medfiles

Novel food and health claim dossiers

– A well done plan guarantees the best outcome

Marine For Health Regulatory Seminar
10 Dec 2019

Mari Lyyra, Regulatory Affairs Manager, Oy Medfiles Ltd

Main regulatory framework for foods and ingredients in EU

Food Information for Consumers *Regulation (EU) 2011/1169*

Nutrition and health claims
Regulation (EC) 1924/2006

Novel foods
Regulation (EU) 2015/2283

Existing forms from new sources and new processing techniques
↓↓↓

Genetically modified foods and feeds *Regulation (EC) No 1829/2003*

Ordinary foods and food ingredients *Regulation (EC) 178/2002* Organic foods *Regulation (EC) 834/2007*	Food supplements *Directive 2002/46/EC*	Foods for Special Groups *Regulation (EU) 609/2013* *Delegated Regulations (EU) 2016/127 (applied from 2020); (EU) 2016/128; (EU) 2017/1798 (applied from 2022)*	Fortified foods *Regulation (EC) 1925/2006*	Food improvement agents *Regulations* Enzymes (EC) 1332/2008 Food additives (EC) 1333/2008 Aromas (EC) 1334/2008

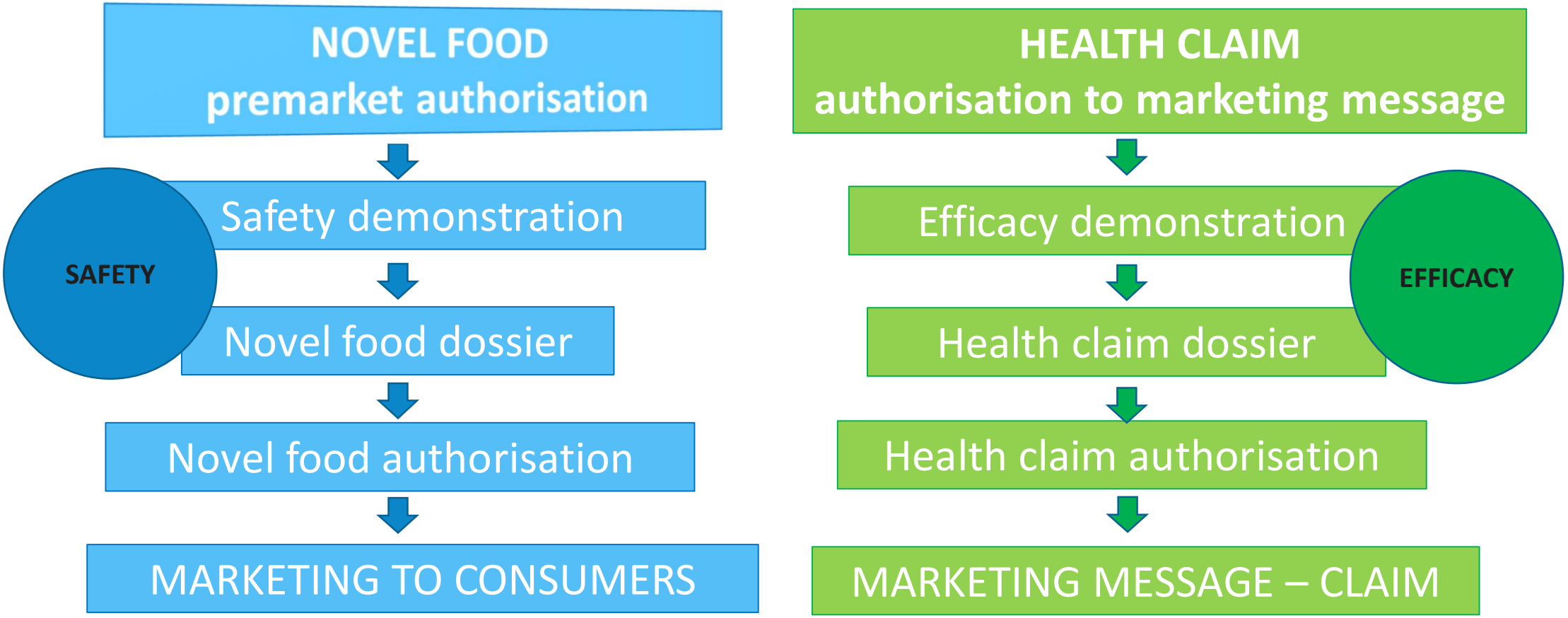
Regulatory positioning for a new food or food ingredient

- **Purpose of use?**
  - A new food (e.g. new species to be used as such)
  - A new food ingredient (e.g. isolated part of a plant or a chemical) to be used in food/food supplement
  - A new source of a mineral or a vitamin
  - Functional food ingredient with health effect
  - Food additive, enzyme, flavouring
- **Regulatory route identification; e.g.**
  - Traditional **or** a novel food
  - Food category; applicable regulations
  - Food additive, food enzyme, flavouring
  - Claims

➡ **Applicable registration process(es)**

If a result is **a novel food with no authorised health claim?**

medfiles



medfiles

Novel foods

Article 1(2) of Regulation (EU) 2283/2015:

The target of novel food regulations is to ensure the effective functioning of the internal market while providing a high level of protection of human health and consumers' interests

Regulations on novel foods in the EU

- **Regulation (EU) 2015/2283 on novel foods**
- Commission Implementing Regulation (EU) 2017/2470 establishing the **Union list of novel foods**
- Commission Implementing Regulation (EU) 2018/1023 correcting Implementing Regulation (EU) 2017/2470 establishing the Union list of novel foods
- Commission Implementing Regulation (EU) 2017/2468 laying down **administrative and scientific requirements concerning traditional foods from third countries**
- Commission Implementing Regulation (EU) 2017/2469 laying down **administrative and scientific requirements for novel food applications**
- Commission Implementing Regulation (EU) 2018/456 on the procedural steps of the **consultation process for determination of novel food status**

Novel food regulation (EU) 2015/2283:
Key definitions:

- **'Novel food'** means any food that was not used for human consumption **to a significant degree** within the Union **before 15 May 1997,** irrespective of the dates of accession of Member States to the Union
- **'Traditional food from a third country'** is a novel food derived from primary production (plants/animals/micro-organisms etc., processed/unprocessed) with a history of safe use in a third country.
  - **'History of safe food use in a third country'** means that the safety of the food in question has been confirmed with **compositional data** and from **experience of continued** use for at least **25 years** in the customary diet of a significant number of people in at least one third country."

