Trusted science for safe food

26 November 2020

Insights on Novel foods Risk Assessment

Nutrition Unit

efsa
European Food Safety Authority

Outline of the Presentation

Introduction

Andrea Germini

Alternative proteins and their sources

Ermolaos Ververis, Ruth Roldán Torres

Novel carbohydrates

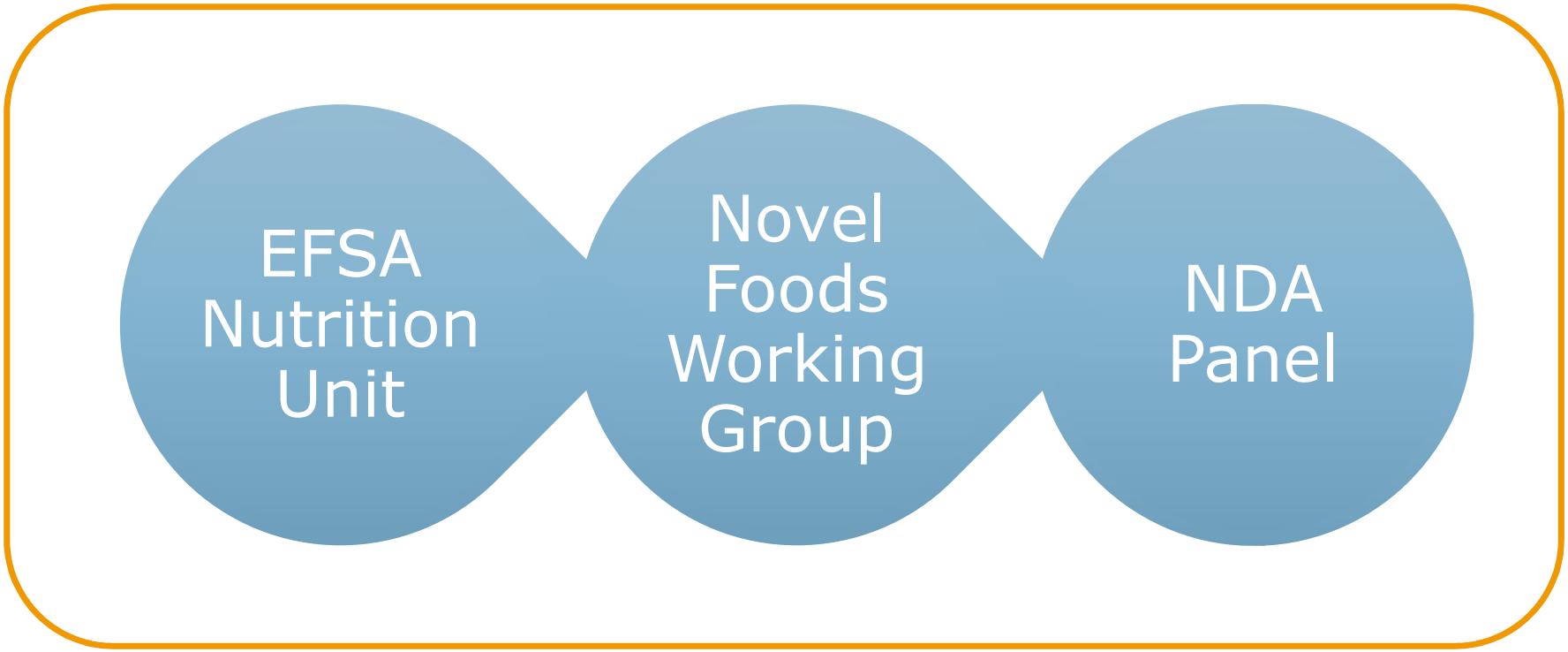
Reinhard Ackerl, Gabriela Precup, Océane Albert

Other Trends in Novel Foods - Food Supplements

Wolfgang Gelbmann, Annamaria Rossi, Andrea Germini

Q&A

Risk Assessment of Novel Foods



Regulation (EU) 2015/2283 on Novel foods

EFSA Novel Foods Framework

WHAT

Novel foods (NF) are "foods or ingredients that have not been used for human consumption to a significant degree in the EU **before 15 May 1997**").

WHY

Regulation (EU) 2015/2283 introduces a **centralised assessment** and authorisation procedure for novel foods as of January 2018.

WHEN

EFSA has a **legal deadline** to adopt its scientific opinion within **9 months** from the date of receipt of a valid application from the EC.

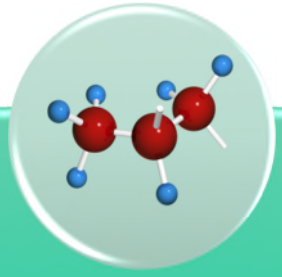
HOW

Data requirements for NF applications are outlined in "**EFSA Guidance on the preparation and presentation of an application for authorisation of a novel food in the context of Regulation (EU) 2015/2283**".

Novel Foods Categories

efsa
European Food Safety Authority

New production process



New or modified molecular structure

Micro-organisms, fungi, algae

From plants or their parts

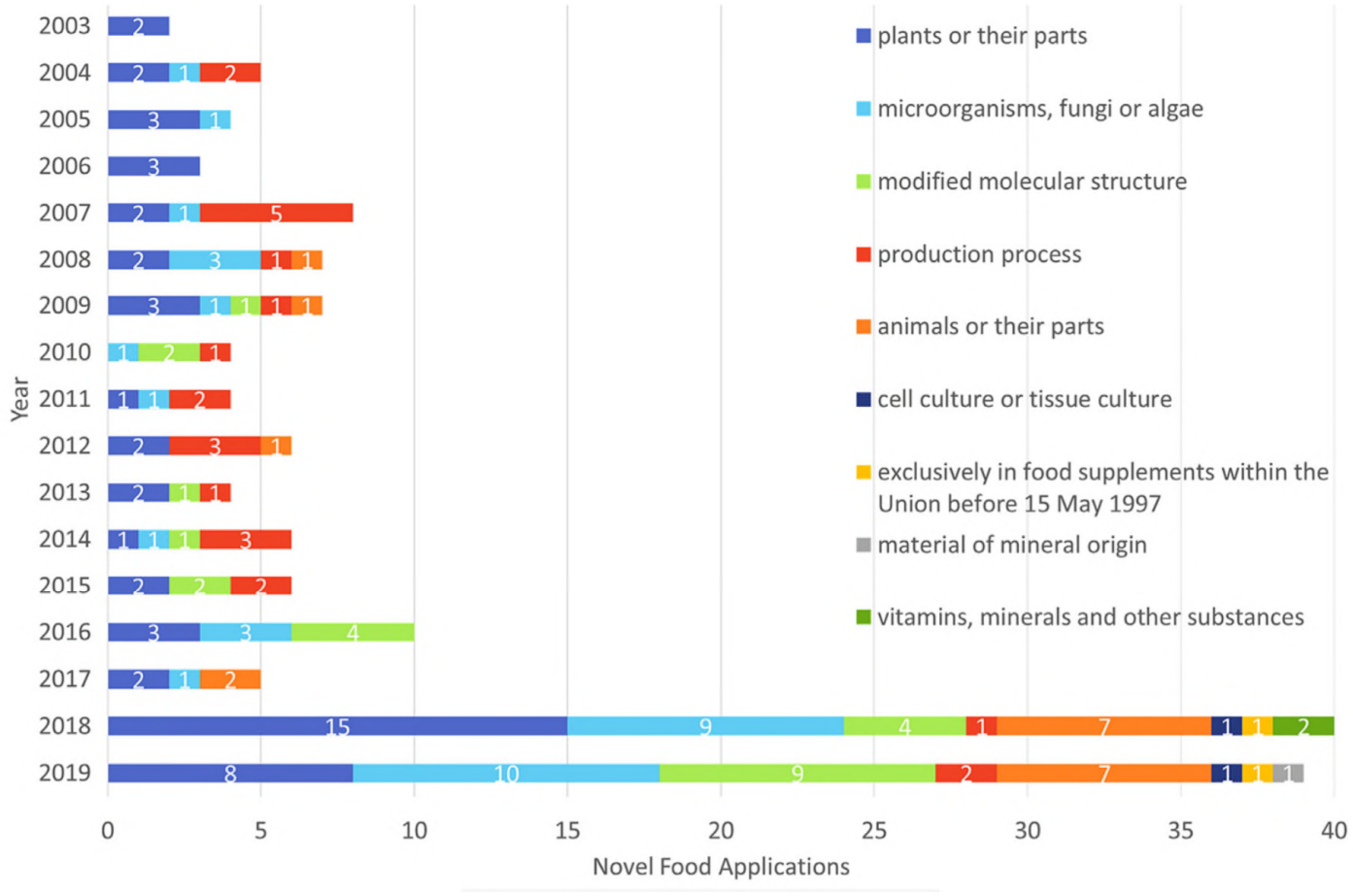
Of mineral origin

From animals or their parts

cell or tissue cultures derived from animals/ plants/ fungi/ algae

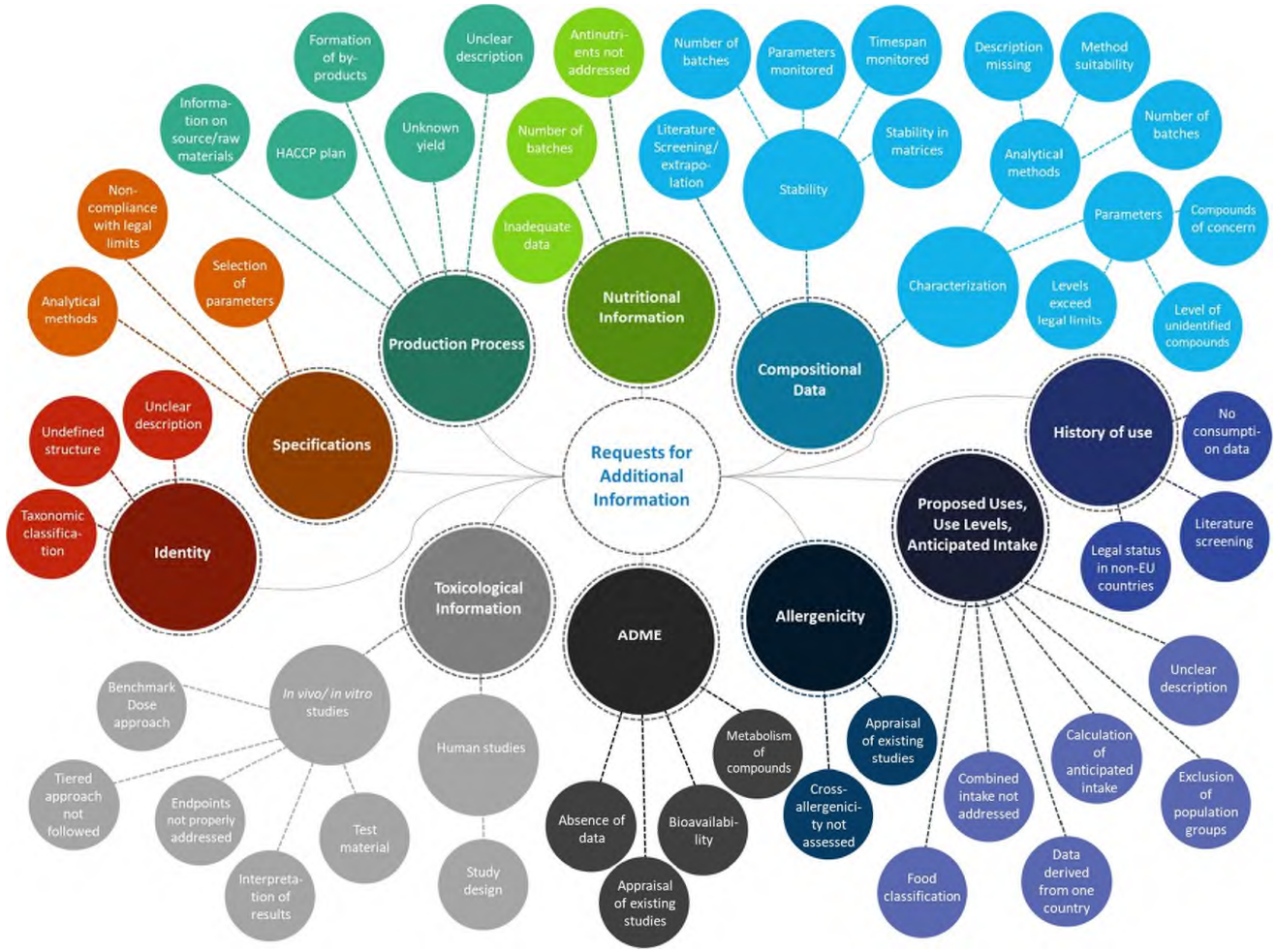
Engineered nanomaterials

Novel Foods Applications by Category



Ververis et al. Food Research International, 2020.

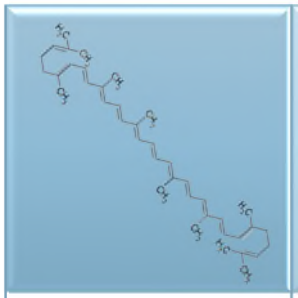
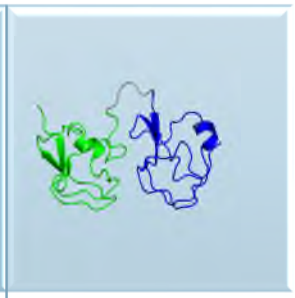
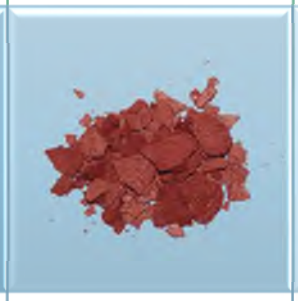
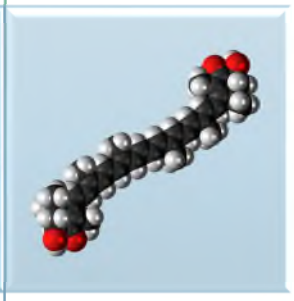
Diversity & Complexity



Ververis et al. Food Research International, 2020.

