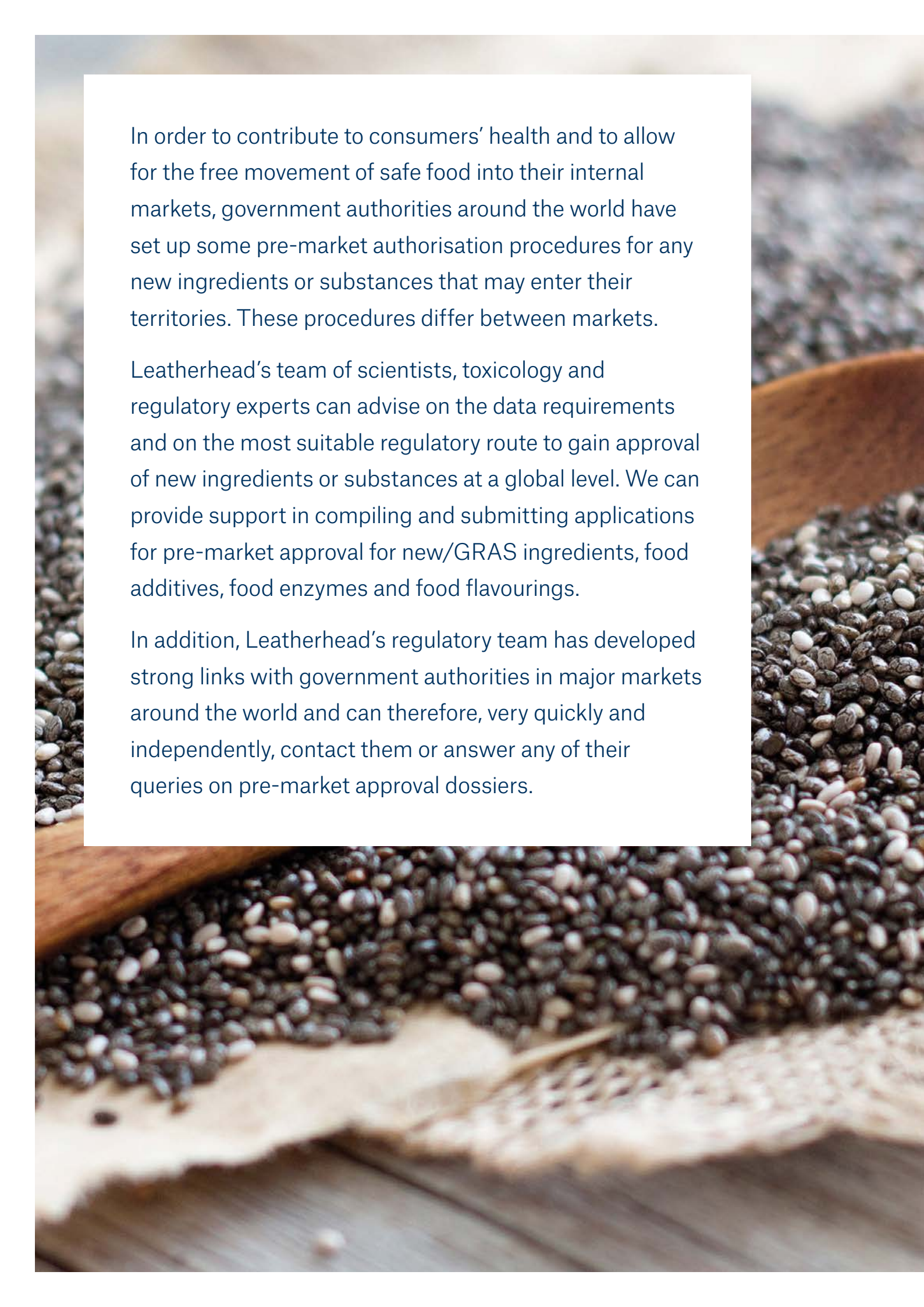


# In focus

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Gaining pre-market approvals for new ingredients and food additives, enzymes and flavourings





In order to contribute to consumers' health and to allow for the free movement of safe food into their internal markets, government authorities around the world have set up some pre-market authorisation procedures for any new ingredients or substances that may enter their territories. These procedures differ between markets.