10 categories defined in Novel food regulation (1)

MEDFILES

1) food with a new or intentionally modified molecular structure
2) food consisting of, isolated from or produced from **microorganisms, fungi or algae**; *e.g. Algal oil from the microalgae Ulkenia sp.*
3) food consisting of, isolated from or produced from material of mineral origin
4) food consisting of, isolated from or produced from **plants or their parts**, *e.g. chia seeds*
5) food consisting of, isolated from or produced from **animals or their parts;** *e.g. Antarctic Krill oil rich in phospholipids from Euphausia superba*
6) food consisting of, isolated from or produced from cell culture or tissue culture derived from **animals, plants, micro-organisms, fungi or algae;** *e.g. Ajuga reptans extract from cell cultures*

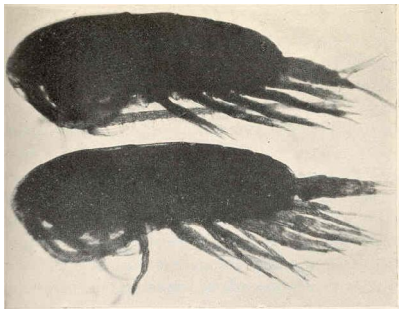
10 categories defined in Novel food regulation (2)

7) food resulting from a production process not used for food production within the Union before 15 May 1997, which gives rise **to significant changes in the composition or structure of a food, affecting its nutritional value, metabolism or level of undesirable substances;** *e.g. UV treated foods (yeast)*
8) food consisting of engineered nanomaterials as defined in the regulation
9) vitamins, minerals and other substances ; when a production process not used for food production within the Union before 15 May 1997 or they contain or consist of engineered nanomaterials; e.g. *new source of vitamin K - menaquinone*
10) food used exclusively in food supplements within the Union before 15 May 1997, where it is intended to be used in foods other than food supplements; *e.g. astaxanthin*

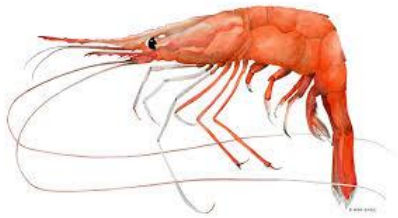
Regulation (EU) 2017/2470
Union list of authorised novel foods

Authorised novel food	Conditions under which the novel food may be used		Additional specific labelling requirements	Other requirements	►M29 Data Protection ◄
***Calanus finmarchicus* oil**	*Specified food category*	*Maximum levels*	The designation of the novel food on the labelling of the foodstuffs containing it shall be 'oil from *Calanus finmarchicus* (crustacean)'		
	Food supplements as defined in Directive 2002/46/EC	2,3 g/day			

***Calanus finmarchicus* oil**	**Description/Definition:** The novel food is ruby coloured, slightly viscous oil with a slight shellfish odour extracted from the crustacean (marine zooplankton) *Calanus finmarchicus*. The ingredient consists primarily of wax esters (> 85 %) with minor amounts of triglycerides and other neutral lipids. **Specifications:** Water: < 1,0 % Wax esters: > 85 % Total fatty acids: > 46 % Eicosapentaenoic acid (EPA): > 3,0 % Docosahexaenoic acid (DHA): > 4,0 % Total fatty alcohols: > 28 % C20:1 n-9 fatty alcohol: > 9,0 % C22:1 n-11 fatty alcohol: > 12 % Trans fatty acids: < 1,0 % Astaxanthinesters: < 0,1 % Peroxide value (PV): < 3,0 meq. O_2/kg



