In focus

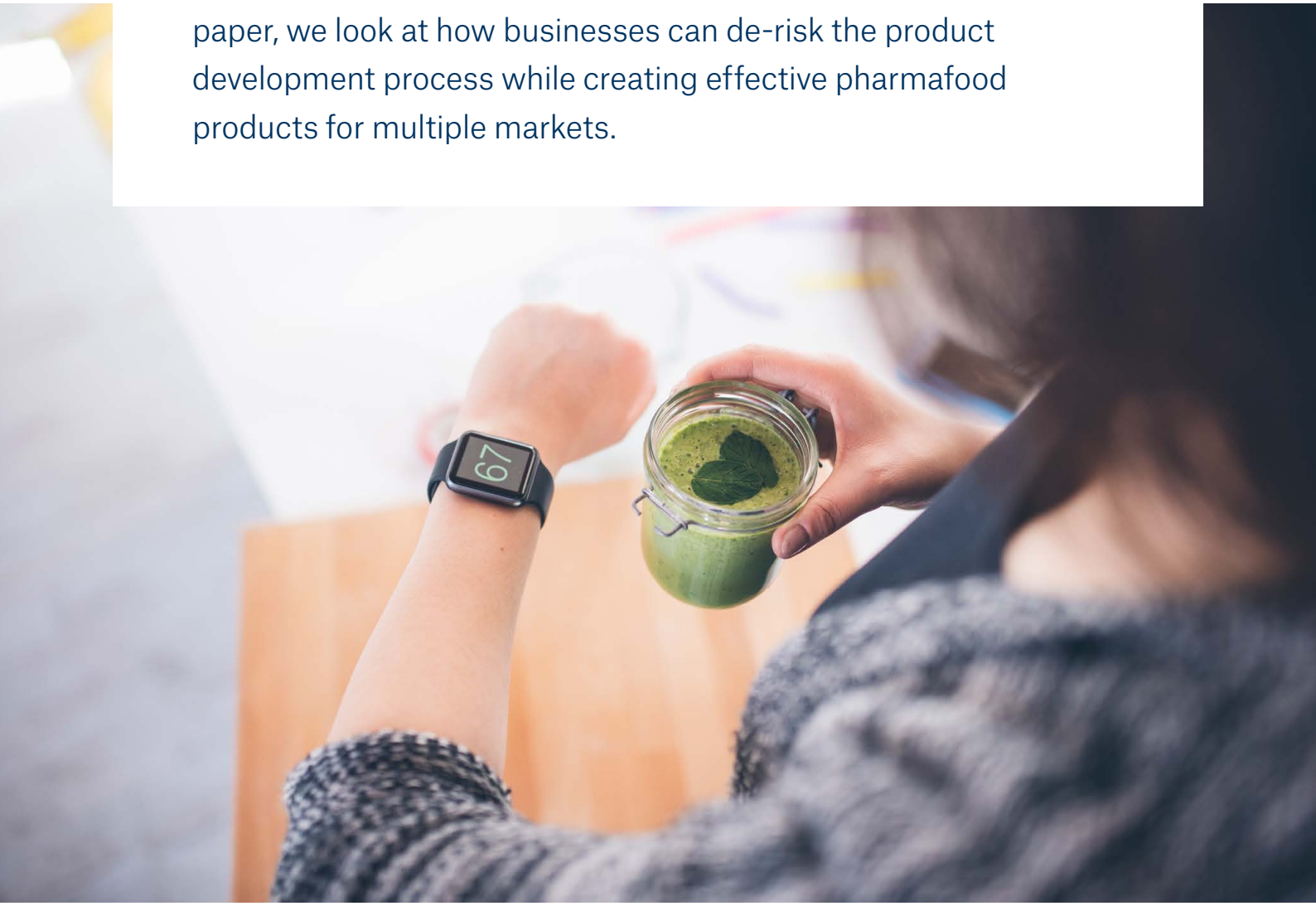
Leverage functional ingredients without falling foul of regulation

Developing compliant food and beverage products focused on cognitive, gut, skin and stress health

leatherhead food research

a **science group** company

The ‘pharmafood’ trend is gaining momentum, with many food and beverage businesses developing products to meet consumers’ evolving health and wellbeing demands. These pharmafood products are food or beverage products that contain an additive or a bioactive that can confer health benefits but don’t require a doctors’ prescription. However, as the boundaries between food and pharmaceuticals blur, there’s a risk of food and beverage products straying into the territory of medicine regulations. What’s more, functional ingredients that are permissible under one country’s food and beverage regulations may be restricted or classified as ‘novel’ in another. In this white paper, we look at how businesses can de-risk the product development process while creating effective pharmafood products for multiple markets.



