text is in line with Recital 32 of Reg 2015/2283 Organisation and content of the notification: Line 294; remove extra '.' 2. Production Process Line 388 - 390: change the wording to '...;the breeding, rearing, feeding, housing, farming conditions and slaughter for farmed animals...'. Also remove the word 'living (L389) as it is repetition. 7. Absorption, distribution, metabolism and excretion (ADME) Line 604: with reference to 'animal models' makes it appear an animal model has to be used. It would be best to change the wording to ' ..selection of the appropriate model' or '...the selection of the appropriate (animal or non-animal) model. Line 606: suggested change of wording to include: ' ...differences between in vitro methods, experimental animals and humans' (even for nano the scientific committee guidance (L875 - 877) includes in vitro methods) Line 628: Is there an error in the Reference given here. The document referenced EFSA SC guidance on RA of the application of nanoscience and nanotechnologies is not EFSA, 2010b as stated here, but rather EFSA 2011a 9.3 Subchronic toxicity

Chapter text	Organisation	Comment text
		Line 719: Include wording: 'Decisions on whether tests are necessary need to be considered in light of the data already available. Comment on 90 day study requirement: There is prevailing sceintific uncertainty with regard to the determination of the necessity of the 90 day feeding trials. EFSA has previously called for case-by-case decisions. (references: Contrary to the announced mandatory requirement for 90-day rodent feeding studies, all guidance documents of the European Food Safety Authority (EFSA) relating to the risk assessmentof GM food and feed advise consideration of the performance of such studies under specific circumstances, determined on a case-by-case basis. EFSA (2011) Guidance for RA of food and feed from GM plants. EFSA Journal 9, 2150 + EFSA (2012) Guidance on the RA of food and feed from GM animals. EFSA Journal 10, 2501 + U.G Sauer & K.A Reid ATLA 40, 183–1 + FP7 GRACE Line 746: EOGRT (OECD 443) not 2 generation testing (OECD 416) as with other EU regulatory requirements. Line 781: reference OECD nano read-across http://www.oecd.org/officialdocuments/publicdisplaydocumentpdf/?cote=env/jm/mono(2016)3&doclanguage=en Line 831: include - ' ...results from in vitro, animal and human studies'

Appendix C – Full list of comments submitted by means of emails

Organisation	Comment text
IPFF	Dear Sir, Dear Madam, Please find attached the IPIFF (i.e. International Platform of Insects for Food & Feed) document "*Insect products as a safe addition to consumer diets*" as referred to in our response to section 9.6.1. This contribution complements the comments we have submitted electronically in the 'consultation template'. We remain at your disposal in case you require any additional information on this document Best regards, IPIFF Secretariat
I.R.C.A. S.p.A. – INDUSTRIA RESISTENZE CORAZZATE E AFFINI	Dear Sirs My complimants on the work done. I have noticed though that there is no mention of the type of packaging that could be eventually used. Eventual interaction or migration of molecules from the packaging especially if it is made of a plastic polymer could add further information on the safety of the food. Best regards [Signed]