Regulation (EU) 2017/2470
Union list of authorised novel foods

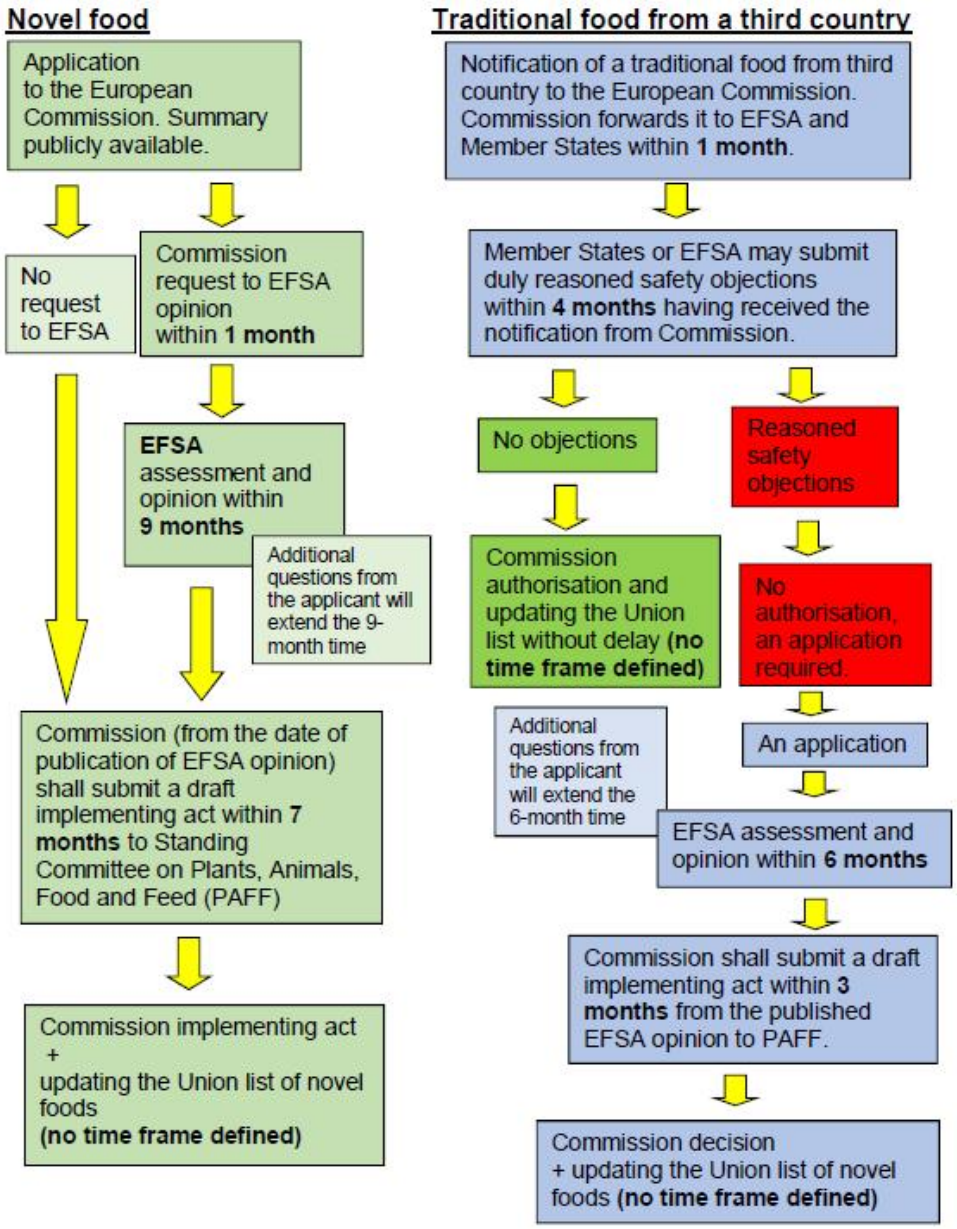
Refined shrimp peptide concentrate	*Specified food category*	*Maximum levels*	The designation of the novel food on the labelling of the foodstuffs containing it shall be 'refined shrimp peptide concentrate'.		Authorised on 20 November 2018. This inclusion is based on proprietary scientific evidence and scientific data protected in accordance with Article 26 of Regulation (EU) 2015/2283.
	Food Supplements as defined in Directive 2002/46/EC for the adult population	1 200 mg/day			
Refined shrimp peptide concentrate	**Description** Refined shrimp peptide concentrate is a peptide mixture obtained from northern shrimp (*Pandalus borealis*) shells and heads via a series of purification steps following enzymatic proteolysis using a protease from *Bacillus licheniformis* and/or *Bacillus amyloliquefaciens*. **Characteristics/Composition** Total Dry matter (%): ≥ 95,0 % Peptides (w/weight dry matter): ≥ 87,0 % of which peptides with molecular weight < 2 kDa: ≥ 99,9 % Fat (w/w): ≤ 1,0 % Carbohydrates (w/w): ≤ 1,0 % Ash (w/w): ≤ 15,0 % Calcium: ≤ 2,0 % Potassium: ≤ 0,15 % Sodium: ≤ 3,5 % **Heavy Metals** Arsenic (inorganic): ≤ 0,22 mg/kg Arsenic (organic): ≤ 51,0 mg/kg Cadmium: ≤ 0,09 mg/kg Lead: ≤ 0,18 mg/kg Total mercury: ≤ 0,03 mg/kg **Microbiological criteria:** Total viable cell count: ≤ 20 000 CFU/g *Salmonella*: ND/25g *Listeria monocytogenes*: ND/25g *Escherichia coli*: ≤ 20 CFU/g Congulase positive *Staphylococcus aureus*: ≤ 200 CFU/g *Pseudomonas aeruginosa*: ND/25g Mould/yeast: ≤ 20 CFU/g CFU: Colony Forming Units ND: Not Detectable			Applicant: Marealis AS., Stortorget 1, Kystens Hus, 2nd floor, N-9008 Tromsø Postal address: P.O. Box 1065, 9261 Tromsø, Norway. During the period of data protection the novel food refined shrimp peptide concentrate is authorised for placing on the market within the Union only by Marealis AS unless a subsequent applicant obtains authorisation for the novel food without reference to the proprietary scientific evidence or scientific data protected in accordance with Article 26 of Regulation (EU) 2015/2283 or with the agreement of Marealis AS. End date of the data protection: 20 November 2023.

tomorrow

medfiles

Novel food registration procedure:

1) Submission to Commission
2) EFSA evaluation
3) Commission handling and authorisation