Pharmafoods present opportunity and risk

Health and wellbeing continue to be a priority for many consumers as they look for food and beverage products with improved nutritional quality that can confer certain health benefits. This is creating increased market opportunities for pharmafoods, but there are risks attached. Figure 1 shows how the interface between food and pharmaceuticals is shifting. As boundaries between food and medicine become less distinct, it's important to be aware of the complexities of the regulatory landscapes, as well as ascertaining which category your product falls into. Mistakes could be costly, potentially resulting in product recalls or withdrawals as well as lasting brand damage.

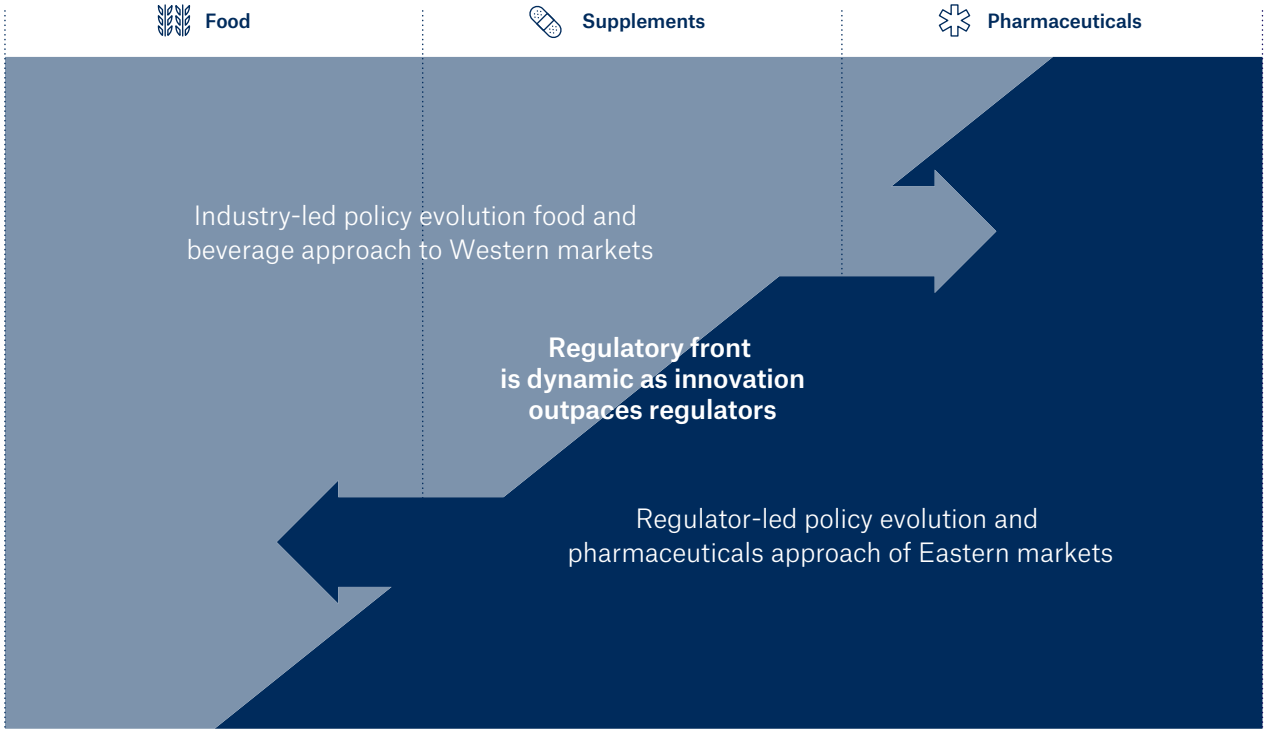


Figure 1. The blurring of regulatory boundaries between food and pharmaceuticals

Functional health ingredients

From an ingredient perspective, we are continually learning about the relationships between functional ingredients and health, both mental and physical. For instance, consumers have long associated caffeine with alertness, but they are increasingly becoming aware of other functional ingredients, such as lemon balm with stress management and turmeric with reduction of inflammation.