Examples of Novel Foods

efsa
European Food Safety Authority

newly synthesized/ isolated compounds				new processes			
	Synthetic Lycopene	Non-sticky chewing gum base	Ice-structuring protein		UV-treated milk	Milk products fermented with *B.xylanisolvens*	UV-treated yeast
traditional foods from non-EU countries				new sources			
	Chia seeds	Baobab fruit	Noni Juice		Krill oil	Lycopene from *B.trispora*	Astaxanthin from *H.pluvialis*

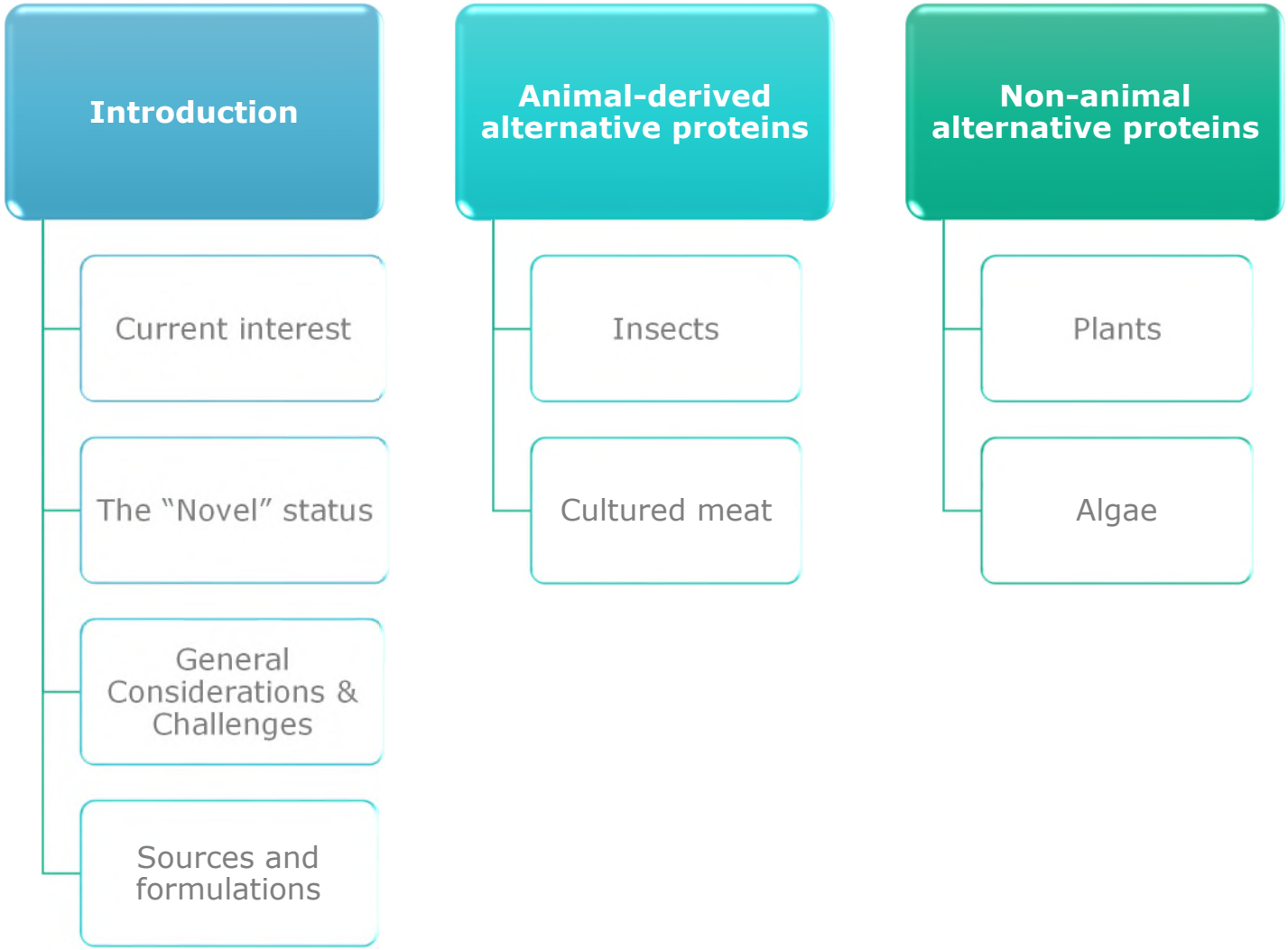
EFSA's Novel Foods Group

Safety Assessment of Alternative Proteins and their Sources as Novel Foods

Ermolaos Ververis, Ruth Roldan Torres

Nutrition Unit

Presentation Outline



Alternative Proteins: Current Interest

efsa
European Food Safety Authority

New technologies

Innovation

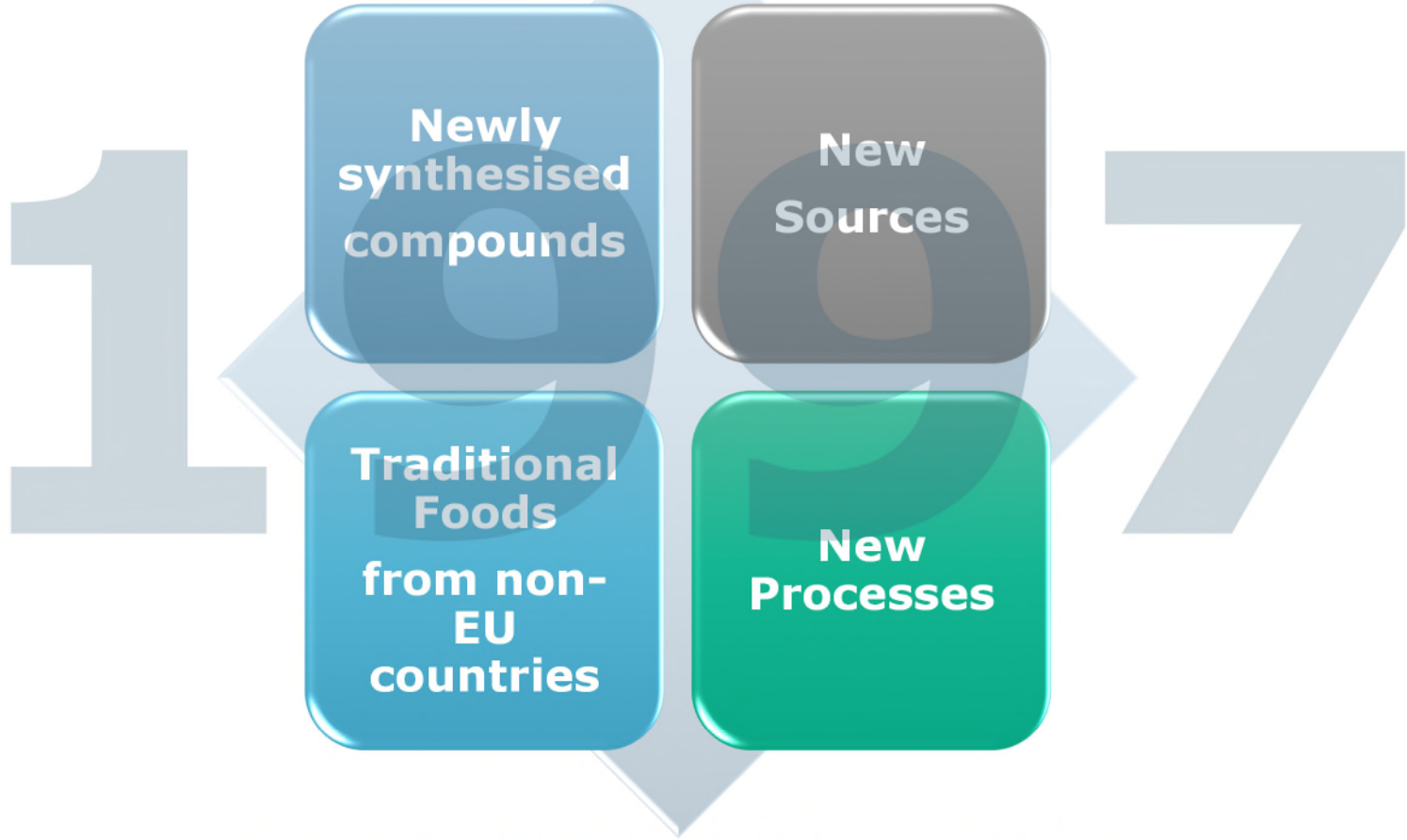
Environmental sustainability

Ethics/Animal welfare

Health considerations

Nutrient Composition

Alternative Proteins: the "Novel" Status



Regulation (EU) 2015/2283 on Novel Foods

EFSA Novel Food Guidance (2016)

- Administrative data
- Introduction
- Identity of the novel food
- Production process
- Compositional data
- Specifications
- History of use of the novel food and of its source
- Proposed uses and use levels and anticipated intake
- Absorption, distribution, metabolism, and excretion
- Nutritional information
- Toxicological information
- Allergenicity
- Concluding remarks
- Annexes, references

EFSA shall consider the following:

- ✓ whether the NF is **safe** under the proposed conditions of use
- ✓ whether the normal consumption of the NF would be **nutritionally disadvantageous**

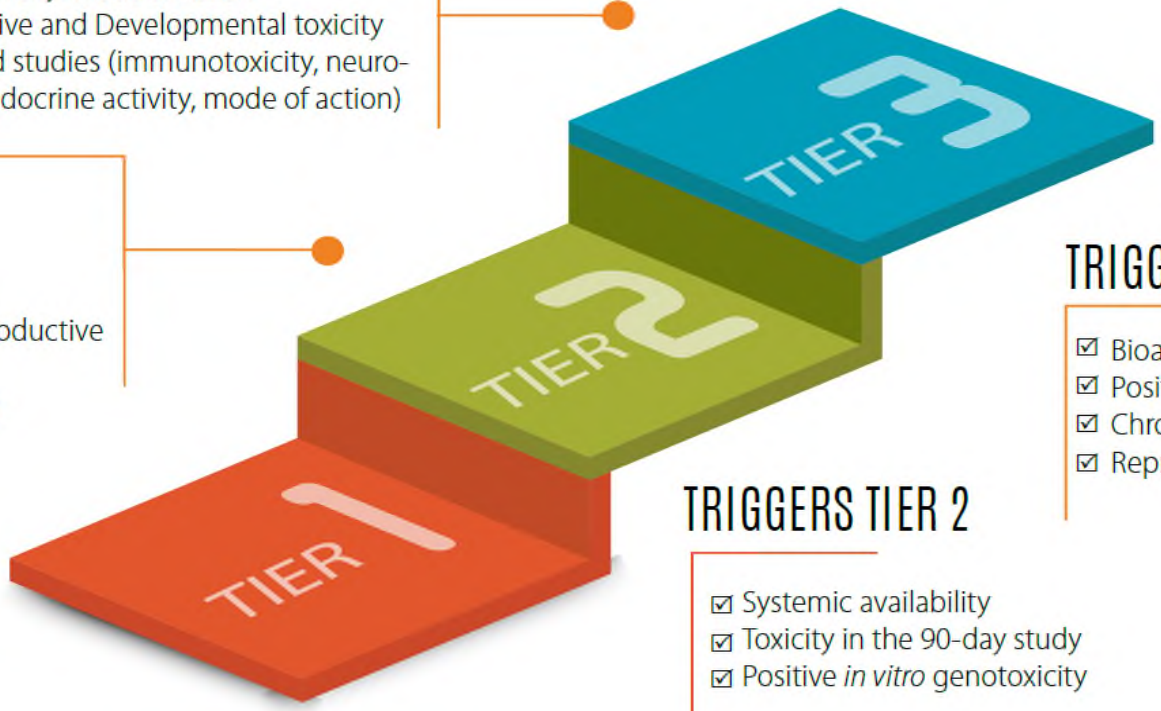
Tiered Toxicity Testing Approach by EFSA

European Food Safety Authority

- ADME: repeated dose, volunteer studies
- Carcinogenicity: *Mode of Action*
- Reproductive and Developmental toxicity
- Specialised studies (immunotoxicity, neuro-toxicity, endocrine activity, mode of action)

- ADME: single dose
- Genotoxity (*in vivo*)
- Chronic toxicity
- Carcinogenicity
- Extended One-Generation Reproductive Toxicity Study (EOGRTS)
- Prenatal developmental toxicity

- Absorption
- Genotoxicity (*in vitro*)
- Extended 90-day toxity study (*in vivo*)



TRIGGERS TIER 3

- ☑ Bioaccumulation
- ☑ Positive *in vivo* genotoxicity
- ☑ Chronic carcinogenicity
- ☑ Repro and developmental toxicity

TRIGGERS TIER 2

- ☑ Systemic availability
- ☑ Toxicity in the 90-day study
- ☑ Positive *in vitro* genotoxicity