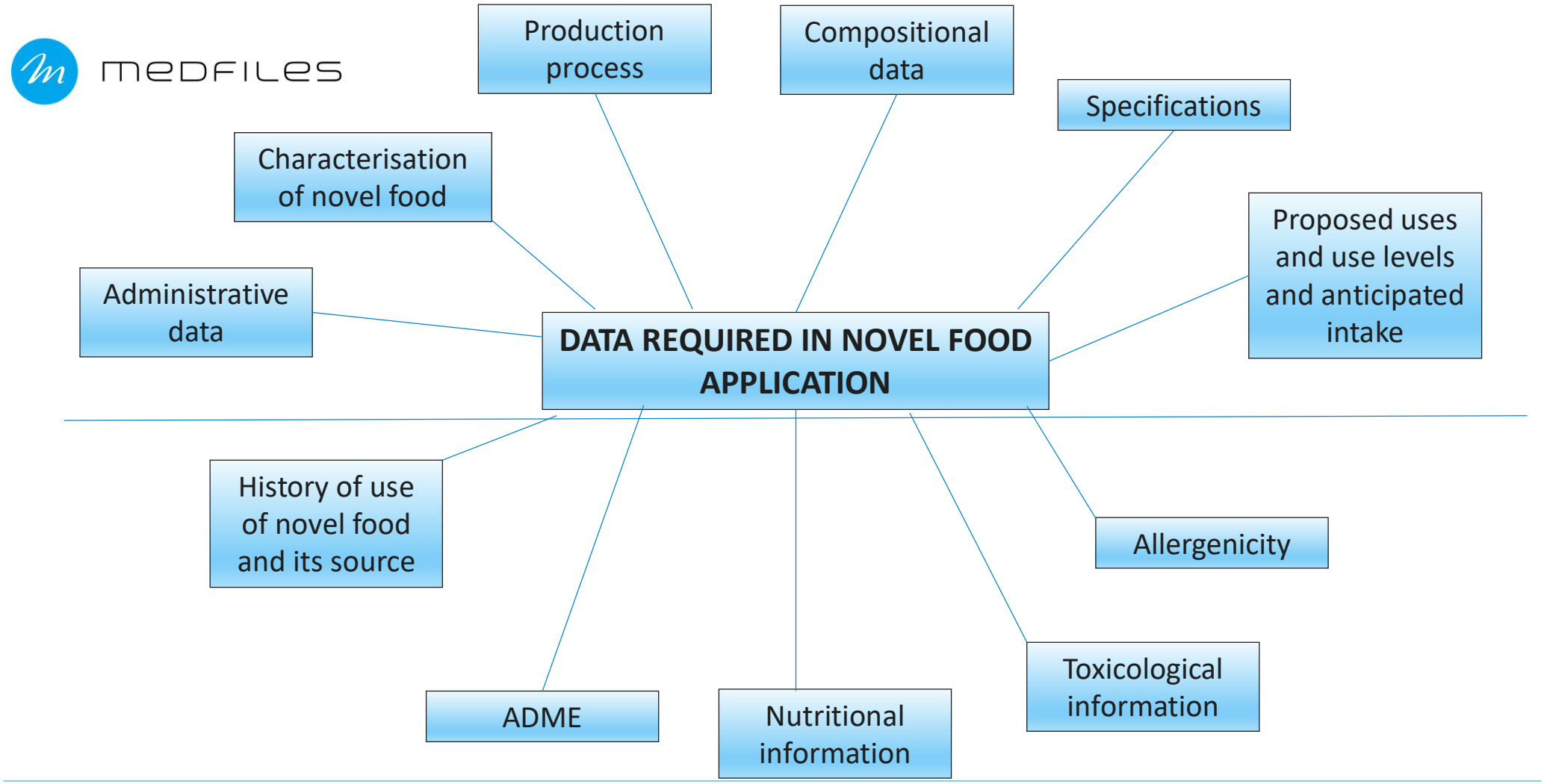
medfiles

Novel food application
What is required?

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

EFSA Panel on Dietetic Products, Nutrition and Allergies (NDA),

EFSA Journal 2016;14(11):4594


medfiles
Production process
Compositional data
Specifications
Characterisation of novel food
Proposed uses and use levels and anticipated intake
Administrative data
DATA REQUIRED IN NOVEL FOOD APPLICATION
History of use of novel food and its source
Allergenicity
ADME
Nutritional information
Toxicological information

Minimum requirements

1) Novel food characterisation

- Detailed information on source species and the end product

2) Production process

- A detailed description of production process + flowchart

3) Compositional data

- Analytical data on nutrients + contaminants and impurities

4) Specification

- Key parametres specific to the product

5) Proposed uses and use levels and anticipated intake

- Food categories, level of addition, calculations on intake

Additional requirements (1)

6) History of use of novel food and/or its source

- Use in the EU and other countries

7) Absorption, distribution, metabolism and excretion (ADME)

- **Absorption** is the key point for all further tests
- Literature, *in vitro*, *in vivo* studies

8) Nutritional information

- To demonstrate that novel food is **not nutritionally disadvantageous** for consumers at the proposed conditions of use
- Refers to the role of novel food in the diet in terms of its **contribution to** or **interaction with nutrient intakes.**
- Content and effect of **anti-nutritional factors and** suspected **interactions with nutrients**
- *In vitro* tests, possibly animal and human studies, depending on novel food

Additional requirements (2)

9) Toxicological information

- Toxicological tests in accordance with international guidelines (e.g. OECD) and according to the principles of Good Laboratory Practices (GLP)
- Basic requirements:
  - ***in vitro* tests of genotoxicity**
    - ✓ a bacterial reverse mutation test (OECD TG 471) i.e. Ames test
    - ✓ an *in vitro* mammalian cell micronucleus test (OECD TG 487)
  - **Subchronic toxicity test to allow the identification of a BMDL (or a NOAEL)**
    - ✓ An extended 90-day subchronic feeding study (OECD TG 408 with extended parameters from the OECD 407: Repeated dose 28-day oral toxicity study in rodents)
- Other tests to be considered case by case
  - Reproductive and developmental toxicity studies
  - Chronic toxicity and carcinogenicity studies

Additional requirements (3)

10) Allergenicity

- Analytical data on composition -> protein
- If the novel food contains any protein -> literature review on its source (including taxonomic relationships), the production process, and available experimental and human data, including information on cross-reactivity
- Further analytics and tests, including human tests

Human studies needed?

- ✓ Not mandatory but often necessary
- ✓ Clinical studies with safety parametres + monitoring of adverse effects

Data protection as part of novel food application

- A novel food approval can be protected for five years if data protection has been granted in a novel food authorization:

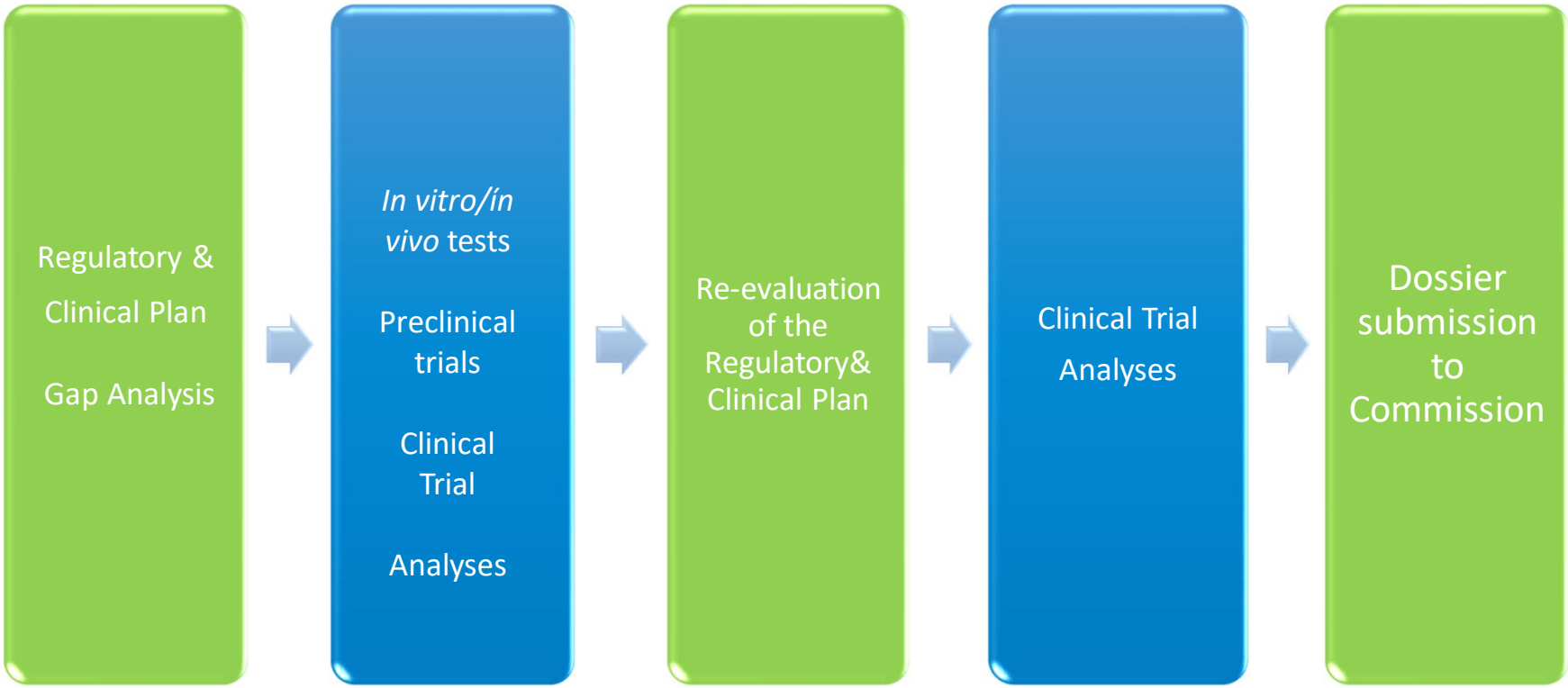
➡ **a company has an exclusive marketing rights for novel food**; toxicological or clinical studies cannot be utilized by other applicants

