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EFSA NOVEL FOOD GUIDANCE UPDATE

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Ad-hoc Meeting with Member States and Observer Countries on the draft EFSA Novel Food Guidance

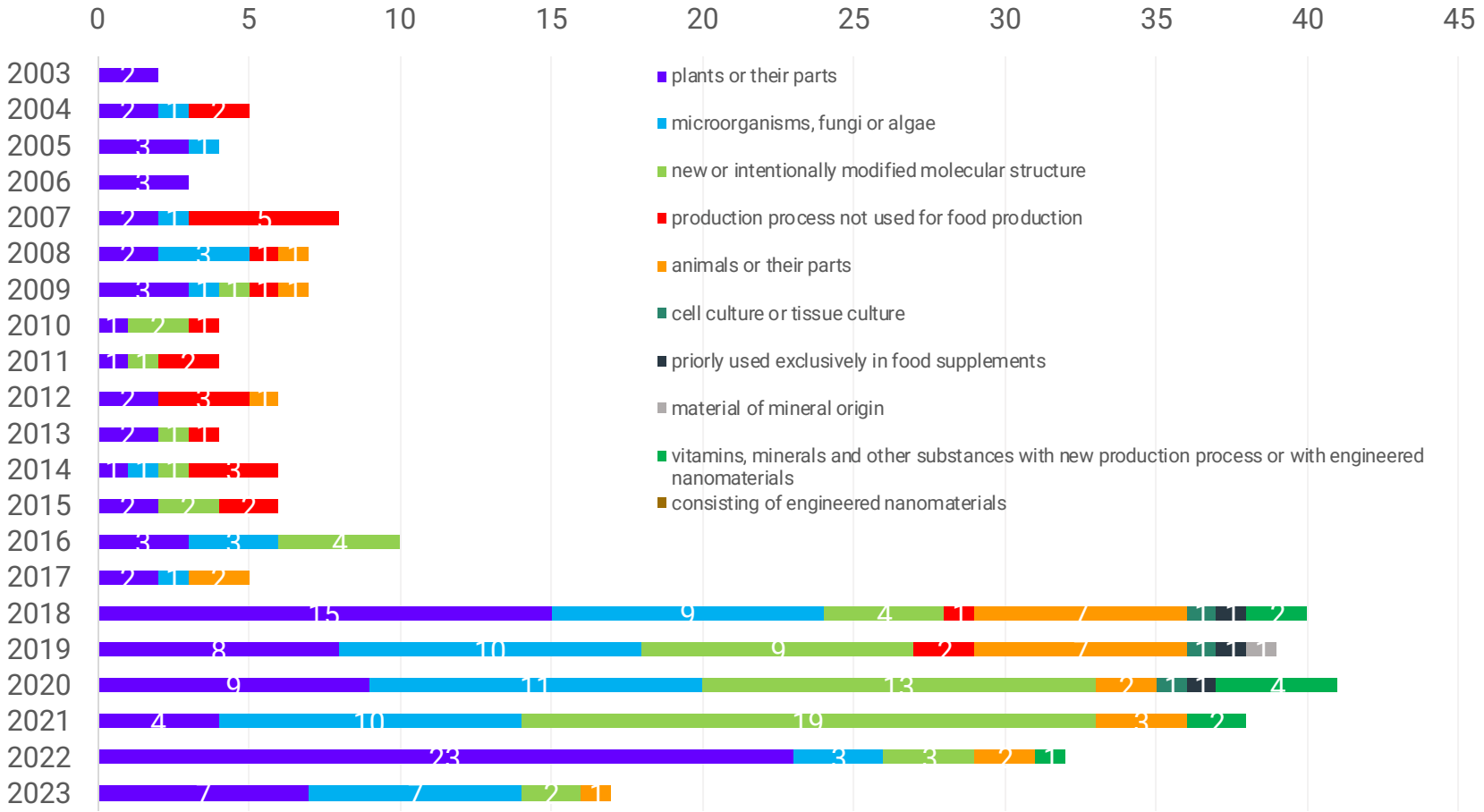
EUROPEAN FOOD SAFETY AUTHORITY

EFSA GUIDANCE ON NOVEL FOODS -UPDATE

EFSA Guidance on the preparation and submission of an application for authorisation of a novel food in the context of Regulation (EU) 2015/2283