Leatherhead's team of scientists, toxicology and regulatory experts can advise on the data requirements and on the most suitable regulatory route to gain approval of new ingredients or substances at a global level. We can provide support in compiling and submitting applications for pre-market approval for new/GRAS ingredients, food additives, food enzymes and food flavourings.

In addition, Leatherhead's regulatory team has developed strong links with government authorities in major markets around the world and can therefore, very quickly and independently, contact them or answer any of their queries on pre-market approval dossiers.

# 1.0 Key drivers for development of new food ingredients and food improvement agents

The ingredient suppliers, together with the food and beverage manufacturers, are challenged and instructed to produce high-quality, healthy, nutritious, and safe products. They are constantly evolving their product ranges by accessing new sources and new technologies to better meet consumer and governmental demands for:

- 1 Clean-label/'natural' ingredients
- 2 Ingredients from ethical sources (i.e. different countries, vegetarianism, veganism, etc.)
- 3 Healthy and nutritious ingredients and products addressing global trends such as reduced sugar, fat and salt themes, fortification, health-promoting ingredients, etc.
- 4 Sustainable and new sources (e.g. omega 3, fatty acids, proteins, etc.)



As a result, the ingredient suppliers are constantly looking at current novel and emerging ingredients and products (Table I) and food processing technologies (Table II) that will enable them to deliver in line with the above-mentioned demands and trends, all of which demonstrate exciting prospects.

In parallel with this technological progress, there needs to be a strong, vigilant awareness of the regulatory requirements, when launching these new/GRAS ingredients, food additives, food enzymes and food flavourings, onto the global market, especially demonstrating that these are safe for human consumption.

**Table I:**  
Examples of new ingredients and products that could be developed from new sources

Exotic foods	Animals
Botanicals and herbs	Minerals & vitamins
Microorganisms	Fungi
Algae and marine plants	Cereal crops

**Table II:**  
Examples of current novel and emerging processing technologies

Bio-fortification	Chemical
Physico-chemical	Enzyme
Ozone treatment	Nanotechnologies
Combinations of above	Fermentation

## 2.0 Gaining a pre-market approval

Prior to launching a new ingredient onto a market, the ingredient supplier needs to follow a regulatory process that will ensure that its ingredient is compliant with the regulatory requirements. These have been designed to ensure that the ingredient is safe for consumption.

The first step for any ingredient supplier is determining the key geographical markets it will market and distribute to. This is because the regulatory requirements differ from country to country, e.g. the European Union (EU), The United States of America (USA) and Canada have different regulatory classification systems and pre-market approval processes.

## 3.0 Supporting the Process

Part of the process for securing pre-market approval involves collating safety data for the Dossier Applications, Food Additive Petitions or GRAS Notifications. It is imperative that the data submitted should not only be robust and comprehensive, but should meet all the requirements, so as to avoid delays and failures.

Toxicological assessment, human exposure estimation and risk assessment are fundamental parts of the regulatory process, and would address critical parameters such as those shown in Table III.

**Table III:**

**Some examples of parameters that should be covered within the safety data needed for pre-market approvals of a novel food ingredient in the EU**

Identity	Nutritional information
Production process	Toxicological information (including: genotoxicity, sub-chronic toxicity, chronic toxicity, reproductive and development toxicity, and human data)
History of use of the new ingredient and / or its formula	Compositional data including stability data
Provided uses of and use levels, and anticipated intake including precautions and restrictions of use	Specifications
Absorption, distribution, metabolism and excretion (ADME)	Allergenicity

## 4.0 The Process

The process for gaining pre-market approvals varies from country to country and a top-line overview for the European, US and Canadian markets are given below. For example, ingredient suppliers in the US may follow a process which relies on self-assessment, whereas those in the European Union follow a process which results

in approval from the relevant authority such as the European Commission. We follow a robust process, as shown below (Figure 1) therefore ensuring a strategic and pragmatic approach at a global level, seeking opportunities to leverage common principles and create data sets applicable to key market requirements.