- <u>Data protection is possible when</u>
  - ✓ Newly developed scientific evidence have not been published
  - ✓ Newly developed scientific evidence is proprietary data of the applicant and the applicant has exclusive right of reference
  - ✓ Newly developed scientific evidence is essential data for safety assessment, i.e. the novel food could not have been authorised without that data

How much novel food authorisation costs and how long it takes?

- Rough cost estimate: 200 000 – 1 000 000 euros
  - Very much **case-dependent**; nature of novel food ingredient affects
  - Analytics: 5 000 - 10 000 euros
  - Toxicological tests: min. 120 000 euros
  - Other tests/studies: Clinical study min. 100 000 euros + potential others (*in vitro, in vivo*)
  - Compiling the application by Medfiles 40 000 – 50 000 €
  - Response to further EFSA questions by Medfiles 5 000 – 10 000 €
- Time estimate:
  - Before novel food application submission: 2-4 years
  - Novel food application procedure 1,5-2 years

Support from a plan to a successful submission and authorisation



medfiles

30 YEARS OF EXPERTISE

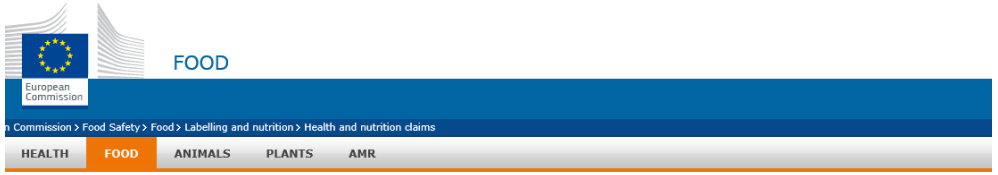
Health claims

A health claim is any statement about a relationship between food and health. The Commission authorises different health claims provided they are based on scientific evidence and can be easily understood by consumers.

Any claim referring to preventing, treating or curing a human disease, or referring to such properties are prohibited.

Regulations on nutrition and health claims in the EU

- Regulation (EC) No 1924/2006 on nutrition and health claims
- Commission Regulation (EU) No 432/2012 establishing a list of permitted health claims made on foods, other than those referring to the reduction of disease risk and to children's development and health:



EU Register on nutrition and health claims

- Individual decisions on applied health claims

medfiles

Regulation (EC) No 1924/2006 on nutrition and health claims

Applies to all commercial communication including
- product labels
- trade marks
- advertising
- symbols
- graphics

Nutrition claims

- Based on composition
- Conditions of use defined for energy, energy nutrients, nutrients, sugar, dietary fibre, salt and omega-3 fatty acids
- e.g. Source of vitamin D; High vitamin D

Health claims article 13.1 (13.2)/13.5

- **Claims relating to functions of the body**
  - E.g. "Daily creatine consumption can enhance the effect of resistance training on muscle strength in adults over the age of 55".
- Claims relating to the **growth and development**
- Claims referring to **psychological and behavioural functions**
- Claims on **slimming or weight-control**

Health claims article 14.1

- **Article 14.1(a) Risk reduction claims**;
  - e.g. "Plant stanol esters have been shown to reduce blood cholesterol. Blood cholesterol is a risk factor in the development of coronary heart disease"
- **Article 14.1(b) Claims referring to children's development**
  - e.g. "Vitamin D is needed for the normal growth and development of bone in children"

Several authorised health claims to vitamins and minerals under Article 13.1 in EU register of nutrient and health claims

Claim type	Nutrient, substance, food or food category	Claim	Conditions of use of the claim / Restrictions of use / Reasons for non-authorisation	Health relationship	EFSA opinion reference / Journal reference	Commission Regulation	Status	Entry ID
Art.13 (1)	Calcium	Calcium contributes to normal blood clotting	The claim may be used only for food which is at least a source of calcium as referred to in the claim SOURCE OF [NAME OF VITAMIN/S] AND/OR [NAME OF MINERAL/S] as listed in the Annex to Regulation (EC) No 1924/2006.	blood coagulation	2009;7 (9):1210	Commission Regulation (EU) 432/2012 of 16/05/2012	Authorised	230, 236
Art.13 (1)	Biotin	Biotin contributes to the maintenance of normal hair	The claim may be used only for food which is at least a source of biotin as referred to in the claim SOURCE OF [NAME OF VITAMIN/S] AND/OR [NAME OF MINERAL/S] as listed in the Annex to Regulation (EC) No 1924/2006.	maintenance of normal hair	2009;7 (9):1209, 2010;8 (10):1728	Commission Regulation (EU) 432/2012 of 16/05/2012	Authorised	118, 121, 2876

Article 13.5 health claims in EU register of nutrient and health claims

Art.13 (5)	Lactitol	Lactitol contributes to normal bowel function by increasing stool frequency	The claim may be used only for food supplements which contain 10 g of lactitol in a single daily quantified portion. In order to bear the claim, information shall be given to the consumer that the bneficial effeft is obtained by consuming 10 g of lactitol in one daily dose. The claim shall not be used for foods targeting children.		Q-2015-00375	Commission Regulation (EU) 2017/676 of 10/04/2017	Authorised	N/A
Art.13 (5)	Sugar beet fibre	Sugar beet fibre contributes to an increase in faecal bulk	The claim may be used only for food which is high in that fibre as referred to in the claim HIGH FIBRE as listed in the Annex to Regulation (EC) No 1924/2006		Q-2011-00972	Commission Regulation (EU) No 40/2014 of 17/01/2014	Authorised	N/A