- Mandate from EC received & accepted by EFSA: June 2023
- Deadline: June 2024
- Considerations:
  - Regulatory Updates: Implementing Regulation (EU) 2017/2469
  - EFSA's experience
  - Advances in science and technologies

EFSA GUIDANCE ON NOVEL FOODS -UPDATE



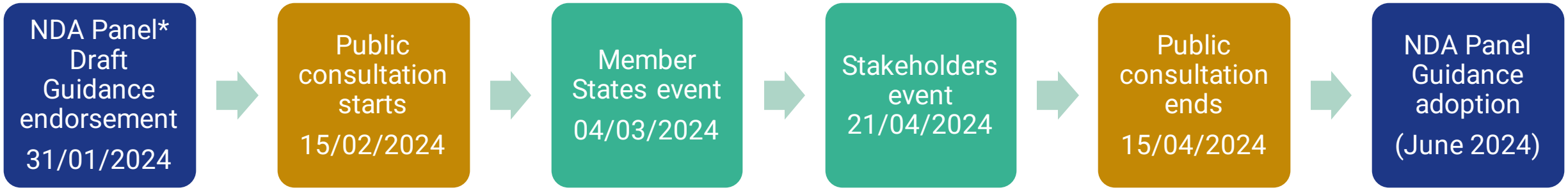
Number of Novel Food dossiers validated for EFSA's Risk Assessment
Adapted from: Ververis et al. (2020), Novel foods in the European Union: Scientific requirements and challenges of the risk assessment process by the European Food Safety Authority. *Food Research International*, 137,109515.

EFSA's experience

- Centralised assessment of multiple & heterogeneous novel food dossiers
- New EFSA cross-cutting guidance applicable
- Risk assessment methodological advances
- New EFSA tools
- Engagement & feedback from stakeholders (e.g., EFSA Scientific colloquium in cell culture-derived foods)

EFSA GUIDANCE ON NOVEL FOODS -UPDATE

Current Timeline



* NDA Panel: EFSA Panel on Nutrition, Novel foods and Food Allergens

IDENTITY OF THE NOVEL FOOD

EXPANDING/EXPLAINING THE FOLLOWING ASPECTS:

- **What is the Novel Food?**
  "the product resulting from the production process, without the addition of non-novel ingredients/excipients"
- When are **excipients** considered part of the NF?
  "[…] they are essential to maintain specific characteristics of the novel food, e.g., stability, physical form."
- **Nomenclature**:
  - *"The name should reflect its characteristic elements e.g., its source, the main part(s) of organisms used, specific elements of the production process, and must bear no nutrition or health claims"*.
  - Commercial names are to be avoided
  - Scientific names according to the most recent taxonomy or scientific nomenclature to be included

IDENTITY OF THE NOVEL FOOD

CURRENT

- Chemical substances
- Polymers
- Foods consisting of, isolated from or produced from microorganisms, fungi or algae
- Food consisting of, isolated from or produced from material of mineral origin
- Food consisting of, isolated from or produced from plants or their parts
- Food consisting of, isolated from or produced from animals or their parts
- Foods consisting of, isolated from or produced from cell culture or tissue culture derived from animals, plants, fungi or algae
- Foods consisting of 'engineered nanomaterials'

PROPOSAL - UPDATE

- Chemical substances, products of mineral origin and polymers
- Foods consisting of, isolated from or produced from microorganisms
- Food consisting of, isolated from or produced from plants, **macro**scopic fungi and algae, or their parts
- Food consisting of, isolated from or produced from animals or their parts
- Foods consisting of, isolated from or produced from cell culture or tissue culture derived from animals, plants, macroscopic fungi or algae
  - Foods consisting of, isolated from or produced from cell culture or tissue culture derived from animals
  - Foods consisting of, isolated from or produced from cell culture or tissue culture derived from plants, macroscopic fungi or algae
- Foods containing or consisting of engineered nanomaterials