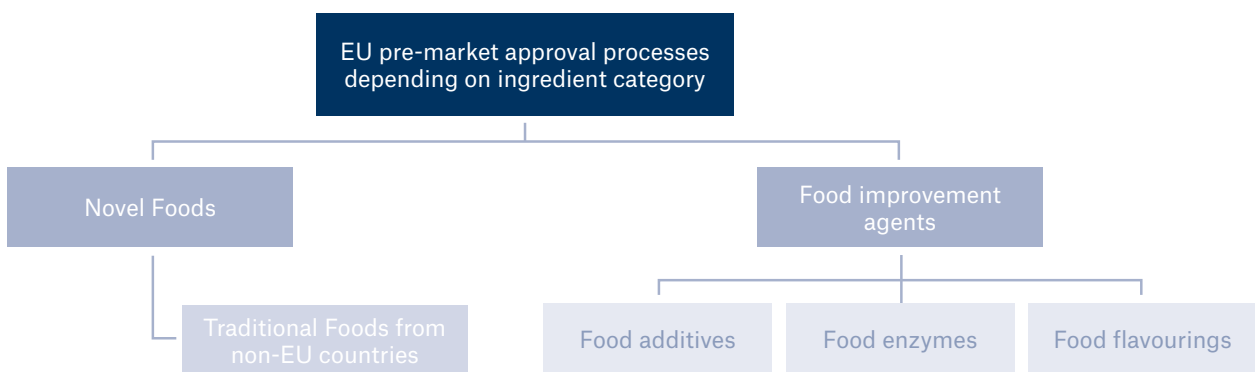
**Figure 1:**  
**Top-line process of key activities from concept to market launch.**



## 4.1 The European Market

In the European market, there are different pathways for gaining pre-market approval for different categories of ingredients as shown in Figure 2. The process for each category is summarised further in Table IV and Figure 3 for novel foods and non-EU traditional foods, and in Table V and Figure 4 for food improvement agents.

**Figure 2:**  
**EU different pathways for gaining pre-market approval**



Once approved, the novel foods, food additives, flavourings or enzymes are subject to the general labelling requirements laid down in Regulation (EU) No 1169/2011 as amended and other relevant labelling requirements in European Union food law. However, in some cases, certain substances may require to be declared using additional labelling information, in particular regarding:

- their description,
- their source,
- their composition, or
- their conditions of intended use.