Article 14 health claims in EU register of nutrient and health claims

Art.14 (1)(a)	Barley beta-glucans	Barley beta-glucans has been shown to lower/reduce blood cholesterol. High cholesterol is a risk factor in the development of coronary heart disease.	Information shall be given to the consumer that the beneficial effect is obtained with a daily intake of 3 g of barley beta-glucan. The claim can be used for foods which provide at least 1 g of barley beta-glucan per quantified portion.		Q-2011-00798	Commission Regulation (EU) 1048/2012 of 08/11/2012	Authorised	N/A
Art.14 (1)(b)	Docosahexaenoic acid (DHA)	Docosahexaenoic acid (DHA) intake contributes to the normal visual development of infants up to 12 months of age.	Information shall be given to the consumer that the beneficial effect is obtained with a daily intake of 100 mg of DHA. When the claim is used on follow-on formula, the food shall contain at least 0,3 % of the total fatty acids as DHA.		Q-2008-211, Q-2008-688, Q-2008-689	Commission Regulation (EU) No 440/2011 of 06/05/2011	Authorised	N/A

medfiles

Article 13 and 14 health claim application process in the EU

Health claim process

Health claim application to the national competent authority of a Member State	Letter of receiving in 14 days	2 wk
		..
National competent authority delivers the whole application to EFSA	"Without a delay", about 2-4 weeks	1 mo
		..
EFSA validates the application	No official time limit, about a month	2 mo
		..
EFSA gives and publishes the opinion	5 mo (+1-2 mo if EFSA asks questions during the process + time answering to questions)	9 mo
		..
Commission authorisation decision	About 2-4 mo	TOTAL TIME: About 13 mo

medfiles

Health claim application

What is required?

General scientific guidance for stakeholders on health claim applications

EFSA Panel on Dietetic Products, Nutrition and Allergies (NDA)

EFSA Journal 2016;14(1):4367

+ guidance on different health areas (e.g. nervous system, physical performance, bone, joints, skin, oral health, weight management, immune system, antioxidants)

medfiles

Main issues addressed by EFSA NDA Panel for health claim evaluation

› **In assessing each specific food/health relationship which forms the basis of a health claim the NDA Panel considers the following key questions:**

(i) the food/constituent is defined and characterised

(ii) the claimed effect is based on the essentiality of a nutrient;

OR

the claimed effect is defined and is a beneficial physiological effect for the target population (i.e. for function claims, the beneficial physiological effect **relates to the maintenance, reduced loss or improvement of a body function**), and can be measured *in vivo* in humans;

(iii) a cause and effect relationship is established between the consumption of the food/constituent and the claimed effect (for the target group under the proposed conditions of use)

EFSA health claim evaluation and outcome

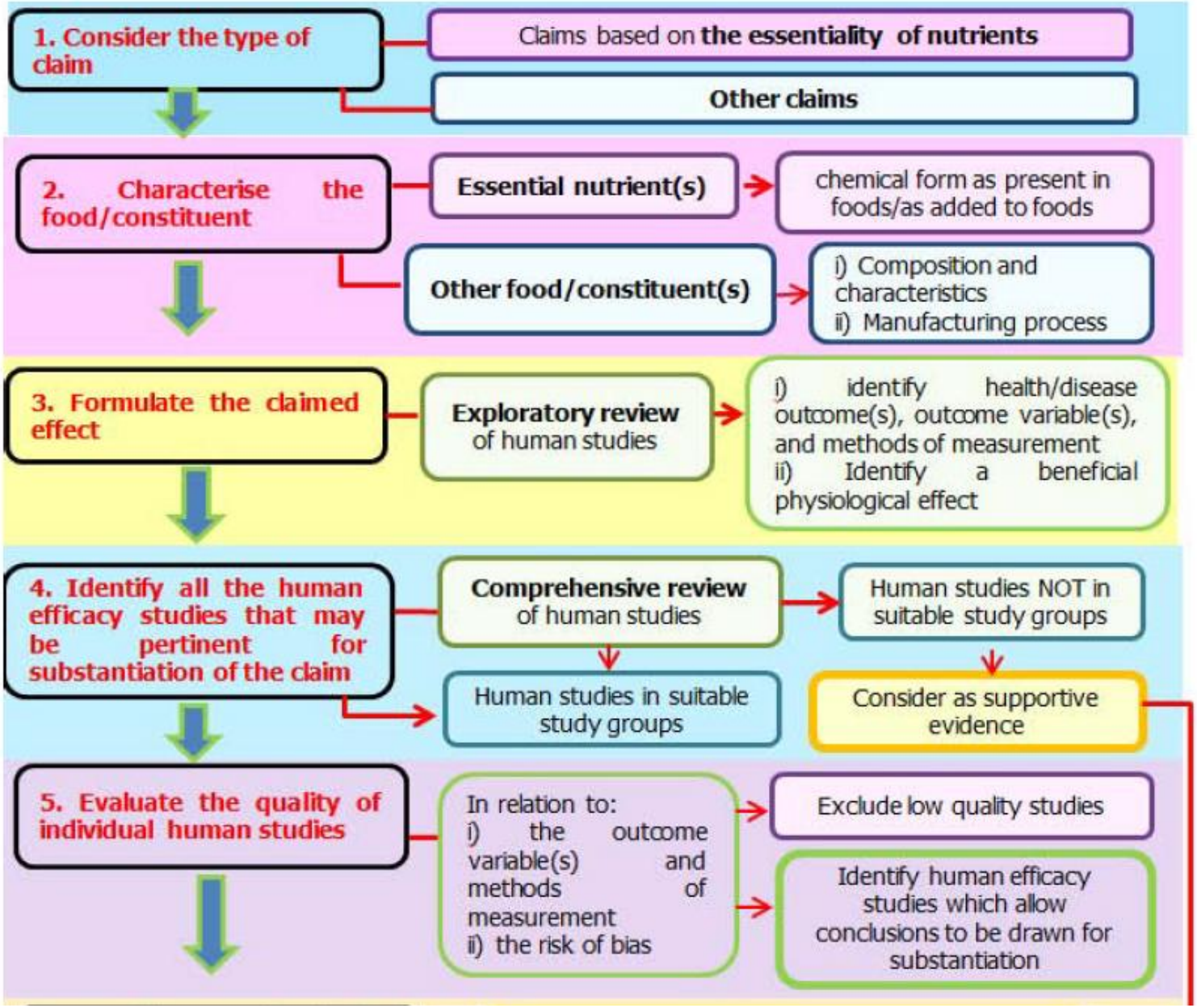
- In assessing each specific food/health relationship which forms the basis of a claim, the NDA Panel **makes a scientific judgement** on the extent to which a cause and effect is established considering
  - the strength, consistency, specificity, dose–response, biological plausibility of the relationship and by weighing the totality of the evidence.