CHEMICAL SUBSTANCES, PRODUCTS OF MINERAL ORIGIN & POLYMERS

- **Chemical names** (IUPAC), when appropriate
- **Multiple new identifiers** (to facilitate also EFSA **registration of cross-cutting substances**) new
- Synonyms, common names, trade names, abbreviations
- **Molecular and structural** formulae
- Molar & molecular mass
- InChI, InChIkey, SMILES new
- Particle size, shape, distribution
- Additional insights **into analytical methods/techniques** for identification new
- Additional requirements regarding **suitable comparators** (e.g., reference material, chemical standards, authentic biological specimens) new
- **Nomenclature**: **ECHA guidance** for identification and naming of substances under REACH and CLP new
- Information on **monomers & reagents** involved in polymerization, chemical modifications
- Degree of polymerization, number average molecular weight, weight average molecular weight and viscosity average molecular weight

FROM MICROORGANISMS

Proposal - update merges information from previous section **"Specific cases - microorganisms"**

In the context of novel foods, microorganisms can have different roles: new

- ✓ as novel food itself, i.e., novel foods consisting of viable cells (active agents) or non-viable cells (biomasses);
- ✓ used in the production of novel foods, e.g., novel foods isolated from or produced from microorganisms (production strains).

- **Unambiguous taxonomic identification** at species level and certificate of deposition
- Characterization of **genes of potential concern** *(i.e., acquired antimicrobial resistance, toxigenicity and pathogenicity traits)*
- Investigate the **production of antimicrobial compounds** unless a QPS Taxonomic Unit (TU) or a TU known not to produce antimicrobials of clinical relevance for use in humans/animals
- **Purpose, characterization, and structure of the genetic modification**(s) for GM production strains new
- **Whole genome sequence** data
- Test the presence of **viable cells & DNA of production strain** (in certain cases, explained) new

FROM PLANTS, MACROSCOPIC FUNGI AND ALGAE

Inclusion of macro fungi, macro algae, and plants within the scope new

- Scientific name & taxonomy
- Synonyms, trivial/common names
- Part(s) used
- **Experimental verification of the identity** of the plant (*e.g., authentic plant specimen deposit in a recognized herbarium, macroscopic/microscopic verification with comparison to an authentic standard, chemical fingerprint compared to standard, DNA-based authentication*) new
- Adherence to EFSA guidance on safety assessment of botanicals and botanical preparations
- Macroscopic fungi and algae: verification of the identity according to **internationally recognized databases and methodology**
- Growing **region(s)** and, when relevant, **season of harvesting** new
- **Growing conditions** to produce the source organism (i.e., cultivated or from the wild, conditions of cultivation) new
- Inclusion of a **non-GMO statement** new

FROM ANIMALS

- Scientific name & taxonomy
- Synonyms, trivial/common names
- **Verification of the identity** (e.g., DNA-based authentication) new
- **Suitability** of the animal sources for human consumption according to Regulation (EU) No 2015/1162 new
- **Health status** of the source animal, age, access to herd/lot health certification new
- Part(s) used
- **Geographical origin** (continent, country, region), **farming and husbandry conditions**
- **Origin of the initial livestock** (e.g., national repository) new
- Inclusion of a **non-GMO statement** new

FROM CELL CULTURE OR TISSUE CULTURE

Creation of two new subsections new

From **animals**

- Identity of the source
- When using **established cell lines**: genetic and phenotypic identity and stability of cells new
- When using **primary cells**: biopsy location or source material, cell type(s) isolated, genetic, and phenotypic identity of cells; new
- Information to attest the compliance with inspection requirements & the absence of any risks of **infectivity from viruses or other zoonotic agents** e.g., testing for viruses (species-specific viruses), testing for prions in the case of limited health information on source animals new
- Information on whether the cells or tissues sourced from a non-GM source have been **genetically modified** new