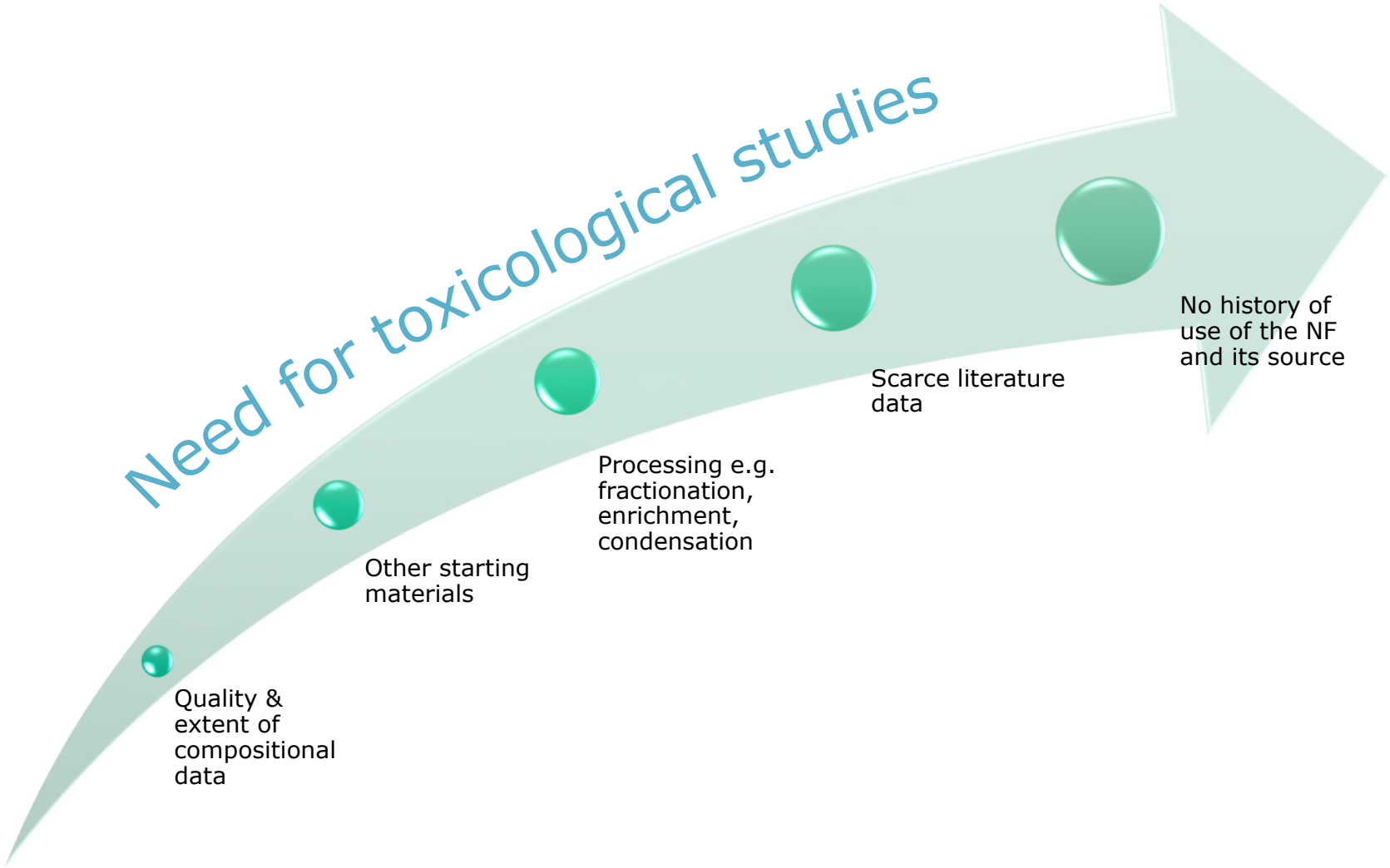
Animal Toxicity Testing: Considerations

Applicable default uncertainty factor:

- Animal → Humans **10**
- Interindividual differences in humans **10**
- Subchronic → chronic exposure **2**

- ✓ UF of **200** (**10 x 10 x 2**) as a default margin of exposure between the reference point (RP) of a subchronic study (no adverse effect level or benchmark dose lower confidence limit) and the estimated high percentile human exposure.
- ✓ UF can be lowered depending on other available data (e.g. nature, type and history of use of the NF and/or its source, compositional data, production process, human data on the endpoint used as the RP etc).
- ✓ NF consisting largely of macronutrients usually cannot be readily tested at doses 100 or 200 times higher than the intended human intake.
- ✓ EFSA Guidance on conducting subchronic toxicity study in rodents on whole food/feed

Animal Toxicity Testing



Alternative Proteins – Examples

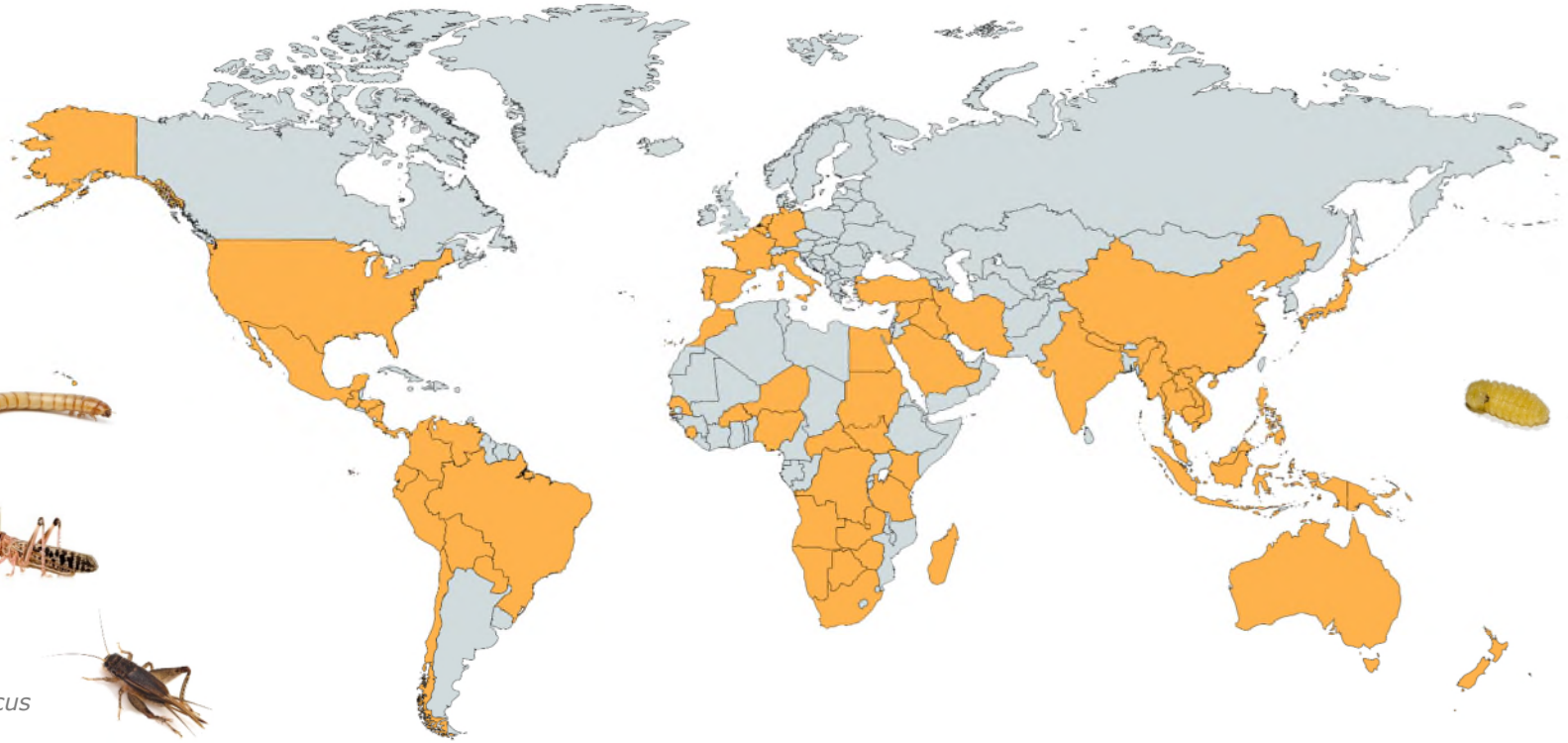
Animal-derived Alternative Proteins and their Sources

Insects & Products thereof

Insects as Food around the World

efsa
European Food Safety Authority

Around 2000 insect species reported to be consumed as food



Mealworm
Tenebrio molitor

Grasshopper
Locusta migratoria

House cricket
Acheta domesticus

Black soldier fly larvae
Hermetia illucens

Caterpillar
Imbrasia belina

Ant eggs
Oecophylla spp

Wasp larvae
Vespula and *Dolichovespula spp*

Silkworm
Bombyx mori

Bee larvae
Apis melifera

Insects & Products thereof as Novel Foods

(NF dossiers received by EFSA)

November 2020

11 EFSA Risk assessment

4 EFSA Suitability check

7 Adults

2+2 *Acheta domesticus*

1+1 *Locusta migratoria*

1 Gryllodes sigillatus

8 Larvae

4 *Tenebrio molitor*

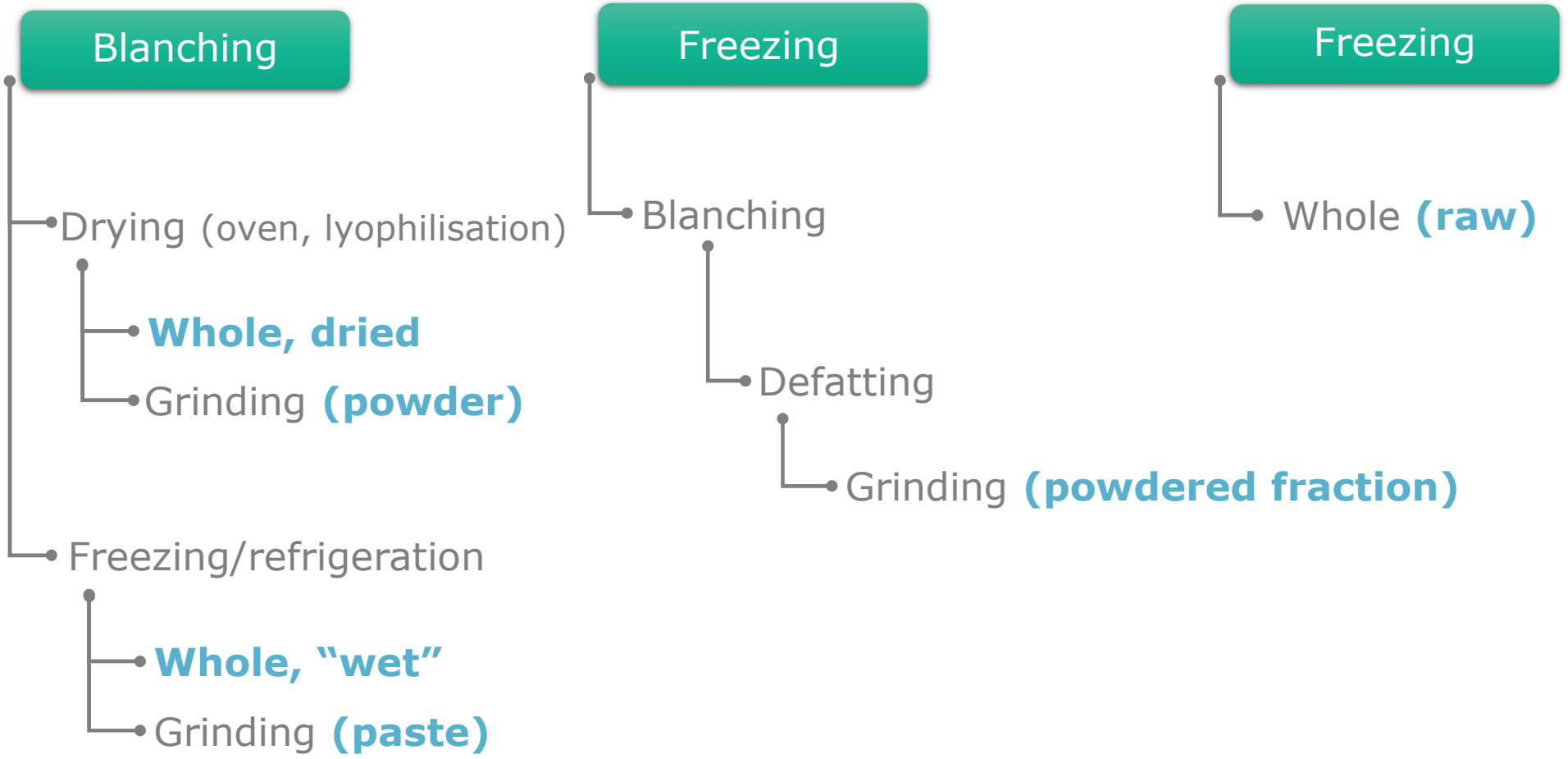
1+1 *Alphitobius diaperinus*

1 *Hermetia illucens*

1 *Apis mellifera*

Processing & Formulations

(in the NF dossiers arrived at EFSA)



Safety Assessment: Main Considerations

Production process

Insect species

- Physical hazards/risks
- Developmental stage
- Endogenously produced compounds

Farming

- Rearing conditions
- Feeding substrate

Harvest & killing

- Fasting step
- Intestinal track not removed
- Separation of insects from frass, decayed animals

Processing

- Microbiological aspects
- Processing contaminants
- Stability

Safety Assessment: Main Considerations

Characterisation & Specifications

- Whole insects: complex foods
- Qualitative and quantitative characterisation of the main constituents & proximate analysis
- Nutritionally relevant constituents (e.g. vitamins, minerals)
- Inherent substances of possible concern to human health
- Impact of feed (bioaccumulation/cross-contamination)
- Collection & extrapolation of data from literature
- Stability (microbiological & oxidative stability of fats)
- Processing contaminants
- Quantification of protein and interference of chitin
- Analytical accreditations are matrix-related

Safety Assessment: Main Considerations

History of Use

- Precautions and restrictions of use (e.g. removal or parts before preparation and consumption)
- Role in the diet of other populations & non-food uses

Proposed Uses, Use Levels & Intake

- Form of uses & food categories to be used must be clear
- Exposure assessment as appropriate

Safety Assessment: Main Considerations

Nutritional Information

- Protein quantification, non-protein nitrogen of chitin, nitrogen-to-protein conversion factor
- Protein quality (e.g. amino acids, digestibility)
- Antinutritional factors (e.g. inhibiting absorption or modifying bioavailability)

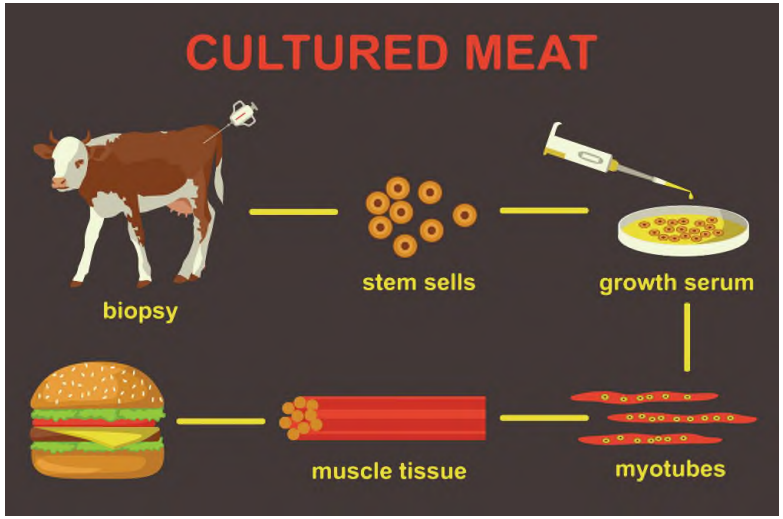
Allergenicity

- *de novo* sensitization
- Cross- reactivity
- Allergens from the feed (e.g. gluten)
- Chitin

Animal-derived Alternative Proteins and their Sources

Cultured (*in vitro*) Meat

What is cultured (*in vitro*) Meat?