→ **EFSA NDA Panel opinion**

- **i.** *A cause and effect relationship has been established between the consumption of the food/constituent and the claimed effect.*
- **ii.** *The evidence provided is insufficient to establish a cause and effect relationship between the consumption of the food/constituent and the claimed effect.*
- **iii.** *A cause and effect relationship has not been established between the consumption of the food/constituent and the claimed effect.*

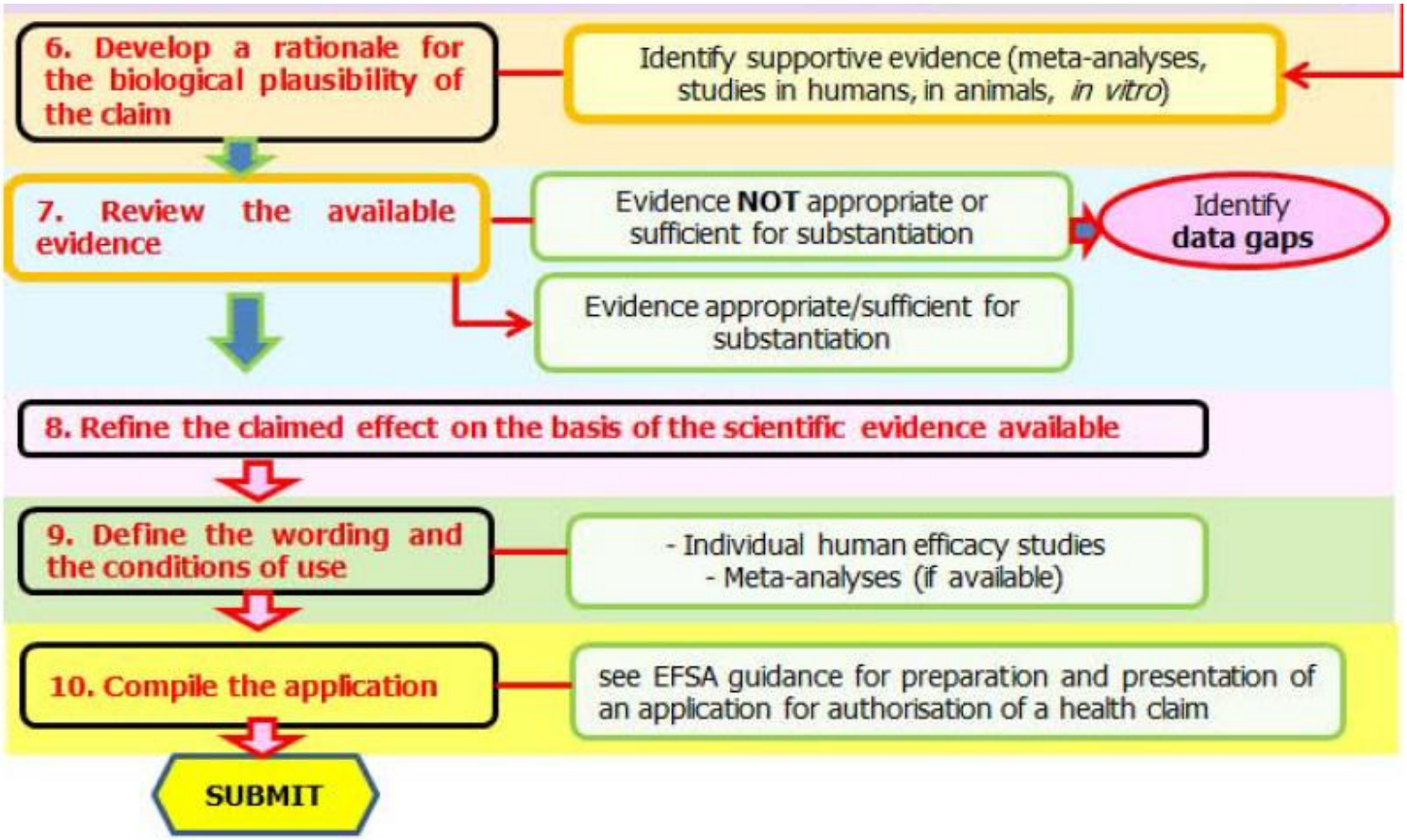
MEDFILES

Key scientific aspects to consider for preparing a health claim application (EFSA NDA Panel, 2016; Figure 2)



medfiles

Key scientific aspects to consider for preparing a health claim application (EFSA NDA Panel, 2016, Figure 2)



medfiles

Clinical studies to support a new health claim application (1)

- **Well-designed and conducted randomised controlled trials are at the top of the hierarchy which informs decisions on substantiation**
  - intervention or observational trials
  - published or unpublished
  - with low risk of bias
  - statistically and clinically significant results!

  investigating the effect of
  - a food/constituent which complies with the specifications of the food/constituent for which the claim is proposed
  - on appropriate outcome variables for the claimed effect,
  - in a suitable study group, and
  - under the conditions of use proposed for the claim

- **Quality of clinical studies is a key issue**
  - Low-quality studies have no value in health claim assessment

Clinical studies to support a new health claim application (2)

› There is no pre-established rule as to how many or which types of studies are needed for health claim substantiation:

According to EFSA guidance on health claim applications ,the applied health effect needs to be documented and repeated:

> ***"The reproducibility of the effect of the food/ constituent, as indicated by the consistency of the findings (within and across studies)****, and the biological plausibility of the effect also need to be considered"*

→ at least two high-quality clinical studies needed if no previous literature available

medfiles

Well-designed plan of a new clinical study to support a new health claim is a key point to achieve a health claim!