From **plants, macroscopic fungi or algae**

- Identity of the source
- **Laboratory or culture collection** sourced (when applicable)
- Identity of the cells or cell lines: part(s) of the organism sourced, cell type isolated, genetic, and phenotypic identity, genetic and phenotypic stability of the cell lines
- Information on whether the cells or tissues sourced from a non-GM source have been **genetically modified** new

CONTAINING OR CONSISTING OF ENGINEERED NANOMATERIALS

*For novel foods **containing or consisting of 'engineered nanomaterials'**, the parameters for identification and characterization of engineered nanomaterials to be provided to support the application are outlined in the "Guidance on risk assessment of nanomaterials to be applied in the food and feed chain" (2021).*

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Compositional information: Novel foods which do not meet the definition of engineered nanomaterial may **contain small particles including particles within the nanoscale**, formed naturally or as by-products in the production process or during handling and processing of the foods

Guidance on technical requirements for regulated food and feed product applications to establish the presence of small particles including nanoparticles (2021).

PRODUCTION PROCESS

Creation of four new subsections new

- General provisions
- Considerations for specific production process steps
- Considerations for specific novel food categories
- Additional considerations

PRODUCTION PROCESS - GENERAL PROVISIONS

- Table with all **input material** used during the production process, with the function and the EU regulatory status alongside certifications/specifications for each input material new
- If **multiple producers**: the applicant should demonstrate the consistency in production new
- **Food Contact Material** compliance new
- Statement for the use of **antimicrobial, pesticidal and parasitic agents** (not necessarily analyses)
- Calculation of **production yield** Information on potential **by-products, impurities, or contaminants**
- Characterise the **novel aspects** of the process (when relevant)
- Measures implemented for **production control and quality and safety assurance** (e.g., HACCP, GMP, ISO).
- **Standardisation criteria** (e.g., chemical markers for the novel food)

PRODUCTION PROCESS - CONSIDERATIONS FOR SPECIFIC STEPS

- Description of **propagation, growth, and harvesting conditions**
- **Breeding, rearing, feeding, and farming practices**
- **Culture conditions** for microorganisms, algae, and cell/tissue cultures, detailing the raw materials used and any additional substances involved
- Consideration of **biological agents** such as parasites, bacteria, and viruses, including **mitigation measures and assessment of their impact on human health** new
- **Post-harvest handling procedures**, encompassing transportation, drying techniques, and storage conditions to maintain food quality and safety
- Processes and operational conditions **for inactivation/removal of food enzymes** of microbial origin used as processing aids, along with **verification of their presence or absence** in the novel food new
- Regulation (EC) No 1332/2008: **status of food enzymes** used in production, including assessment status by EFSA new
- **Provision of additional data on microorganisms used in food enzyme production** if risk assessment is ongoing or if the enzymes have not been previously assessed new

PRODUCTION PROCESS - CONSIDERATIONS FOR SPECIFIC CATEGORIES

- **Plant, fungi, algae, or animal - derived:** conversion processes from raw materials to food products, including heat treatment, extraction, distillation, fermentation, etc.
- **Chemical synthesis - derived:** Description of reaction sequences, side reactions, and purification steps, including reaction conditions and purification methods.
- **Microorganism-employed production processes**: removing/inactivating microbial cells during downstream processing, ensuring full provision of operational conditions and viability maintenance methods; investigation of potential toxic compound formation new
- **Cell culture or tissue culture - derived:** new

- type of cells used, purification steps, cell isolation, cell selection, genetic stability, and compliance with Good Cell Culture Practices and relevant standards.
- Information on primary cells or established cell lines, including source, preparation, banking process, and passage number, along with any modifications made to the cells.
- Description of processes for treatment, extraction, screening, and selection of cell lines or tissues, including chemicals and biological materials used, and impurities resulting from their use.
- Compliance with applicable standards, such as those outlined in the EMA Guidance documents