Safety Assessment: Main Considerations

Identity

Foods consisting of, isolated from or produced from cell culture or tissue

- Biological source (International codes of nomenclature)
- Organ and tissue or part of the organism
- Information on the identity of cells
- Type of culture
- Stem cells, laboratory, culture collection
- Cell or tissue substrate used as a novel food

Characterisation

- Identities and quantities of impurities, by-products or residues, antimicrobial residues
- Nutritionally relevant constituents
- Biological hazards: BSE/TSE, viruses (source, zoonotic), microbiological contaminants
- Type and spectrum of target analytes depending on sources and production process

Safety Assessment: Main Considerations

Production Process

Detailed description including:

- Treatment, modification, immortalisation of cells
- Raw materials, starting substances, medium/ substrate, growth factors/hormones, culture conditions, antimicrobials, hygiene measures, description of the equipment.

Generic issues related to manufacturing processes using cultured cells:

- Potential by-products, impurities, contamination, stability of cells, consistency of the production process
- Operational limits and key parameters of the production process

Safety Assessment: Main Considerations

Nutritional Information

- Role of the NF in the diet (based on the intended uses)
- Comparative approach with conventional meat
- Quality and quantity of macro & micronutrients

Allergenicity

- Basis: comprehensive compositional data
- Potential use of «omics» tools (genomics, transcriptomics, proteomics, metabolomics)

Non-animal Alternative Proteins and their Sources

Plants & Products thereof

Plants & Products thereof as Novel Foods

Processing & Formulations

Input

Whole plants

Grains or seeds, and their derivates (e.g. flours)

Part of plants (e.g. leaves, roots)

Processing

Output

Protein-based powders/extracts

Protein isolates/ concentrates

Others (e.g. fermented protein mixtures)

Safety Assessment: Main Considerations

Production process

INPUT

- Fertilizer composition
- Pesticide residues
- Growth medium
- Primary/secondary metabolites
- Water/ground contamination
- Environmental and transportation conditions

PROCESSING

- Heat-treatment
- Reduction of antinutrients
- Off-flavours
- Extraction solvents
- Process enzymes
- Fermentation
- Toxic compounds from Maillard reaction

Safety Assessment: Main Considerations

Characterisation & Specifications

- Contaminants & undesirable substances

(e.g. primary & secondary metabolites, process enzymes and heavy metals, residues of cultivation conditions)

- Microbiological aspects

(e.g. pH, water activity, microbial counts & toxins)

- Processing contaminants

(e.g. thermal processing: lysinoalanine, Maillard reaction products, acrylamide)

- Stability markers

(e.g. lipid oxidation markers, organoleptic attributes)

- Macro- and micro- nutrients
- Antinutritional factors
- Toxicants/allergens

Safety Assessment: Main Considerations

Characterisation & Specifications

Alfalfa protein concentrate

- 45 - 60 % protein
- L-canavanine
- Phytoestrogens (coumestrol and isoflavones)
- Saponins
- Phytate

Rapeseed powder & protein isolate

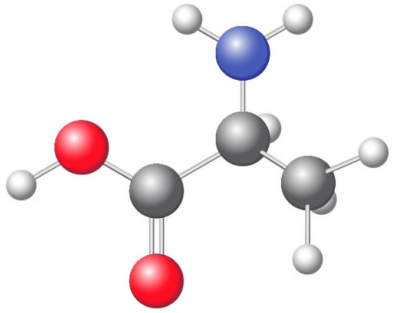
- Powder 33–43 % protein, isolate ≥ 90 % protein
- Glucosinolates
- Phytate
- Erucic acid

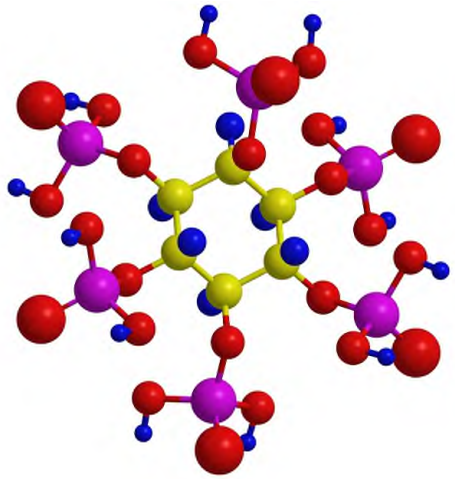
Chia seeds

- seeds 15-26 % proteins, powder ≥ 40 % protein
- Phenolic acid derivatives and flavonoids
- Process contaminants

Safety Assessment: Main Considerations

Nutritional Information



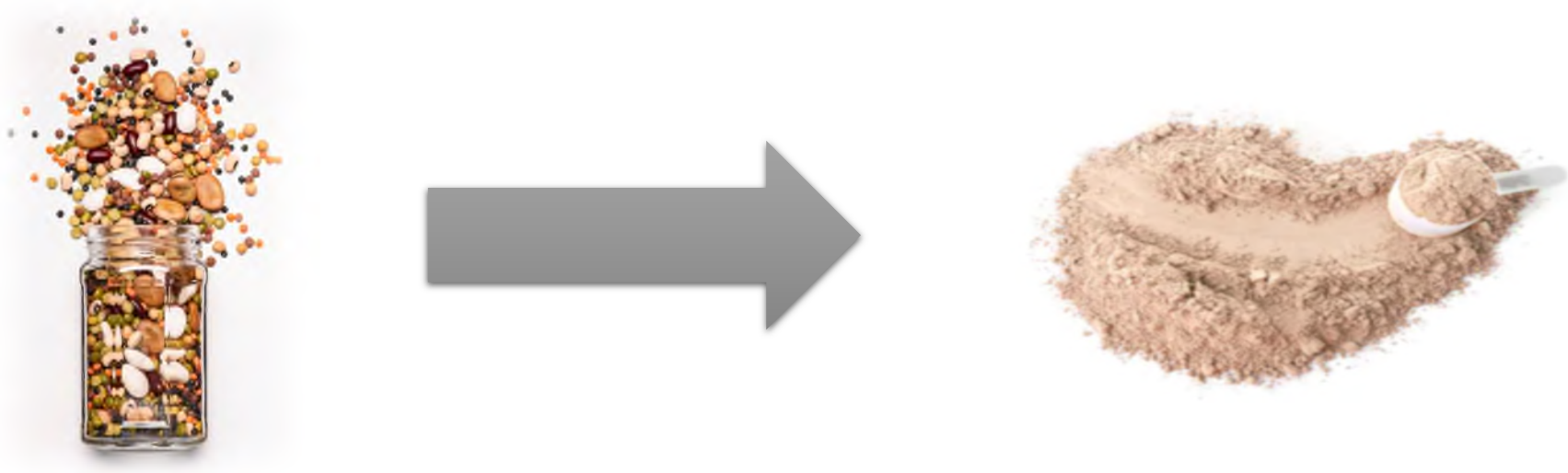


- Protein digestibility
- Aminoacid profile
- Antinutrients

Safety Assessment: Main Considerations

Allergenicity

- Scarce evidence in the existing literature
- *de novo* sensitization
- Cross reactivity (e.g. rapeseed with mustard)
- Potential impact of the production process
- Mixture of various proteins



Non-animal Alternative Proteins and their Sources

Algae & Products thereof

Algae & Products thereof as Novel Foods

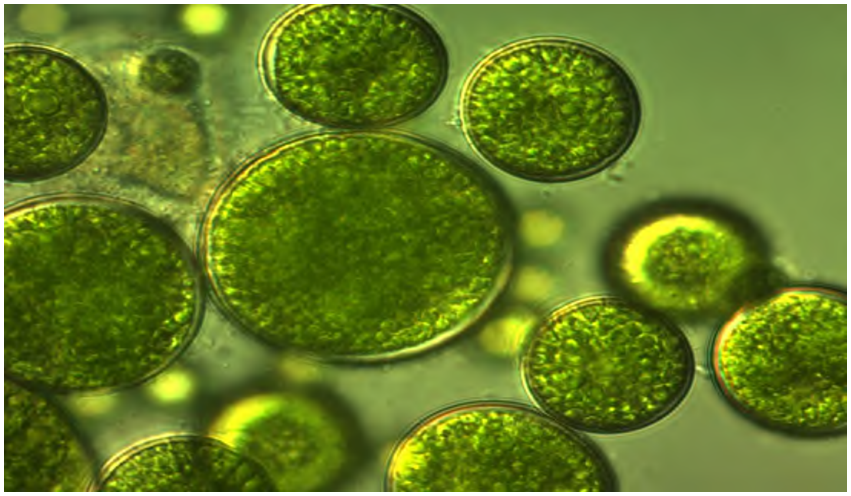
Examples of NF applications

Macroalgae

- *Laminaria digitata*

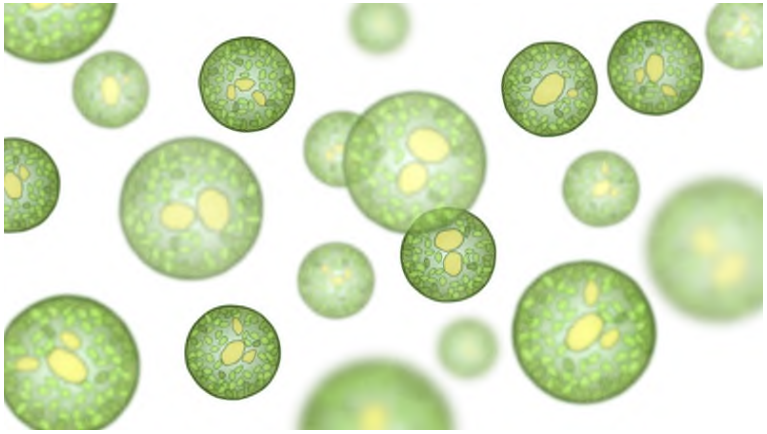
Microalgae

- *Galdieria sulphuraria*
- *Schizochytrium* sp.
- *Phaeodactylum tricornutum*
- *Tetraselmis chuii*



Safety Assessment: Main Considerations

Identity



- Scientific name & synonyms
- Verification according to internationally recognized databases and methodology
- Deposition in an officially recognized culture collection
- Qualified Presumption of Safety (QPS) status

Production Process

- Fermentation/cultivation conditions (e.g. time, temperature, pH, presence of light, open vs. close systems)
- Culture medium constituents
- Downstream processing
- Absence/ presence of viable cells of the production strain in the NF

Safety Assessment: Main Considerations

Characterisation

- Nutritional composition (e.g. iodine)
- Algal toxins and other toxic substances (e.g. accumulation of heavy metals)
- Particle size distribution in case of dried biomass (powder)
- Stability tests in relation to their composition and the indented uses

Allergenicity

- Potential risk from algal proteins
- Potential use of proteomic analysis

efsa
European Food Safety Authority

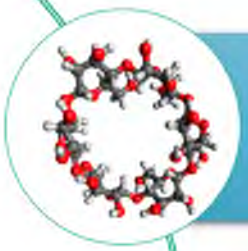
Q&A

Novel Carbohydrates as Novel Foods

Reinhard Ackerl, Gabriela Precup, Océane Albert

Nutrition Unit

Outline



Novel fibre

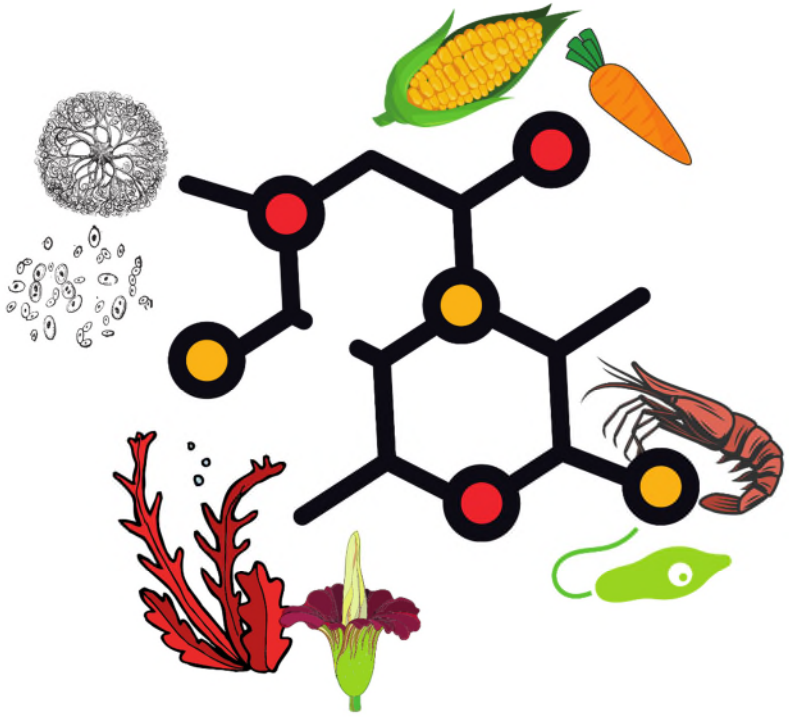
Human identical milk oligosaccharides

Novel Foods intended to replace sugars

Novel Carbohydrates as Novel Foods

Novel Fibre

Manifold Sources and Production Processes



Sources:

- Plants
- Fungi
- Bacteria
- Yeast
- Algae
- Animals

Production processes:

- Chemical
- Enzymatic
- Fermentation

etc.