- Randomisation, controlling and blinding, monitoring background diet and habits
  - low risk of bias important
- Suitable study group (part of general healthy population)
  - With no/mild disease / medication
- The intervention product complies with the food specification in the application
- Study design in accordance under the conditions of use proposed (e.g. within a meal, once/twice a day, before physical activity, in free-living subjects) for the claim
- Appropriate outcome variables (primary and secondary) to substantiate the applied claim
  - Power calculations -> correct sample size
- Appropriate valid outcome measurement methods and appropriate study durations
- Appropriate pre-planned statistical methods (e.g. difference between the groups or an absolute number) and intention-to-treat analysis; post-study secondary analyses are not recommended; how to handle protocol deviations
- Detailed reporting

medfiles

Data protection

Article 21 of Regulation (EC) 1924/2006 on claims

- Proprietary data of applicant -> data protection
  - Possible for unpublished studies –> 5 yrs protection for unpublished, proprietary, essential data with exclusive right by applicant

Article 21

Data protection

1. The scientific data and other information in the application required under Article 15(3) may not be used for the benefit of a subsequent applicant for a period of five years from the date of authorisation, unless the subsequent applicant has agreed with the prior applicant that such data and information may be used, where:

(a) the scientific data and other information has been designated as proprietary by the prior applicant at the time the prior application was made; and

(b) the prior applicant had exclusive right of reference to the proprietary data at the time the prior application was made; and

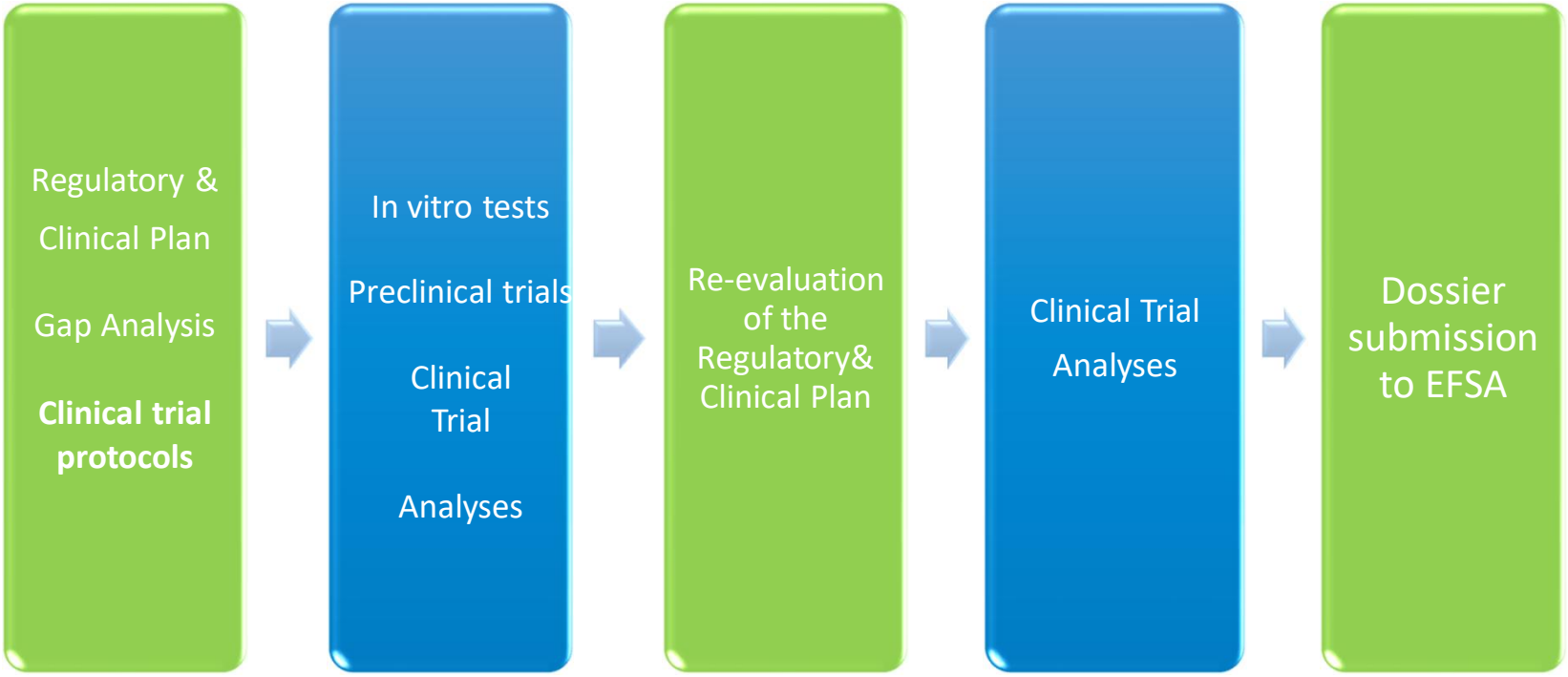
(c) the health claim could not have been authorised without the submission of the proprietary data by the prior applicant.

How much health claim authorisation costs and how long it takes?

- Rough cost estimate for a new ingredient: 100 000 – 700 000 euros
  - Very much claim (effect) dependent
  - Analytical costs (2 000 – 5 000 euros)
  - Minimum 2 clinical studies (á 20 000 – 300 000 €)
  - Compiling the application by Medfiles 40 000 – 50 000 €
  - Response to further EFSA questions by Medfiles 5 000 – 10 000 €
- Time estimate:
  - Prior to health claim application submission: 2-3 years
  - Health claim application procedure: approximately 1 year

medfiles

Support from a plan to a successful submission



A well done plan guarantees the best outcome!


medfiles
THANK YOU!
Securing a healthier tomorrow
www.medfiles.eu
Follow us in:
in
YouTube

Contact persons-Non-drugs

Food and Nutrition

Mari Lyyra (> 20 years of experience food regulatory, **novel foods**, labelling)

Regulatory Affairs Manager, M.Sc.
mari.lyyra@medfiles.eu
tel. +358 20 7446 849

Pia Karjalainen (> 10 years of experience food&feed regulatory, **health claims**, labelling)

Senior Regulatory Affairs Expert, M.Sc.
pia.karjalainen@medfiles.eu
tel +358 40 643 1957

In addition: several pharmacists, chemists, toxicologist, medical experts available

Non-drugs team: 8 persons
Clinical team (food &pharma): 23 persons