COMPOSITIONAL DATA

Explanation on the role of compositional data in the risk assessment new

General requirements Creation of four new subsections new

- Analytical methods
- Addressing compositional variability
- Sampling practices
- Compositional analytes

Single substances and simple mixtures

Complex mixtures and whole foods

Stability Creation of a new subsection new

- Impact of processing on the novel food in the proposed-for-use matrices

COMPOSITIONAL DATA

ANALYTICAL METHODS

- Validated methods, preferably nationally or internationally
- LOD/LOQ
- Information on the matrix accreditation new
- Description and validation of in-house methods

ADDRESSING COMPOSITIONAL VARIABILITY

- At least 5 representative batches of the novel food that have been independently produced
- Address potential compositional variations (e.g., seasonal) of the raw materials
- Cover the variability spectrum of the production process parameters new

COMPOSITIONAL DATA

SAMPLING PRACTICES

- Principles of representative sampling should be applied new
- Information on sampling protocols new

COMPOSITIONAL ANALYTES

- Identity and the quantity of impurities or by-products, residues and chemical and microbiological contaminants
- Guidance on the selection of analytes new
- Novel protein sources – specific requirements new
- Engineered nanomaterials vs nanoparticles new
- Novel foods that do not require a priori a nano-specific risk assessment new

COMPOSITIONAL DATA

SINGLE SUBSTANCES & SIMPLE MIXTURES

- Information on the identities and the relative ratios of all components
- Elaboration of a mass balance
- Analyses as per identity requirements new

COMPLEX MIXTURES & WHOLE FOODS

- Qualitative and quantitative characterization of the main constituents
- Proximate analysis for whole foods
- Amount of unidentified components
- Characterization of main classes of components
- Nutritionally relevant components, substances of possible concern
- To investigate the impact of processing new
- Literature search
- Comparison with conventional comparators

COMPOSITIONAL DATA

STABILITY

- Investigation of **compositional integrity and safety**
- Testing of compositional qualifiers, constituents, and parameters **susceptible to changes** during storage
- Chemical, physicochemical, and microbiological stability **under intended storage conditions**
- **At least five representative batches**, independently produced, with continuous monitoring from initiation to completion
- Use of stability testing results to **establish relevant specification parameters**, ensuring compliance throughout the proposed shelf-life
- Cover **at least the proposed shelf-life** duration in stability testing, considering **intermediate intervals** and potential use of **accelerated conditions** with proper **extrapolation evidence**
- Disclosure of any **added ingredients for stability enhancement**
- Impact of additional processing on the novel food in the proposed-for-use matrices (new subsection)

SPECIFICATIONS

Specifications encompass chemical, physicochemical, nutritional, and microbiological parameters defining the identity and safety of novel foods.

- Role in Risk Management new
- Inclusion of key descriptors, source names, microbial strains, and production process details.
- Major constituents, proximate analytes, characteristic components, safety parameters, and quality/stability indicators.
- Applicants must justify each parameter and its limits, supported by compositional and stability analysis data.
- Specifications should be verifiable using the indicated analytical techniques, with information on method's sensitivity provided.

HISTORY OF USE OF THE NOVEL FOOD AND/OR ITS SOURCE

History of Use of the Source

- Data on composition, production, and experience from the use of products from the source may provide relevant aspects for consideration.
- Relevant information may be found in EFSA's Compendium on Botanicals for foods derived from plants.

History of Use of the Novel Food

- Data may exist on the use of the novel food as food in countries outside the EU and on non-food uses.
- Information could include the extent of use as food and/or for non-food purposes, population groups for which it's been a dietary component, its role in the diet, handling, and preparation methods.
- A comprehensive literature review of human studies reporting on safety outcomes should be conducted.
- The literature search should not be limited to the novel food itself but should also include studies with safety-relevant components and similar foods.