Adequate Intake for Dietary Fibre set by EFSA

Age group (years)	Dietary fibre (g/d)
1	10
2–3	10
4–6	14
7–10	16
11–14	19
15–17	21
≥ 18	25

Scientific Opinion on Dietary Reference Values for carbohydrates and dietary fibre (EFSA NDA Panel, 2010): https://efsa.onlinelibrary.wiley.com/doi/epdf/10.2903/j.efsa.2010.1462

Fibre Intake generally below Adequate Intake

- Mean dietary fibre intake in g/day in the EU:

Adults			
Males		**Females**	
AT	19.5	**AT**	20.1
DK	21.0	**DK**	19.0
FI	24.0	**FI**	21.0
FR	18.7	**FR**	15.7
HU	24.2	**HU**	21.7
IE	23.2	**IE**	17.4
IT	21.8	**IT**	18.9
LT	20.9	**NO**	21.0
NO	25.0	**PL**	19.7
PL	**29.7**	**PT**	23.7
PT	23.5	**SE**	16.0
SE	18.0	**ES**	16.9
ES	19.2		

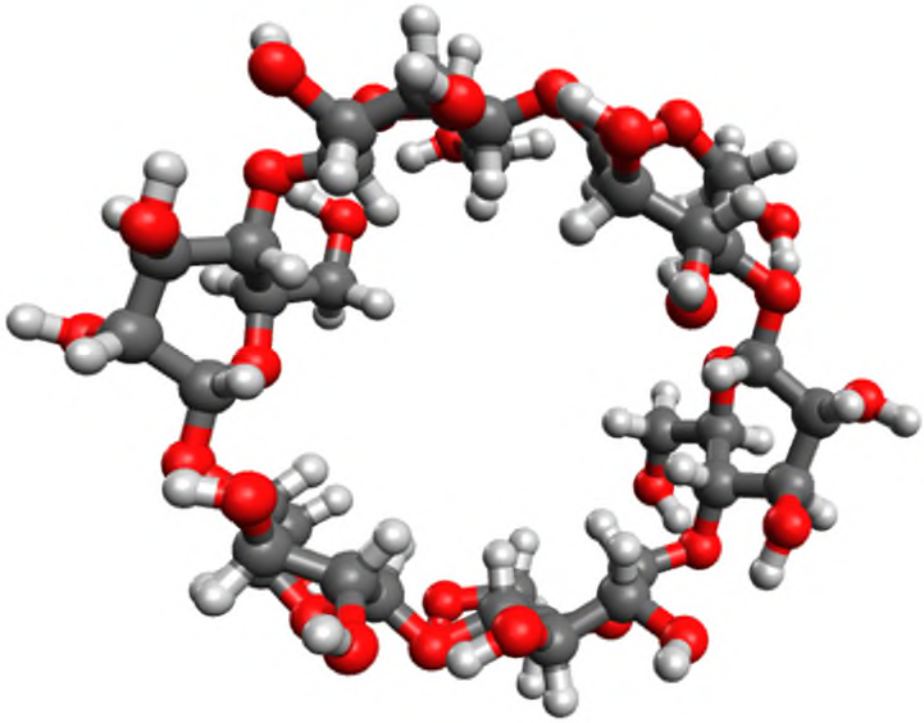
Children 7-9 years			
Males		**Females**	
AT	15.0	**AT**	14.3
DE	**17.5**	**DE**	**16.8**
DK	**18.0**	**DK**	**17.0**
FR	13.5	**FR**	12.2
NL	**17.0**	**IT**	15.2
NO	**16.0**	**NL**	15.0
PL	**19.6**	**NO**	14.0
PT	**20.2**	**PL**	**17.4**
SE	14.0	**PT**	**19.4**
		SE	13.0

Scientific Opinion on Dietary Reference Values for carbohydrates and dietary fibre (EFSA NDA Panel, 2010): https://efsa.onlinelibrary.wiley.com/doi/epdf/10.2903/j.efsa.2010.1462

Alpha-cyclodextrin

- Starting material: starch, i.e. polymeric carbohydrate of numerous glucose units
- Converted enzymatically into a molecule with circular structure
- Six glucose subunits linked end to end via α-1,4 linkages

  → cannot be hydrolysed by human amylases (salivary, pancreatic) anymore

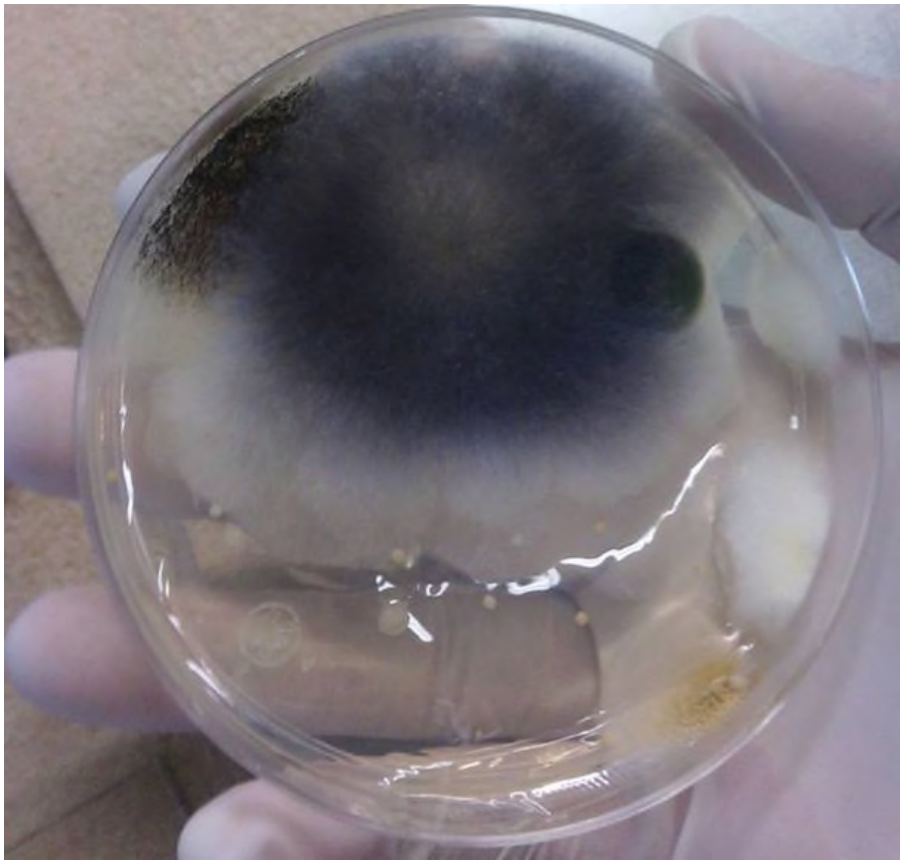


Resistant Starch – chemically modified

- Source: high amylose maize starch
- Chemically modified (starch chains cross-linked and esterified with phosphate groups)
  - ↪ Creation of phosphated distarch phosphate = resistant starch (Type IV)
  - ↪ Digestibility is decreased

Chitin-glucan from *Aspergillus niger*

- Derived from the cell wall of the mycelium of *Aspergillus niger*
- Contains 90% chitin glucan
- Obtained by fermentation
- Non-toxic non-pathogenic strain (used for citric acid production)



Fibre-rich NF from Yeast - *Yarrowia lipolytica*

- Dried biomass
- History of use as feed not food, but it can be found in many types of cheese/dairy products
- ~25% fibre (beta-glucan)
- Yeast species received qualified presumption of safety (QPS) (based on extensive literature search)
- Yeast cells are heat-killed during the manufacturing process

Selenium-enriched *Yarrowia lipolytica*

Chromium-enriched *Yarrowia lipolytica*

Fibre-rich NF from Algae - *Euglena gracilis*

- Single-cell alga extensively used in laboratory as model organism
- History of food outside EU (Japan)
- Received qualified presumption of safety (QPS)
- >50% fibre (beta-glucan) in the NF, i.e. dried biomass.

Combination of 3 non-starch Polysaccharides

- Mixed in a specific (proprietary) ratio to produce the Novel Food ("PGX")

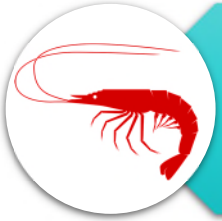
Konjac glucomannan
[*Amorphophallus konjak*]

Xanthan gum
[*Xanthomonas campestris*]

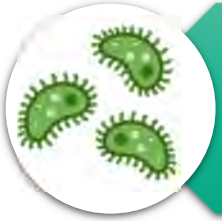
Sodium alginate
[Brown seaweed]

Ongoing Assessments

Rhamnogalacturonan I - enriched carrot fibre (from carrot pomace)



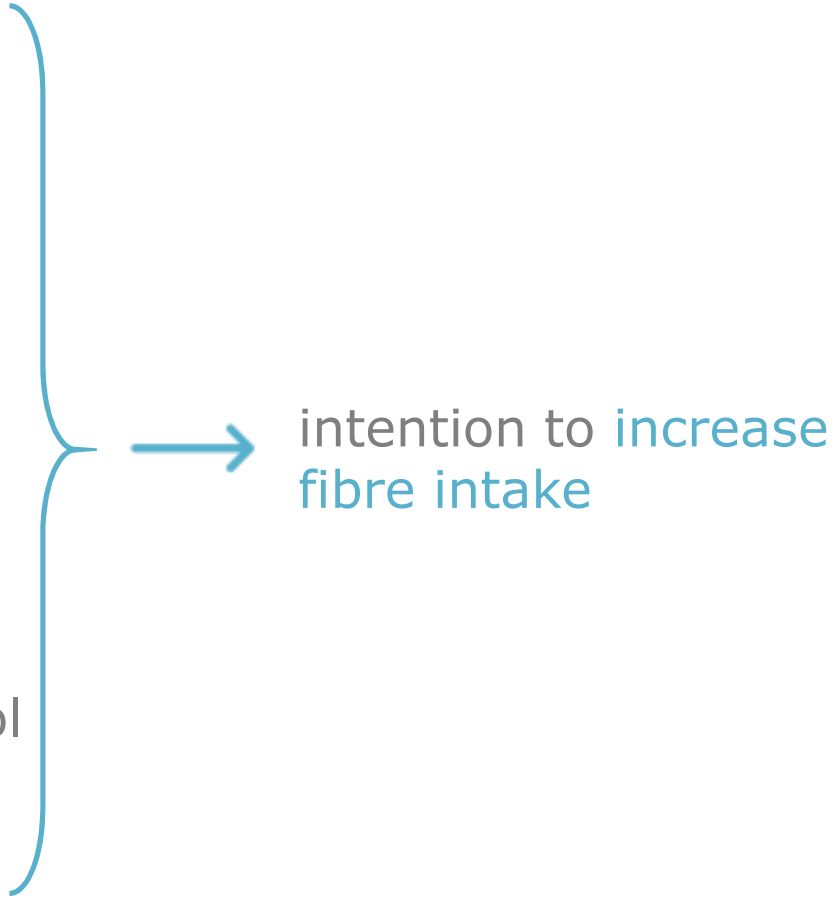
Chitosan - from exoskeletons of crustaceans



Bacterial cellulose aqueous suspension (obtained by fermentation with *Komagataeibacter sucrofermentans*)

How Novel Foods enter the Food Chain

- Breads
- Biscuits/cookies
- Cereals/cereal bars
- Pasta
- Milk shakes
- Yoghurts
- Fruit and vegetable juices
- Non-alcoholic beverages
- Dairy desserts
- Meal replacement for weight control
- Infant and follow-on formula
- Food supplements



Implications for the Risk Assessment

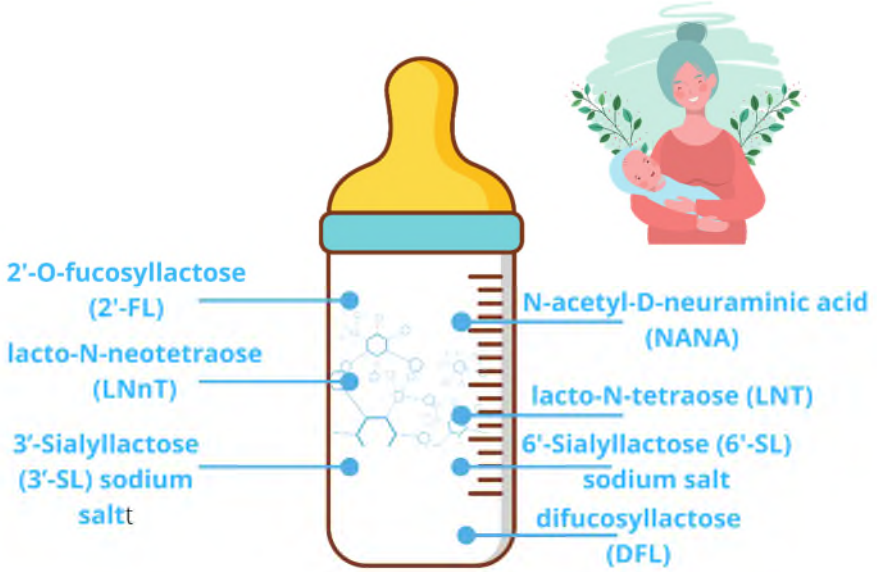
- Live microorganism/heat-killed/pasteurised?
- History of use?
- Qualified presumption of safety (QPS)?
- Reagents of production process/residuals?
- Chemical contamination?
- Hygiene/microbiological risk (waste used as source)?
- Secondary metabolites/anti-nutrients of concern?
- Species (or closely related ones) toxin producer (e.g. aflatoxin)?
- Tolerable Upper Intake Levels (ULs) exceeded (e.g. Se-enriched *Yarrowia*)?

