Guidance on Novel Foods

Composition, production process and specification

Prof. Marina Heinonen
University of Helsinki
Member of the NDA Panel and
EFSA's WG on Novel Foods

Info-Session
06 March 2017
Parma

efsa
European Food Safety Authority

OUTLINE

- **Presenting the two EFSA Guidance documents**
- **Aspects raised in the public consultation**
- **Requests for additional information**
  Examples from the past and considerations of the NDA Panel.

STRUCTURE OF THE Novel Food GUIDANCE

- **Part 1: Administrative data**
- **Part 2: Characterisation, technical & scientific data**
  - 2.1. Introduction
  - 2.2. Identity of the NF
  - 2.3. Production process
  - 2.4. Compositional data
  - 2.5. Specifications
  - 2.6. History of use of the NF and/or of its source
  - 2.7. Proposed uses and use levels and anticipated intake
  - 2.8. Absorption, distribution, metabolism, and excretion
  - 2.9. Nutritional information
  - 2.10. Toxicological information
  - 2.11. Allergenicity
  - 2.12. Concluding remarks

- **Part 3: Annexes to the dossier**

2.1. INTRODUCTION

- **Brief description**
  - Source
  - Principle of production process
  - Typical compositional features
  - Purpose and intended use

2.2 IDENTITY OF THE NF (1)

2.2.1. Chemical substances

2.2.2. Polymers

Foods consisting of, isolated from or produced from….

2.2.3. Microorganisms, fungi or algae

2.2.4. Material of mineral origin

2.2.5. Plants or their parts

2.2.6. Animals or their parts

2.2.7. Cell or tissue cultures derived from animals, plants, fungi, algae

2.2.8. Foods consisting of “engineered nanomaterials”

2.2 IDENTITY OF THE NF (2)

2.2.1 Chemical substances

- Chemical name, when appropriate, according to IUPAC nomenclature rules
- CAS number (if this has been attributed) and other identification numbers
- Synonyms, trade names, abbreviations
- Molecular and structural formulae; stereochemistry
- Molecular mass (Da)

2.2 IDENTITY OF THE NF (3)

2.2.5 NF consisting of, isolated from or produced from plants or their parts

- Scientific (Latin) name (botanical family, genus, species, subspecies, variety with author's name, chemotype, if applicable)
- Synonyms (botanical name) that may be used interchangeably with the preferred scientific name
- For plants, verification of the identity according to internationally recognised databases and methodology
- Common names (if a trivial or a common name is used, it should be linked to the scientific name and part used)
- Part(s) used (e.g. root, leaf, seed, etc.)

- Geographical origin (continent, country, region)

2.3. PRODUCTION PROCESS (1)

2.3.1. Detailed description of the production process

- e.g. chemical synthesis, enzyme-catalysis, fermentation, isolation from natural source
- Information on potential by-products, impurities and contaminants that could raise safety concerns
- Characterization of novel aspects of the process (if applicable)
- Raw materials, starting substances
- Handling of sources

animals: breeding, farming, hunting conditions
microorganisms: culture conditions

plants: cultivation practice, time of harvest, EFSA guidance on safety assessment of botanicals and botanical preparations (EFSA, 2009)

2.3. PRODUCTION PROCESS (2)

- Operational limits and key parameters of the production process

  e.g. • Novel Foods obtained via chemical synthesis:

  - reaction sequence, side reactions
  - purification methods (solvents, extraction, crystallisation etc.)
  - reaction conditions (reagents, temperature, time etc.)

  • Conversion of raw material into an ingredient for a preparation

- Measures implemented for production control and quality assurance (e.g. HACCP, GMP, ISO)

- Production flow chart, including quality control checks

⇨ **Should allow conclusions on the impact of the process on safety and nutritional value of the NF**

2.4. COMPOSITIONAL DATA (1)

⇨ Qualitative and quantitative data on composition, physicochemical, biochemical and microbiological properties

- Identities and quantities of impurities, by-products or residues, chemical & microbiological contaminants
- Nutritionally relevant inherent constituents (e.g. micronutrients),
- Toxic, addictive, psychotropic, allergenic or other substances of possible concern to human health
- Type and spectrum of target analytes depending on sources and production process

  e.g. chemical synthesis > residual starting materials and by- products, fermentation > undesirable metabolites, extraction > residual solvents

2.4. COMPOSITIONAL DATA (2)

2.4.2. Single substances and simple mixtures thereof

Single substances

- Identity tests (e.g. UV-VIS, IR, NMR, GC-MS, LC-MS)
- Physicochemical properties (e.g. appearance, melting point, boiling point)
- Solubility data in water and other common solvents
- Particle size, shape and distribution
- Minimum purity value
- Density and/or viscosity for liquid preparations

Simple mixtures (can be fully chemically characterised)

- Information on the identities and the relative ratios of all components
- Elaboration of a complete mass balance

2.4. COMPOSITIONAL DATA (3)

2.4.3. Complex mixtures and whole foods

Complex mixtures (e.g. extracts, protein hydrolysates)
Whole foods (e.g. milk, meat, fruits, seeds)

⇨ not all constituents can be fully chemically characterised and/or identified

- Qualitative and quantitative characterisation of the main constituents - at least via sum parameters
- Whole foods: proximate analyses (i.e. ash, moisture, protein, fat and carbohydrates)
- For the classes of naturally or chemically derived components which characterise the nature of the NF: comprehensive qualitative and quantitative data
- Setting up of a mass balance
- Indication of the amount of unidentified components