PROPOSED USES AND USE LEVELS AND ANTICIPATED INTAKE OF THE NOVEL FOOD

Target population

- The target population is the general population when no labelling restrictions can be applied new
- When labelling restrictions can be applied (e.g. food supplements), the target population can be restricted to a group of the general population

Proposed uses and use levels

- Mandatory information that needs to be provided by applicants when the NF is an ingredient
- Specific requirements for whole foods, food supplements and particular food categories (total diet replacement, meal replacement) new

Anticipated intake of the NF

- Reference to DietEx tool and update of FAIM tool new
- Reference to opinions already adopted to explain how to perform combined exposure when a NF is proposed to be used in different forms (e.g. ingredient, whole food, food supplements) new

PROPOSED USES AND USE LEVELS AND ANTICIPATED INTAKE OF THE NOVEL FOOD

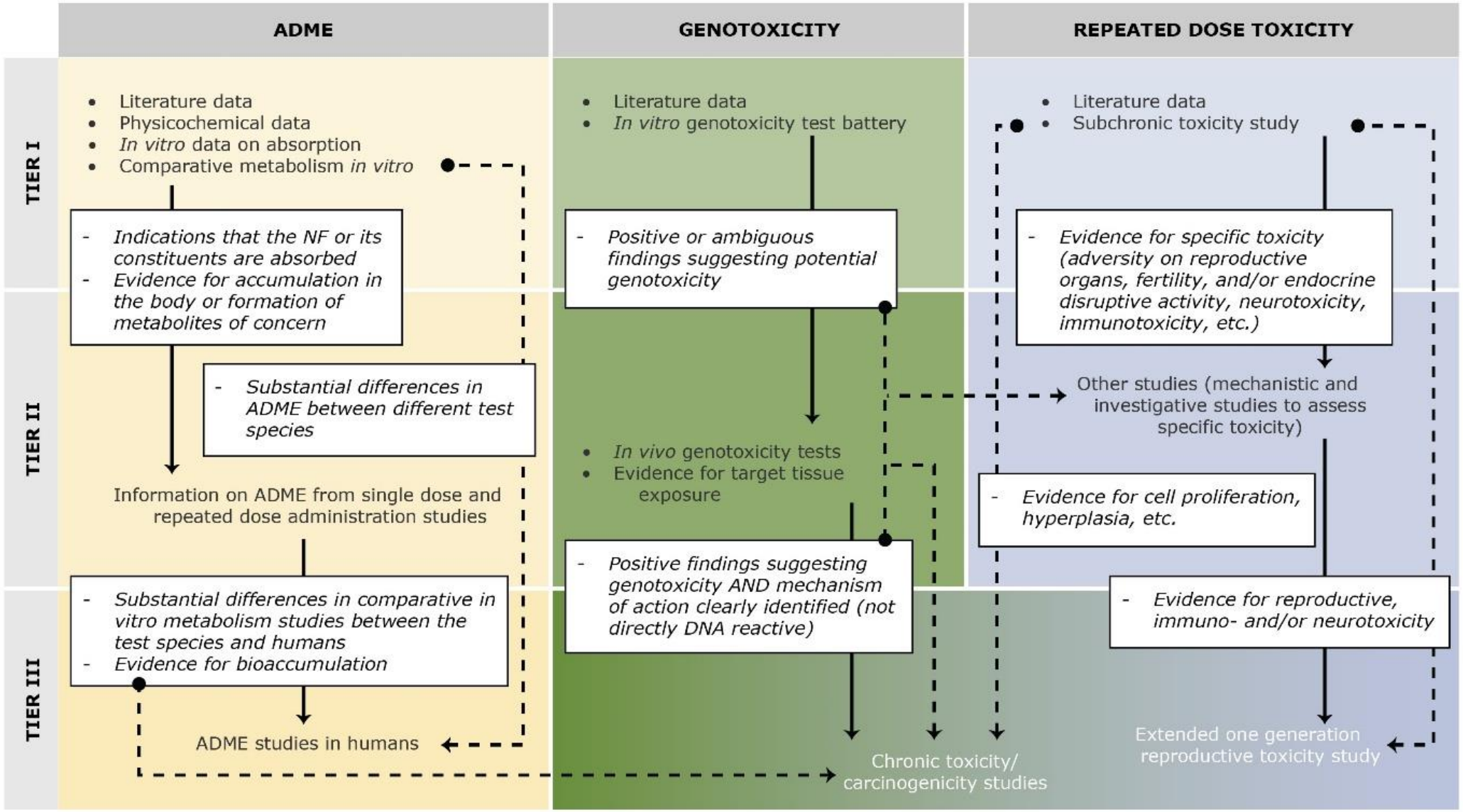
Combined intake considering other sources of the NF or its main constituents