Novel Carbohydrates as Novel Foods

Human identical Milk Oligosaccharides (HiMOs)

Human Milk Oligosaccharides: Interest

- HMOs: 3rd largest solid component (after lipids and lactose) of the breast milk
- More than 150 HMOs identified
- HiMOs: main components of the NF-identical to HMOs
- Applications in food products and for infant nutrition (IF, FOF)



Human identical Milk Oligosaccharides as Novel Foods in the EU

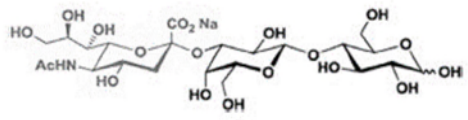
- 2'-O-fucosyllactose (2'-FL) (EFSA, 2015)
- lacto-N-neotetraose (LNnT) (EFSA, 2015)
- LNnT and 2'-FL in food supplements for children (EFSA, 2015)
- N-acetyl-D-neuraminic acid (NANA) (EFSA, 2017)
- 2'-FL/difucosyllactose mixture (EFSA, 2019)
- lacto-N-tetraose (LNT) (EFSA, 2019)
- 6'-Sialyllactose (6'-SL) sodium salt (EFSA, 2020)
- 3'-Sialyllactose (3'-SL) sodium salt (EFSA, 2020)
- Lacto-N-neotetraose (EFSA, 2020)
- 3-fucosyllactose (3-FL)(2) (EFSA, 202X)
- 2'-FL (EFSA, 202X)
- 3'-Sialyllactose (3'-SL) (EFSA, 202X)
- 6'-Sialyllactose (6'-SL) (EFSA, 202X)
- Lacto-N-tetraose (LNT) (EFSA, 202X)

European Commission

Summary of applications

Main Considerations for Safety Assessment

Identity



- Food with a new or intentionally modified molecular structure*
- Food consisting of, isolated from or produced from microorganisms, fungi or algae *
- Information on the NF source
- Chemical & structural characterization of the NF vs natural HMOs

*Regulation (EU) 2015/2283

Production Process

- Chemical synthesis or fermentation by genetically modified microorganisms (GMM, e.g. *E.coli*)
  - check for absence of DNA, byproducts and antimicrobial resistance genes
  - impurities and solvents

Main Considerations for Safety Assessment

Characterisation & Specifications

- Qualitative and quantitative characterisation of the main constituents & proximate analysis
- Substances of possible concern to human health (residual endotoxins)

Main Considerations for Safety Assessment

Proposed uses, use levels and anticipated intake

- Uses for infant and follow-on formulae, variety of food and food supplements as proposed
- Appropriate exposure assessment from different foods in various population categories

Main Considerations for Safety Assessment

Anticipated intake:

- Define an appropriate natural level (representative concentration of a given HMO) in breast milk, based on literature data
- Estimate a possible maximal natural intake of the HMO per kg bodyweight of infants
- Estimate a possible maximal intake of the HiMO per kg bodyweight of infants further to NF intake
- Compare the intake of HiMO per kg bodyweight to the natural intake of HMOs from breast milk

- A possible consumption that does not exceed a natural intake is considered **safe**

Main Considerations for Safety Assessment

Toxicological information

- Limited toxicological studies (Tier I) as per guidance
- Genotoxicity studies to rule-out specific concerns (e.g. for impurities)
- Sub-chronic studies (e.g. 90-day) provide insight on the behaviour of the NF
- Sometimes limited margin of exposure in comparison with the anticipated intake

Nutritional information

- Non-digestible oligosaccharides, negligible nutritional impact
- Demonstration that they are not nutritionally disadvantageous

Novel Carbohydrates as Novel Foods

Intended to replace Sugars

Food Additives or Novel Foods?

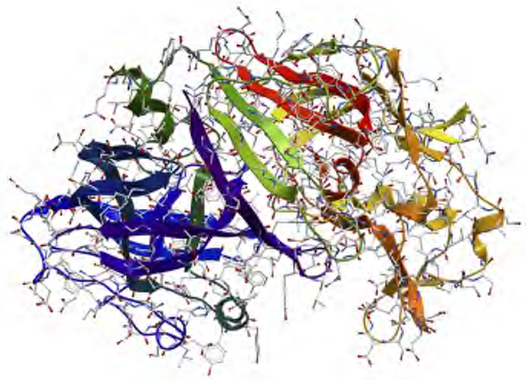
- Food Additives Regulation (EC) 1333/2004 Article 3(2)(a)(i):

*"**monosaccharides, disaccharides or oligosaccharides** and foods containing these substances used for their sweetening properties **are not considered to be food additives**"*

- Therefore, all mono-, di- and oligo-saccharides with new or intentionally modified molecular structure, where that structure was not used as, or in, a food within the Union before 15 May 1997 are considered **NOVEL FOOD**

Challenges from the Production Process (1)

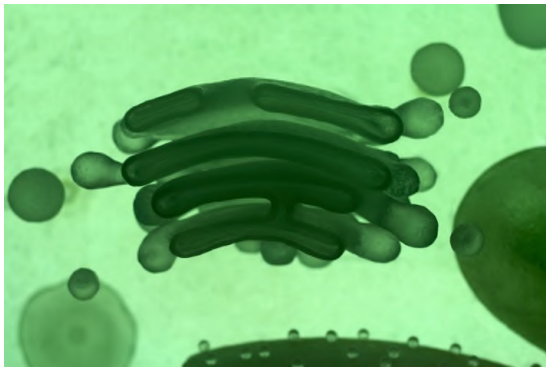
- NF intended to replace sugars are often obtained by enzymatic reactions
- Food enzymes covered by Regulation (EC) No 1332/2008, not by the Novel food Regulation (EC) 2015/2283



However:

- Evaluation of food enzymes ongoing at EFSA
- No Union List of authorized enzymes established by the EC yet

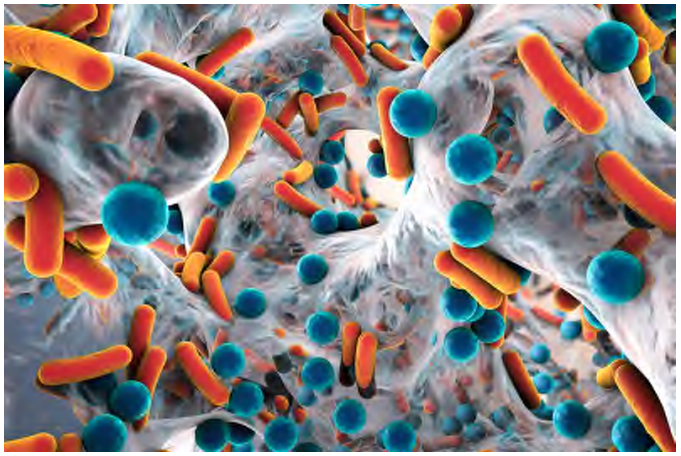
Request for information according to the Guidance on the characterisation of microorganisms used as feed additives or as production organisms (EFSA, 2018) and Characterisation of microorganisms used for the production of food enzymes (EFSA, 2019)



Challenges from the Production Process (2)

If a NF consists, contains or is produced:

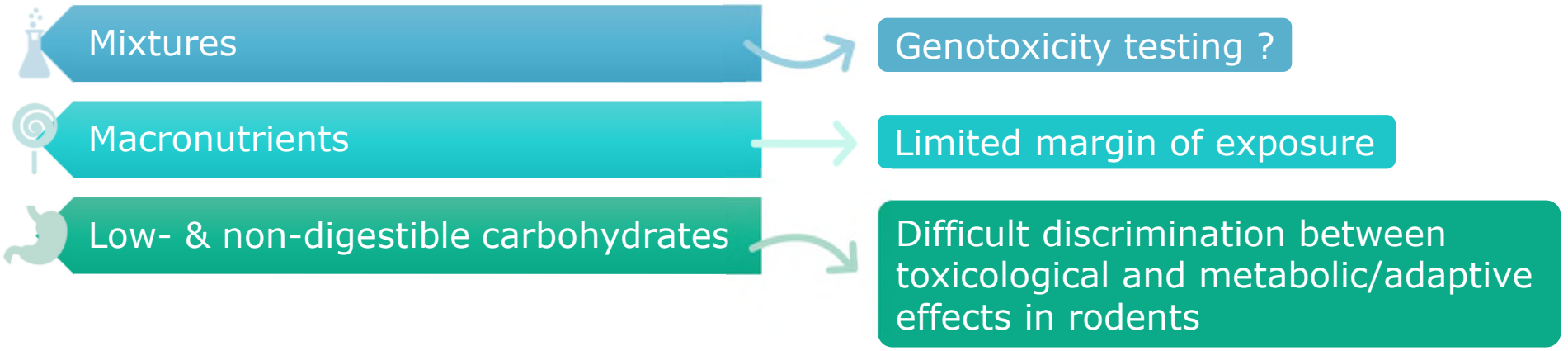
- with a microorganism
  - ↪ evaluation for Qualified Presumption of Safety (QPS) by the Biohazard Panel
- with a microorganism which has been granted QPS
  - ↪ the NDA Panel would not question the safety of that microorganism
  - ↪ other safety aspects of a Novel Food will have to be assessed and additional data may be requested



QPS is granted at the taxonomic species level
QPS is generally not applied to genetically modified microorganisms

Challenges in Toxicity Testing

- Default tiered toxicological approach (including Tier 1 absorption, genotoxicity and subchronic toxicity studies) not always optimal/possible



- Possible alternatives/solutions:
  - Good compositional characterisation of the NF
  - Control group(s)
  - Human studies

What role for Human Data?

- Human clinical trials may provide supportive evidence to investigate potential adverse effects provided they are:

RELEVANT

- Test material
- Study population
- Studied dose
- Duration
- Safety-related parameters reported

etc.

RELIABLE

- Study design
- Execution (risk of bias?)

etc.

- Absence of adverse effects in human clinical trials is not necessarily evidence of safety
- History of use (human consumption) outside the EU can also prove useful

efsa
European Food Safety Authority

Q&A

Other Trends in Novel Foods

Food Supplements

Wolfgang Gelbmann, Annamaria Rossi, Andrea Germini

Nutrition Unit

Outline

Plant extracts

(Synthetic) cannabidiol

Engineered nanomaterials

Focus on Food Supplements

Food Supplement Directive 46/2002

- Vitamin and mineral substances in Annex I + II
- Art 4(6): EFSA assessed about 280 vitamin and mineral substances the majority until 2009

No harmonised EU approach	No EU harmonised minimum or maximum levels for vitamins and minerals	No EU harmonised use of "*other substances*" (incl. botanicals)
Notification to the EU member state(s) may be required	UL, DRV and background intake to be considered (but subject to manufacturers & national limits)	National provisions

≠ (Reg EU 1925/2006 other food stuff)

If safety concerns are raised – risk managers, on its own initiative, EFSA could be tasked

- Novel Foods intended for FS may be also a new "nutrient sources"

FS in the EU – Role of the EFSA NDA Panel

- Vitamins and minerals: DRVs including ULs
- "Other substances" (safety – only upon request or own initiative)
- Health Claims (efficacy) – *botanicals on hold*
- New nutrient sources (safety and bioavailability)
- **Novel Foods (safety)**

- Other EFSA Panels for additives (e.g. food colour), GMO etc.

Novel Foods in Food Supplements

- **Specific target and restrictions of target population** possible, e.g. adults only. This is not applicable for NF intended to be added to foods like breakfast cereals, beverages, dairy products, breads, etc…. - Art 5 (6) of Implementing rules for Art 10 NF applications - Regulation (EU) 2017/2469. **Reasoning for restrictions**

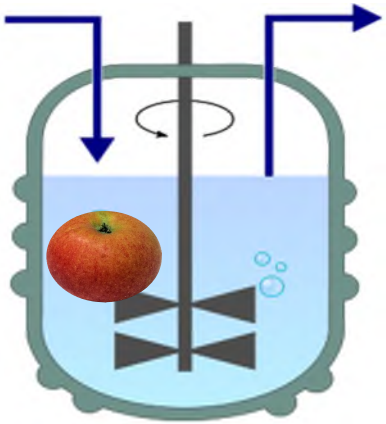
- **Exposure assessment** = proposed maximum intake (possibly background intake) for the proposed target population
- **History of use (HoU) in food supplements** in third countries does not qualify for traditional foods from third countries.
- **HoU in food supplements within the EU**
- **HoU as drug**
- **HoU**: limited weight in establishing the safety of the NF, especially for plant extract given their diversity of their sources, processing, composition, historical conditions of use. However, data may be important.