2.4. COMPOSITIONAL DATA (4)

- Preferably, data on at least five representative batches that have been independently produced
- Use of validated analytical methods, preferably nationally or internationally-recognised (e.g. AOAC, ACS, EP)
- Description of methods
  - limit of detection (LOD)
  - limit of quantification (LOQ)
  - references
- Certificates of analyses and information on the accreditation of laboratories
- In-house methods: full description and validation of procedures

2.4. COMPOSITIONAL DATA (5)

2.4.4. Stability

Identification of hazards which might arise during storage and transport:

- Consideration of constituents/parameters
  - susceptible to changes during storage
  - direct effect on safety or indicator for safety-relevant alterations
- Physicochemical, biochemical and microbiological stability of the NF under normal conditions of storage
  - effects of packaging, storage temperature and environment
- Use of the novel food as an ingredient added to other foods

⇨ investigation of stability in the processed foods

2.5. SPECIFICATIONS

- Define key parameters which characterise and substantiate the identity of the NF
- Provide a rationale for the selected parameters on the basis of analytical characterisation of the NF
- Set a limit regarding minimal purity
- Set acceptable limits for impurities and degradation products, in particular for those of toxicological and nutritional relevance
- In the absence of legal requirements, include maximum levels of contaminants
- Provide the methods used for analysis of all parameters
- Table format

PUBLIC CONSULTATION (1) – IDENTITY

- *The classes in the guidance do not correspond to the categories of NFs listed in the Regulation.*
- *In relation to foods from microorganisms, fungi or algae, further guidance on the genetic methods was requested which can be used for identification of the strain concerned.*

The classes are based on scientific considerations (chemistry, source, production process) and are not meant to reflect the categories of the Regulation.

Guidance on the identification and characterisation of foods from microorganisms, fungi or algae was extended, referring to internationally accepted molecular methods. Reference to the EFSA guidance on Health Claims was added on the approach for the identification of bacteria and yeasts.

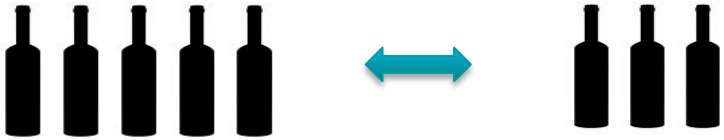
PUBLIC CONSULTATION (2) – PRODUCTION

- *The relevance of providing the reaction conditions was questioned, considering that NF authorisations would be generic. A similar comment was made on the need for exact methods used to rear and process insects – as these may vary amongst producers.*

The Panel considers that detailed Information on the production process is needed, because EFSA is asked to perform its assessment on a specific NF and to indicate risks and uncertainties.

PUBLIC CONSULTATION (3) – COMPOSITION

Why 5 independently manufactured batches (while only 3 for drugs or chemical)?



The compositional parameter of whole foods and complex mixtures such as flour, extracts and juice generally have a larger range and variability than drugs, chemicals and single substances. Results from five independent batches provide more reassurance that the NF under the applied production process consistently meets the proposed specifications. General principle No. 9 provides flexibility. Deviations from requirements should be justified.

PUBLIC CONSULTATION (4) – COMPOSITION

Considerations and arguments for five batches:

- complex mixture
- high proportion of unidentified compounds
- novel source with no history of human consumption
- small margin of exposure (= MoE on anticipated human exposure versus adverse effect in toxicologal testing)

Considerations and arguments for three batches

- single chemical substances and simple mixtures
- high purity
- negligible amounts of undefined substances
- High MoE

PUBLIC CONSULTATION (5) – COMPOSITION

If several production processes are applied, the applicant should provide the details of each applied production process and propose specifications for all these NFs?

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 NF derived from all these production processes.

Example from the past: synthetic lycopene: the last step formulations differed, resulting in three different specifications - still only one application and one opinion. In other cases where the differences in the production process results in larger differences in the composition, or amount of undesirable substances, ... separate assessments may be applicable.

REQUESTS FOR ADDITIONAL INFORMATION (1)

- **Inadequate information on methods and labs**

  e.g. information (and certificates) on the accreditation of laboratories, absence of analytical reports from such laboratories, description of the applied analytical method, references to the analytical methods, inappropriate analytical method applied - inadequate LOD, missing info on LOD/LOQ.

- **Incomplete information on composition**

  e.g. information on protein content, type of polysaccharides, type of polyphenols, secondary plant metabolites..., significant amount of unidentified compounds/impurities, no information on the presence of undesirable substances even if information is available for the source of the NF or closely related species.

REQUESTS FOR ADDITIONAL INFORMATION (2)

- **Specification of the NF**

  e.g. critical components from the source or production process not added to the specification (e.g. Pd used as a catalysator, residual solvents from an extraction process..)

- **Batch testing**

  Missing, insufficient information (source, year, independently produced, results not complying with specifications...)

- **Stability testing**

  Missing, insufficient information (on the batches, on conditions, lacking reports), proposed conditions of use not considered and addressed

REQUESTS FOR ADDITIONAL INFORMATION (3)

- **Production process**

  Steps missing, insufficient information on source, raw materials, reagents used and conditions, equipment, catalysts, enzymes, extraction solvent used process, pore size of filtrations, flow-chart, production yield, quality assurance system in place, HACCP; insufficient considerations and investigations on the effect of the production process applied to the NF (e.g. effects of excessive heating or UV treatment on the food).

  Heated (1h at 75° C) milk products fermented with *B. xylanisolvens*: EFSA asked to provide analyses on vitamins B2, B12, lysine, and furosine content, as a marker for Amadori products formed from early Maillard reactions before and after this heat treatment.

Thank you for your attention!