- Explanation of combined intake (e.g. when the NF is also used in other domains like food additive or food colouring; combined exposure of the main constituents of the NF and background diet)
- Reference to opinions already adopted to explain how to perform the combined exposure new

Estimated exposure to undesirable substances

- Use the maximum limit of an undesirable substance in the NF and the 95th percentile anticipated exposure of that undesirable substance from the NF.
- The 95th percentile exposure of the undesirable substance should be compared with the reference value.

ADME & TOXICITY TESTING - TIERED APPROACH



NUTRITIONAL INFORMATION

Creation of five new subsections new

- Excess intake of nutrients
- Inadequate intake of essential nutrients
  - antinutrient content
  - replacement of foods in the diet
- Specific considerations for novel foods proposed as new sources of micronutrients
- Specific considerations for novel protein sources
- Additional information

NUTRITIONAL INFORMATION

Excess intake of nutrients

- Novel food are considered nutritionally disadvantageous if consumption could lead to excess intake of nutrients exceeding Tolerable Upper Intake Levels (ULs) or HBGVs if ULs not available
- Discussion and justification of a potential increase in nutrient intake compared to background diet (if no HBGV available)

Inadequate Intakes of Essential Nutrients

- Identification of antinutrients & comparison of antinutrient content in the novel food with that of comparable foods
- Consideration of potential adverse effects on nutrient absorption and bioavailability
- Demonstration that nutritional composition of novel food does not differ unfavorably from conventional foods it intends to replace.
- Attention to essential nutrients below recommended levels in European populations.

NUTRITIONAL INFORMATION

Specific Considerations for Micronutrient Sources

- Application of EFSA guidance on new sources of micronutrients for novel foods proposed as new sources of vitamins and minerals
- Assessment of micronutrient bioavailability compared to reference sources.