Other Trends in Novel Foods

Plant Extracts

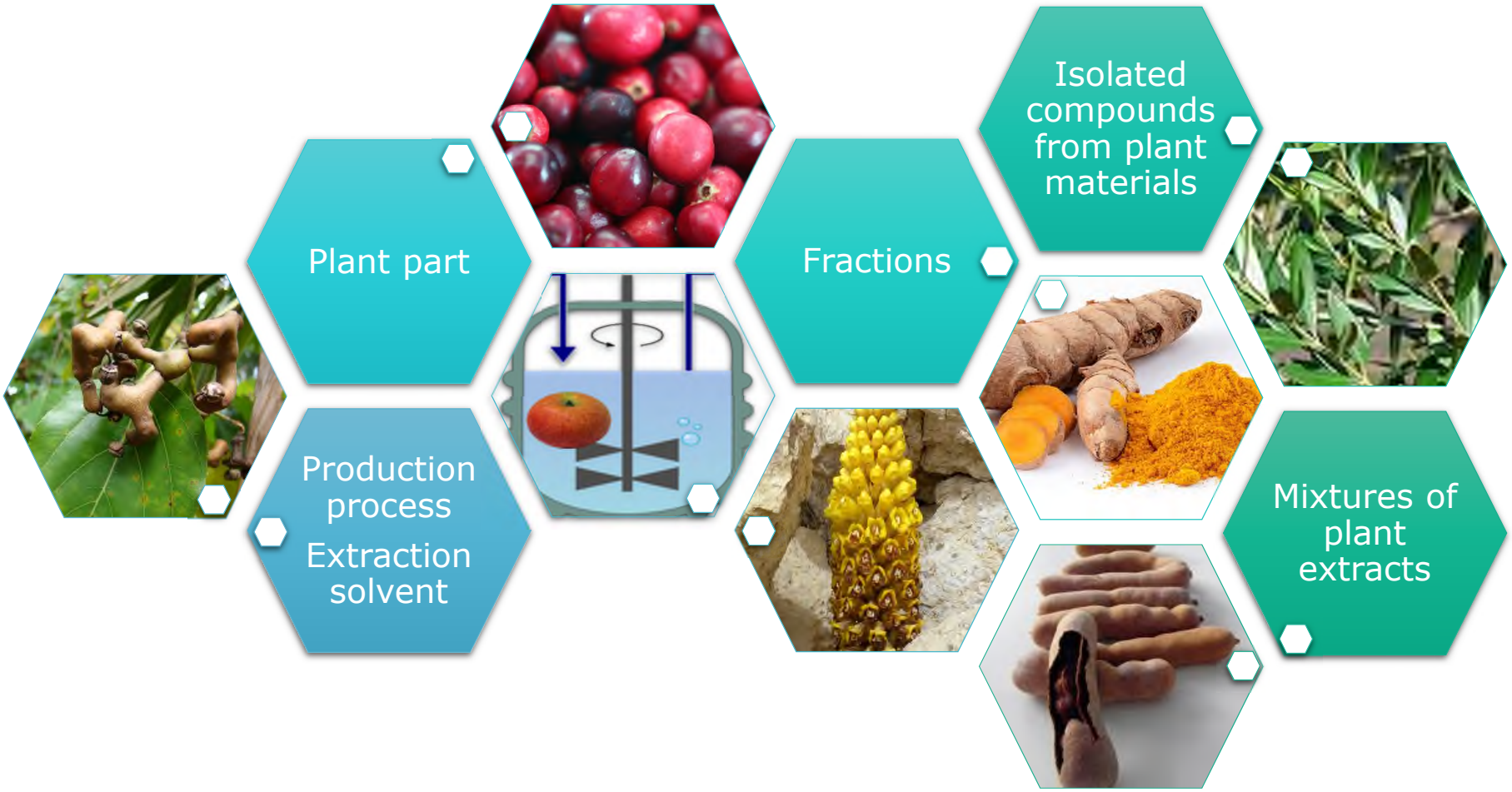
Plant Extracts – Diversity of Sources



With or without history of use of the source, its parts, for food, drug or other uses.

Diversity of the Production Process



Hazard Identification

Available knowledge (botanicals & naturally-occurring substances)

- Identity of the plant source
- Chemical composition of the plant/ plant part used
- Impact of manufacturing process to chemical composition

Available knowledge on reported toxicity/ adverse effects

- Toxicity of plants/ plant preparation
- Toxicity of naturally occurring chemical substances (follow-up)
- Case reports

Literature search

EFSA Compendium of Botanicals*

*Database of naturally occurring substances of possible concern for human health when present in food
https://www.efsa.europa.eu/en/data/compendium-botanicals

Other Aspects – Plant Extracts

- **Safety perspective** on presumed beneficial effects, mode of action
- **Toxicological aspects:** usually mixtures and uncharacterised fraction
    - Representativeness of the test material
    - Tiered toxicological approach (default UF of 200 on subchronic studies)
    - Genotoxicity assessment – usually a mixture

Genotoxicity Assessment of Novel Food

EFSA Genotoxicity testing strategies (2011)

European Food Safety Authority

EFSA Journal 2011;9(9):2379

SCIENTIFIC OPINION

Scientific opinion on genotoxicity testing strategies applicable to food and feed safety assessment [1]

EFSA Scientific Committee[2, 3]

European Food Safety Authority (EFSA), Parma, Italy

This Scientific Opinion, published on 3 October 2012, replaces the earlier version published on 30 September 2011.

EFSA Genotoxicity testing strategies (2011)

efsa
European Food Safety Authority

Tier 1

In vitro genotoxicity testing recommended test battery:

- Bacterial reverse mutation (Ames) assay (OECD TG 471)
- *In vitro* mammalian cell micronucleus test (OECD TG 487)

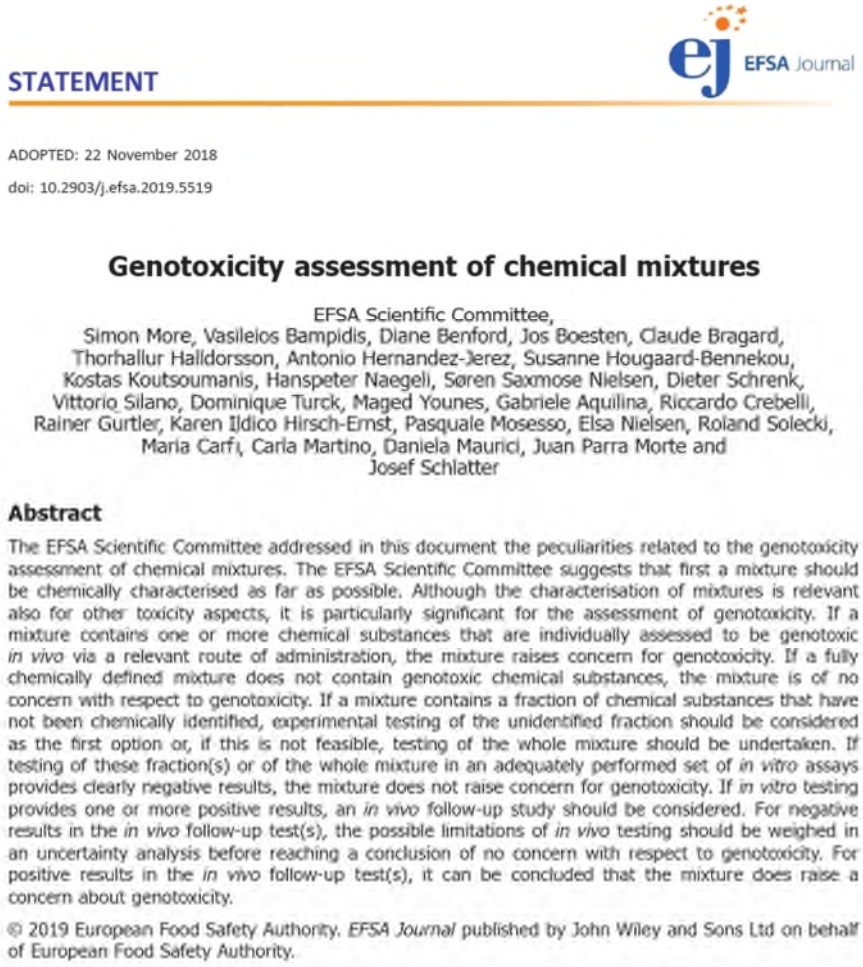
Tier 2 *(follow-up of in vitro positives, to be selected case-by-case based on in vitro test results, SAR, metabolic and toxicokinetic considerations, etc.)*

In vivo genotoxicity testing recommended tests:

- *In vivo* micronucleus test (OECD TG 474)
- *In vivo* comet assay (OECD TG 489)
- Transgenic rodent mutagenicity (TGR) assay (OECD TG 488)

The guidance continues considering examples of different scenarios for the *in vivo* follow up

Genotoxicity of mixtures



STATEMENT

EFSA Journal

ADOPTED: 22 November 2018

doi: 10.2903/j.efsa.2019.5519

Genotoxicity assessment of chemical mixtures

EFSA Scientific Committee,
Simon More, Vasileios Bampidis, Diane Benford, Jos Boesten, Claude Bragard, Thorhallur Halldorsson, Antonio Hernandez-Jerez, Susanne Hougaard-Bennekou, Kostas Koutsoumanis, Hanspeter Naegeli, Søren Saxmose Nielsen, Dieter Schrenk, Vittorio Silano, Dominique Turck, Maged Younes, Gabriele Aquilina, Riccardo Crebelli, Rainer Gurtler, Karen Ildico Hirsch-Ernst, Pasquale Mosesso, Elsa Nielsen, Roland Solecki, Maria Carfì, Carla Martino, Daniela Maurici, Juan Parra Morte and Josef Schlatter

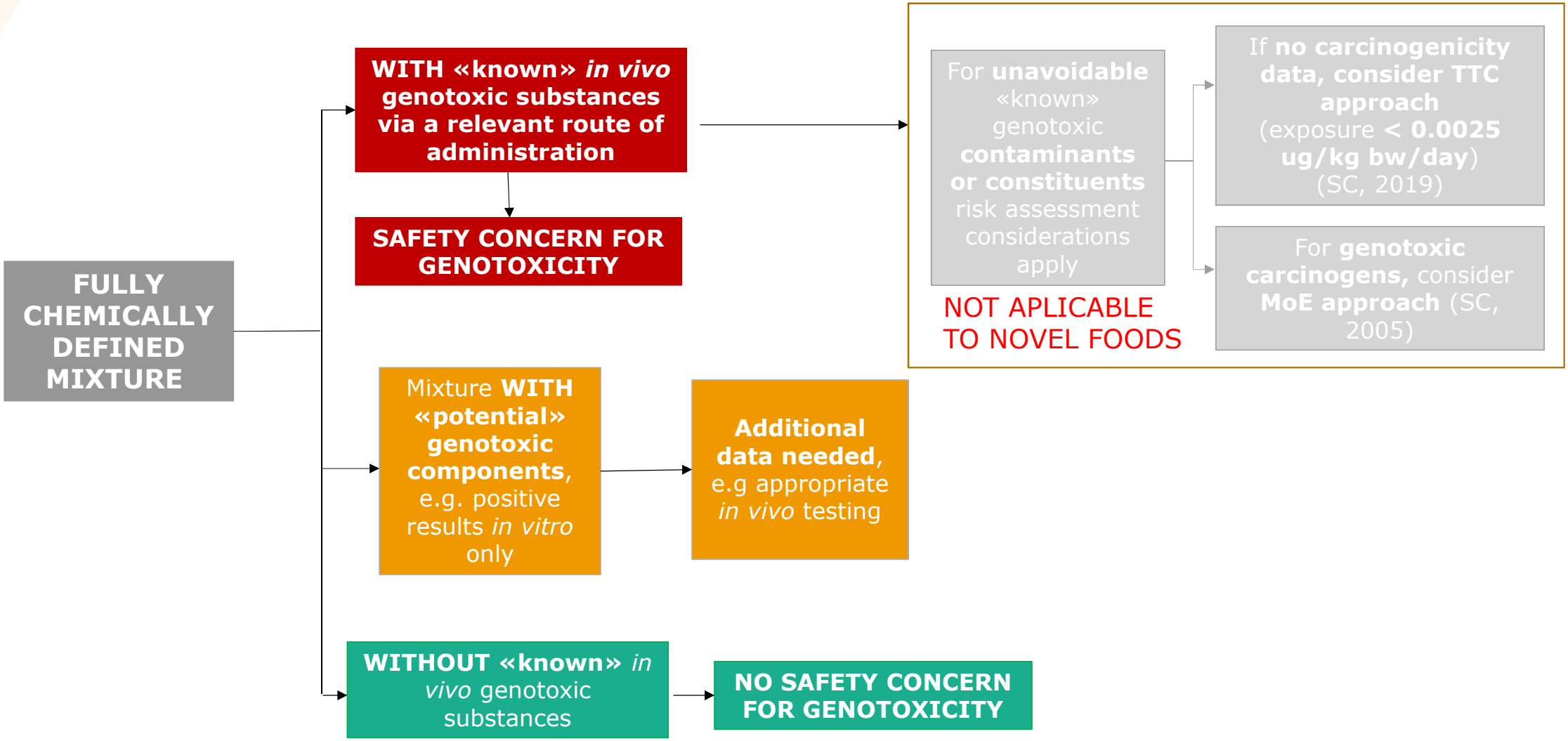
Abstract

The EFSA Scientific Committee addressed in this document the peculiarities related to the genotoxicity assessment of chemical mixtures. The EFSA Scientific Committee suggests that first a mixture should be chemically characterised as far as possible. Although the characterisation of mixtures is relevant also for other toxicity aspects, it is particularly significant for the assessment of genotoxicity. If a mixture contains one or more chemical substances that are individually assessed to be genotoxic *in vivo* via a relevant route of administration, the mixture raises concern for genotoxicity. If a fully chemically defined mixture does not contain genotoxic chemical substances, the mixture is of no concern with respect to genotoxicity. If a mixture contains a fraction of chemical substances that have not been chemically identified, experimental testing of the unidentified fraction should be considered as the first option or, if this is not feasible, testing of the whole mixture should be undertaken. If testing of these fraction(s) or of the whole mixture in an adequately performed set of *in vitro* assays provides clearly negative results, the mixture does not raise concern for genotoxicity. If *in vitro* testing provides one or more positive results, an *in vivo* follow-up study should be considered. For negative results in the *in vivo* follow-up test(s), the possible limitations of *in vivo* testing should be weighed in an uncertainty analysis before reaching a conclusion of no concern with respect to genotoxicity. For positive results in the *in vivo* follow-up test(s), it can be concluded that the mixture does raise a concern about genotoxicity.