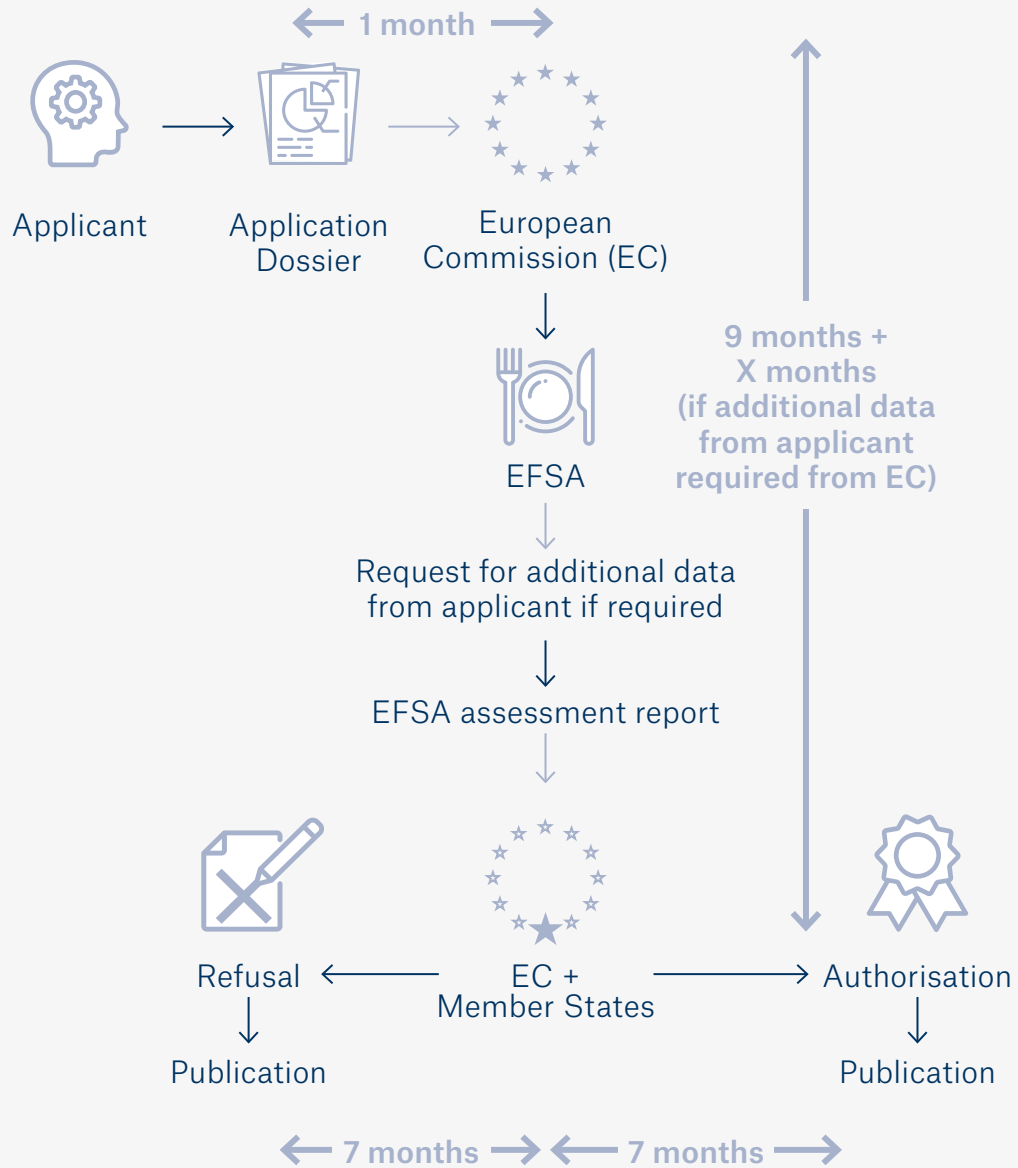
This way consumers will be informed of the nature and safety of the substance, particularly with regard to vulnerable groups of the population.

Table IV:

Overview of the EU pre-market approval process for novel and traditional foods

Category	Descriptions
<p>Novel foods and traditional foods</p>	<p><b>Foods or food ingredients</b> that have not been used for human consumption to a significant degree within EU before 15 May 1997 are typically considered as “novel foods/food ingredients” and will require pre-market authorisation in the EU.</p> <p>The Novel Food Regulation (EU) Regulation 2015/2283 has updated the EU novel food application dossier process in January 2018, following incorporation of new measures to centralise and streamline the process. The benefit of this updated process is to have simpler, faster and more efficient process, so that businesses can bring new and innovative food to the EU market more easily, while still maintaining a high level of food safety for European consumers.</p> <p>Novel foods must be:</p> <ol style="list-style-type: none"> <li>1. safe for human consumption,</li> <li>2. labelled appropriately, so as not to mislead consumers and</li> <li>3. must not differ from the food it intends to replace in such a way that its normal consumption would be nutritionally disadvantageous for consumers.</li> </ol> <p>As of this moment, the process involves key steps, which are:</p> <ol style="list-style-type: none"> <li>1. the submission of a safety dossier to the European Commission</li> <li>2. the assessment of the dossier by the European Food Safety Authority and</li> <li>3. final decision made by the European Commission and the EU Member States for authorisation/refusal.</li> </ol> <p>This process takes 17 months from the date of submission if no additional data is requested from applicants.</p> <p><b>Traditional foods from non-EU countries</b> - Traditional foods from third countries could be considered novel foods in the EU. If they are considered novel, they benefit from a relatively short authorisation process (5 months in total if no safety concerns are raised) under the Novel Food Regulation (EU) Regulation 2015/2283 to gain EU market access. Where safety concerns are raised, the European Food Safety Authority (EFSA) is consulted. EFSA will have 6 months to produce an opinion. The European Commission will then have 3 months to make a final decision on the approval of the product, based on the obtained EFSA opinion. The applicant may withdraw its application at any time, so terminating the procedure.</p> <p>The process for gaining pre-market novel food approval is summarised in Figure 3.</p>