Specific Considerations for Novel Protein Sources

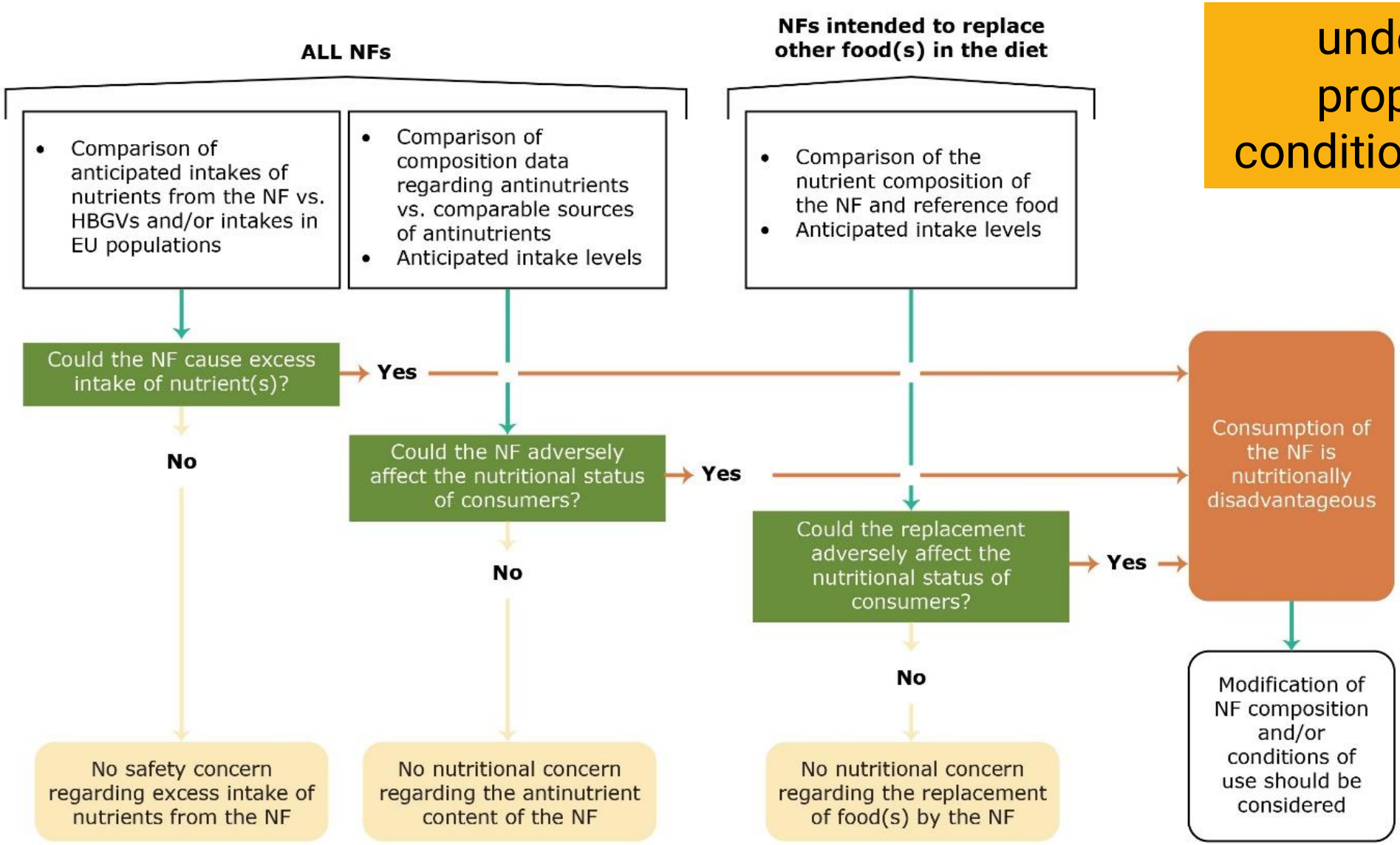
- Evaluation of protein quality in terms of true ileal digestibility and indispensable amino acid composition
- Calculation of Digestible Indispensable Amino Acid Score (DIAAS)
- Consideration of protein content estimation methods and expected contribution to total protein intake

Additional Information

- Consideration of in vitro, in silico, animal models, and/or human studies to address interaction of novel food with diet and nutrients.
- Necessity for such studies may arise from information on source, composition, and production of novel food, documented experience on its use, and outcomes of relevant studies.

INVESTIGATING THE NUTRITIONAL IMPACT OF THE NOVEL FOOD

under the proposed conditions of use



ALLERGENICITY

- (a) **to inform risk managers** about the allergenic properties of a NF which may serve them for their marketing authorisation decisions including those with regards to possible labelling requirements and
- (b) **to collect the available evidence** related to the allergenicity of a NF and **to generate a limited set** of data in order gain some knowledge about the respective properties of the NF.

NF divided in four sub-categories Creation of four new subsections new

1. NF with NO protein content derived from the production process
2. NF derived from allergenic foods subject to MANDATORY ALLERGEN LABELLING with no proteins from other sources
3. NF derived from allergenic foods NOT subject to mandatory allergen labelling
4. NF for which the allergenic potential is UNKNOWN
   - Single protein & simple protein mixtures
   - Complex protein mixtures and whole foods

Each NF subcategory has different data requirements.

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