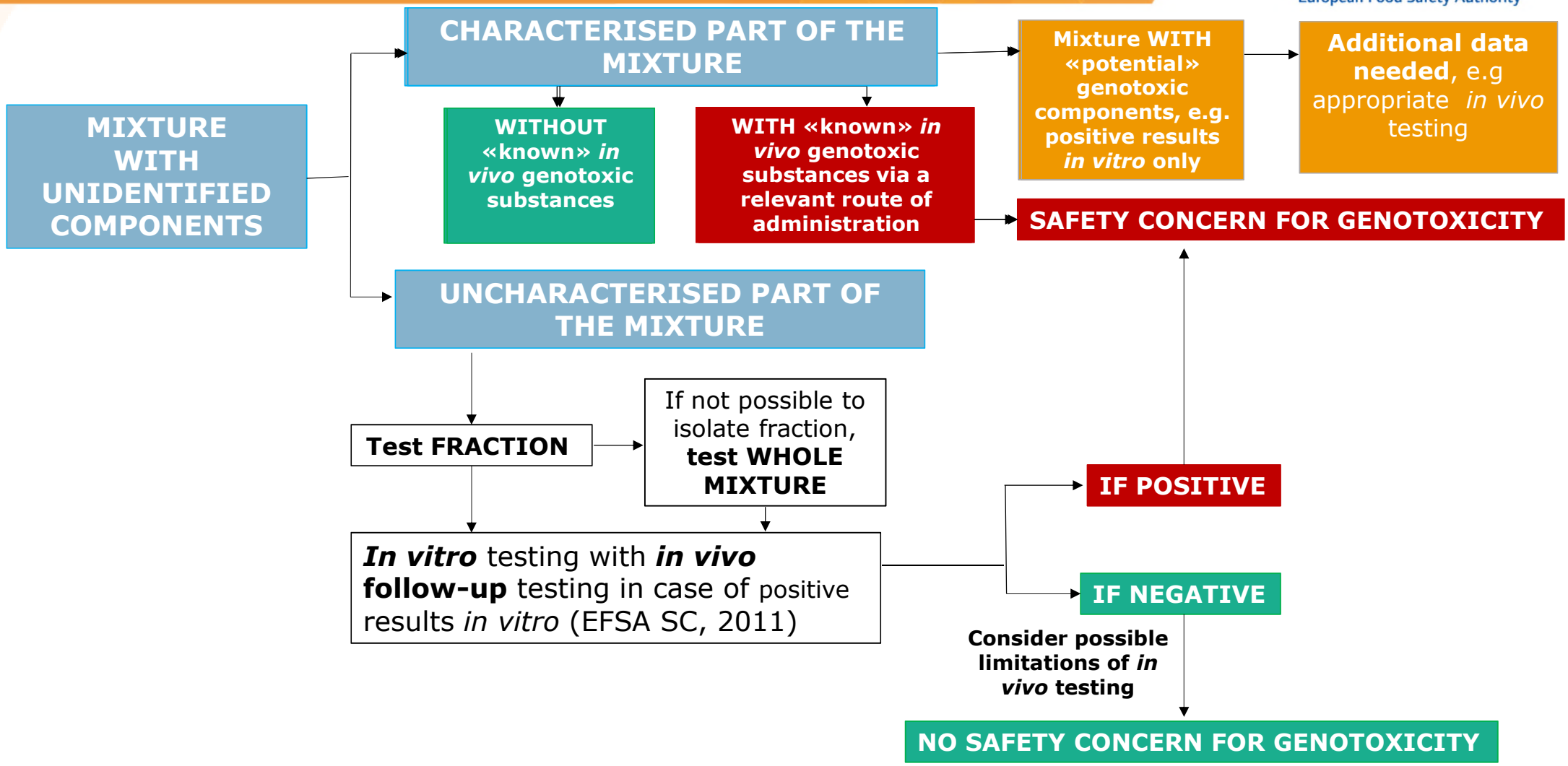
Source: https://www.efsa.europa.eu/en/efsajournal/pub/5519

- **Chemically fully defined mixtures**: assessment of all the components, *i.e.* component-based approach
- **Mixtures containing substantial fraction of unidentified components**: identified components assessed individually, *i.e.* component-based approach
- **Unidentified fraction** should be tested as first option. If not feasible, testing of the whole mixture should be undertaken, *i.e.* whole-mixture approach

Fully Chemically Defined Mixtures–Component Based Approach



Mixture with Unidentified Components



Other Trends in Novel Foods

Synthetic Cannabidiol

“Cannabis” – Cannabinoids - Cannabidiol

Novel Food Catalogue

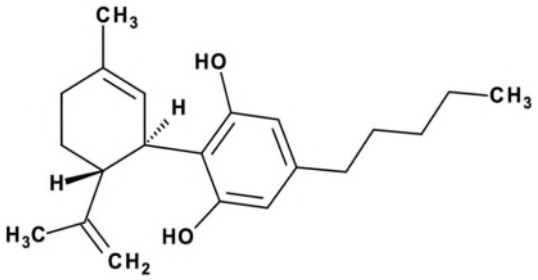
- Cultivation of *Cannabis sativa* L. is permitted provided they are registered in the EU’s ‘Common Catalogue of Varieties of Agricultural Plant Species’ and THC content does not exceed 0.2 % (w/w)
- Extracts of *Cannabis sativa* L. and derived products containing cannabinoids are considered novel foods
- Synthetically obtained cannabinoids are considered as novel

3 CBD under EFSA RISK ASSESSMENT

Cannabidiol

- EMA has recently approved Epidyolex which active substance is CBD from the milled botanical raw material (Cannabis sativa L.). Epydiolex is an adjunctive therapy for seizures associated with Lennox Gastaut syndrome (LGS) or Dravet syndrome (intractable childhood epilepsy) for patients 2 years of age and older.

- EFSA assessment will perform an **independent RA**:
  - Assessment is NOT based on risk-benefit
  - EFSA target general population, not patients
  - Different production process



- Evaluation of CBD will follow the approach from EFSA NDA Guidance for NF

Other Trends in Novel Foods

Engineered Nanomaterials

Nanomaterials and Novel foods

REGULATION (EU) 2015/2283

Article 3

Definitions

(f) 'engineered nanomaterial' means any intentionally produced material that has one or more dimensions of the order of 100 nm or less or that is composed of discrete functional parts, either internally or at the surface, many of which have one or more dimensions of the order of 100 nm or less, including structures, agglomerates or aggregates, which may have a size above the order of 100 nm but retain properties that are characteristic of the nanoscale.

Properties that are characteristic of the nanoscale include:

(i) those related to the large specific surface area of the materials considered; and/or

(ii) specific physico-chemical properties that are different from those of the non-nanoform of the same material.

Nanomaterials EFSA GDs

Engineered nanomaterials

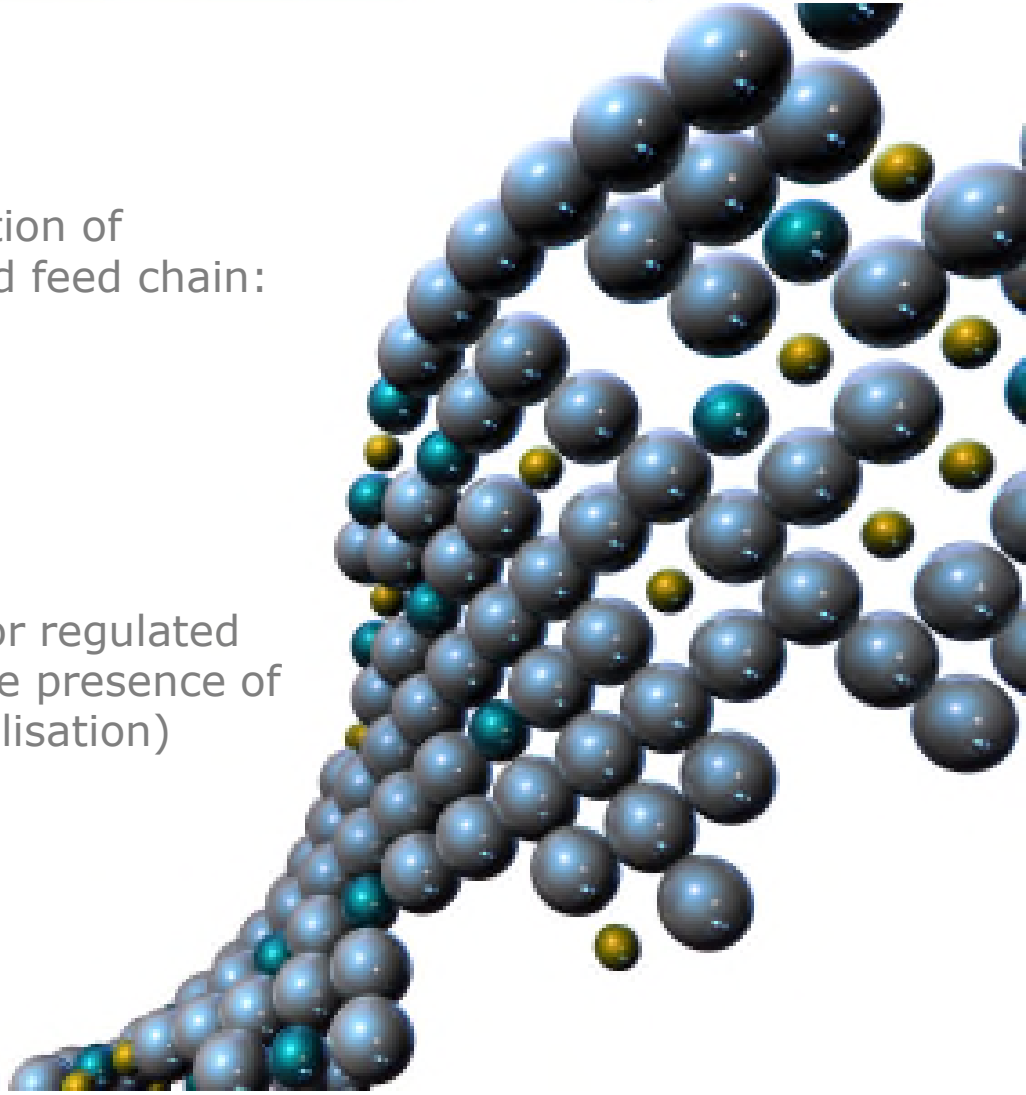
EFSA Guidance on risk assessment of the application of nanoscience and nanotechnologies in the food and feed chain: Part 1, human and animal health (2018)

- 1 NF application as source of iron

Nanoparticles

Draft EFSA Guidance on technical requirements for regulated food and feed product applications to establish the presence of small particles including nanoparticles (under finalisation)

- 7 NF applications under evaluation



efsa
European Food Safety Authority

Q&A

Ongoing works and mandates of NDA Panel

Trusted science for safe food

efsa
European Food Safety Authority

Ongoing Works and Mandates

Novel foods / Nutrient sources	▪Art 10 NF applications: **74** in progress (of which 54 stop-clock for supplementary data) ▪NS applications: **1** stop-clock for supplementary data
Foods for special groups	▪Safety & suitability of Protein-hydrolysate formula: **4** stop-clock for supplementary data Efficacy in reducing risk of developing allergy: **1** stop-clock for supplementary data ▪Total Diet Replacement for weight control: due **02/2021**
Health claims	▪Art 13(5) new science/proprietary data: **2** in progress, **3** under validation
Tolerable Upper Levels	▪Dietary sugars: due **12/2021** (Public consultation Summer 2021, Technical meeting with stakeholders September 2021) ▪Selenium: due **03/2022**
Other mandates	▪Safety of Alpha lipoic acid and insulin autoimmune syndrome (Art 8): due **04/2021** ▪Dietary Folate Equivalent_CaLMF_5LTHF glucosamine salt: due **08/2022**
Transparency Regulation	▪Updating eight Guidance documents: due **12/2020 / 01/2021**

Stay connected

European Food Safety Authority

Subscribe to

efsa.europa.eu/en/news/newsletters
efsa.europa.eu/en/rss

Receive job alerts

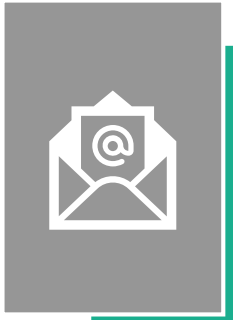
careers.efsa.europa.eu – job alerts

Follow us on Twitter

@efsa_eu
@plants_efsa
@methods_efsa
@animals_efsa

Follow us Linked in

Linkedin.com/company/efsa



Contact us

efsa.europa.eu/en/contact/askefsa