Figure 3:  
EU general novel food pre-market approval process flow diagram



**Table V:**  
**Overview of the EU pre-market approval process for Food Improvement Agents**

Category	Descriptions
Food Improvement Agents: food additives, enzymes or flavourings	<p>Food enzymes, food additives and flavourings are regulated under Regulations (EC) 1332/2008, 1333/2008 and 1334/2008 (as amended) respectively. All new food improvement agents are approved in the EU via a common procedure laid down in Regulation (EC) 1331/2008.</p> <p><b>'Food additives'</b> are defined in the EU as any substance not normally consumed as a food in itself and not normally used as a characteristic ingredient of food, whether or not it has nutritive value, the intentional addition of which to food for a technological purpose in the manufacture, processing, preparation, treatment, packaging, transport or storage of such food results, or may be reasonably expected to result, in it or its by-products becoming directly or indirectly a component of such foods</p> <p><b>'Flavourings'</b> are defined in the EU as substances that are:</p> <ul style="list-style-type: none"> <li>(i) not intended to be consumed as such, which are added to food in order to impart or modify odour and/or taste;</li> <li>(ii) made or consisting of the following categories: flavouring substances, flavouring preparations, thermal process flavourings, smoke flavourings, flavour precursors or other flavourings or mixtures thereof.</li> </ul> <p><b>'Food enzymes'</b><sup>1</sup> are defined in the EU as any products obtained from plants, animals or micro-organisms or products thereof including a product obtained by a fermentation process using micro-organisms:</p> <ul style="list-style-type: none"> <li>(i) containing one or more enzymes capable of catalysing a specific biochemical reaction; and</li> <li>(ii) added to food for a technological purpose at any stage of the manufacturing, processing, preparation, treatment, packaging, transport or storage of foods.</li> </ul> <p>The process for gaining pre-market approval as a food improvement agent is summarised in Figure 4.</p>

**Figure 4:**  
**EU food improvement agents common procedure pre-market approval process flow diagram**



<sup>1</sup>Applications for the approval of food enzymes were submitted by the 2015 deadline to the European Commission which is currently assessing those dossiers to create an EU list of approved enzymes for the EU (EU Member States national measures apply in the meantime). However, this is not a closed list and new applications can be made or applicants can re-submit if their applications were not successful.



## 4.2 The US Market

Introduction of new ingredients onto the US market typically relies on one of two pathways (Figure 5):

1. **Pathway 1:** submitting a Food Additive Petition (FAP) to the US FDA
  - A food additive is any substance that is reasonably expected to become a component of food either directly or indirectly; these require pre-market approval.
2. **Pathway 2:** notifying the FDA of a new substance that is Generally Recognized as Safe (GRAS).
  - GRAS substances on the other hand are exempted from the definition of “food additive” and instead are defined as “substances that are generally recognized, among experts qualified by scientific training and experience to evaluate their safety as having been adequately shown through scientific procedures . . . to be safe under the conditions of their intended use.”
  - Section 201(s) of the Food, Drug, and Cosmetic Act of 1938 allows a substance that is GRAS for a particular use to be marketed for that use without pre-market approval.

The primary determinant of which pathway should be chosen, FAP or GRAS notification, comes down to the consensus of safety among qualified experts.

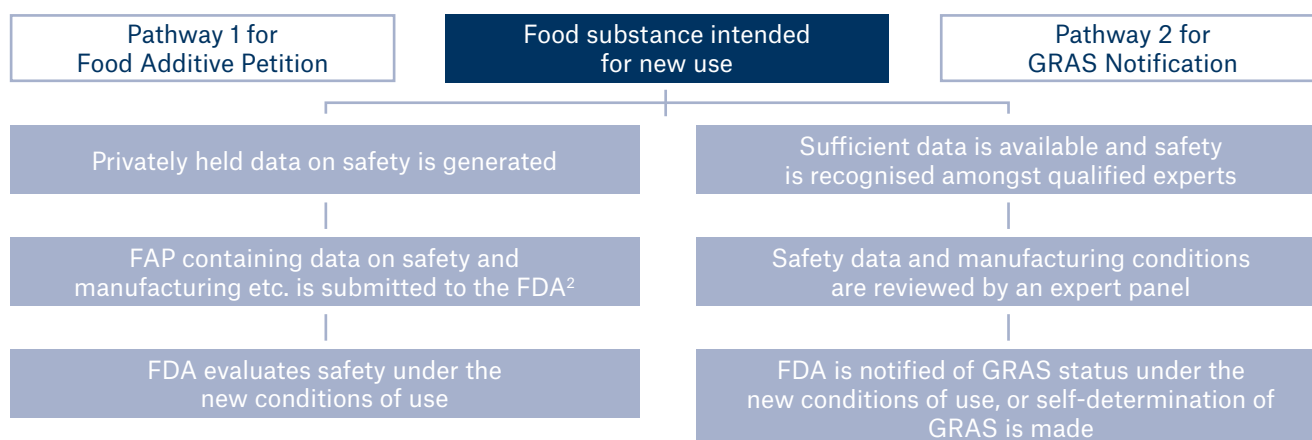


A food additive petition relies on privately generated data and information that are submitted to the FDA for review and determination of safety.

The GRAS notification relies on broadly available, published information and data on the substance that can serve as the basis of the safety determination made by experts outside the FDA.

The FAP process relies on a robust FDA review followed by federal rulemaking, no regulations are issued for a GRAS notification. The FDA evaluates whether a GRAS determination is sufficient and sends a letter to the notifier stating that it either does not question the basis for the notifier’s GRAS determination or that the notice does not provide a sufficient basis for a GRAS determination. Alternately, a GRAS self-determination can be made without FDA involvement.

**Figure 5:**  
**Regulatory process on US landscape**



<sup>2</sup>Should FDA find the data to be insufficient it will request the applicant provide additional data; this will of course delay the process.



## 4.3 The Canadian Market

### Novel foods in Canada can be one of the following

1. a substance, including a microorganism, that does not have a history of safe use as a food;
2. a food that has been manufactured, prepared, preserved or packaged by a process that
  - a) has not been previously applied to that food, and
  - b) causes the food to undergo a major change;
3. a food that is derived from a plant, animal or microorganism that has been genetically modified such that
  - a) the plant, animal or microorganism exhibits characteristics that were not previously observed in that plant, animal or microorganism,
  - b) the plant, animal or microorganism no longer exhibits characteristics that were previously observed in that plant, animal or microorganism, or
  - c) one or more characteristics of the plant, animal or microorganism no longer fall within the anticipated range for the plant, animal or microorganism [B.28.001, FDR].

The Regulations require that, prior to the sale or advertisement of a novel food, Health Canada be notified with sufficient accompanying information, as outlined in B.28.002(2) of the Regulations, to conduct a safety assessment. If Health Canada deems the novel food to be safe for consumption, a letter of no-objection is issued notifying the petitioner to that effect.



### About Leatherhead Food Research ▾

Leatherhead Food Research provides expertise and support to the global food and drink sector with practical solutions that cover all stages of a product's life cycle from consumer insight, ingredient innovation and sensory testing to food safety consultancy and global regulatory advice. Leatherhead operates a membership program which represents a who's who of the global food and drinks industry. Supporting all members and clients, large or small, Leatherhead provides consultancy and advice, as well as training, market news, published reports and bespoke projects. Alongside the member support and project work, our world-renowned experts deliver cutting-edge research in areas that drive long term commercial benefit for the food and drink industry. Leatherhead Food Research is a trading name of Leatherhead Research Ltd, a Science Group Company.

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