There is no doubt that functional ingredients from familiar edible plants (e.g. St. John's Wort, lavender and basil) as well as the more exotic (e.g. ashwagandha and Chanca Piedra) will continue to dominate the food and beverage scene. With the health benefits they confer, manufacturers can create products which address the nutritional and health needs of specific cohorts, such as the elderly, women and athletes or those with specific health issues such as acid reflux or joint inflammation.

Consumers expect these products and their ingredients to satisfy fundamental criteria such as safety and effectiveness as well as transparent, sustainable and natural sourcing. There are also regulations surrounding the use of these ingredients, and claims made by the products containing them. Such regulations can vary greatly across different geographical markets.

In this white paper, we look at four core areas that are gaining attention from consumers and manufacturers:

- Cognitive health
- Gut health
- Skin health
- Stress health

Then we identify important factors which must be considered to de-risk the product development process.

Cognitive health (nootropics)

Nootropics (also known as smart drugs or cognitive enhancers) are gaining attention as non-prescription substances that can enhance cognitive performance or prevent decline of cognitive function. It is thought that they could offer much potential in the prevention and management of dementia.

These substances can be synthetic or found naturally in foods. Within the natural realm, bioactives (e.g. caffeine), botanicals (e.g. *Gingko biloba, Rhodiola*), phytochemicals, omega fatty acids and vitamins are classic examples.

It is thought that herbal nootropics, such as *Gingko biloba*, work by increasing dopamine and adrenergic receptor activity and inhibiting the norepinephrine uptake. Others like *Panax ginseng* and *Bacopa monnieri* are thought to increase acetylcholine and/or glutamate reception activity while inhibiting acetylcholinesterase.

Gut health (postbiotics)

Postbiotics and paraprobiotics are touted as a new class of substances, in addition to probiotics and prebiotics, that can influence the gut microbiome.

Postbiotics are functional fermentation compounds, released or produced by probiotics, which exert a positive effect on the host's health. Paraprobiotics are generally defined as 'inactivated/dead microbial cells of probiotics'. However, the terminology is evolving and, 'postbiotics' can be used to encompass both aspects[1].

Research on these substances is ongoing, but it is thought that they could play a role in managing inflammation, obesity, hypertension, coronary heart diseases, cancer and oxidative stress[2]. Their inclusion within food matrices is an attractive proposition for food and beverage manufacturers looking to offer products with superior nutritional quality.

Skin health (skin microbiome cosmetics)

Although studies on the skin microbiome are still in their early days, it is becoming clear that it plays a key role in maintaining good skin condition.

There is a rising trend for cosmetic products that support the skin microbiome. This can be seen in the formulation of microbiome-friendly products that don't over-sanitise the skin as well as products containing prebiotics to help balance the microbiome. New approaches, such as adding probiotics to products, are also being explored.

Carbohydrate complexes have been developed that influence microbial species like *Malassezia furfur* and *Staphylococcus epidermidis* on the scalp, to improve hydration and decrease flaking. Inulin, which promotes bacterial growth, may also be used to improve skin condition. Some skincare brands are adding *Lactobacillus* species to formulations to help rebalance the skin microbiome; others are developing proprietary bacteria either as an ingredient or an ingredient delivery mechanism.

It's important to note that safety issues may arise if microorganisms are used in formulas. Further research is required to understand the effects of these products on global skin health.

Stress health (adaptogens)

Adaptogens are herbs that help the human body adapt to stress, support normal metabolic process and restore balance[3]. Following clinical trials, they are considered effective in facilitating optimal performance in times of stress, as well as addressing acute symptoms of anxiety[4]. However, their mechanism is still unknown.

One hypothesis is that they suppress a stress-activated kinase, JNK (c-Jun N terminal protein kinase), which is triggered by the presence of inflammatory cytokines. It has been reported that adaptogens stimulate the formation of HSP70 (heat-shock protein) which is known to inhibit JNK[5].

Examples of adaptogens include: Tulsi/Holy basil (*Ocimum sanctum*), Eleuthero root (*Eleutherococcus senticosus*) and Schisandra (*Schisandra chinensis*).

How to de-risk R&D with regulatory insight

The product development lifecycle (Figure 2) can be costly and resource-intensive. Understanding the potential impact of regulatory constraints from the outset, or at point of ideation (1), can de-risk and accelerate the process while improving effectiveness and robust compliance.

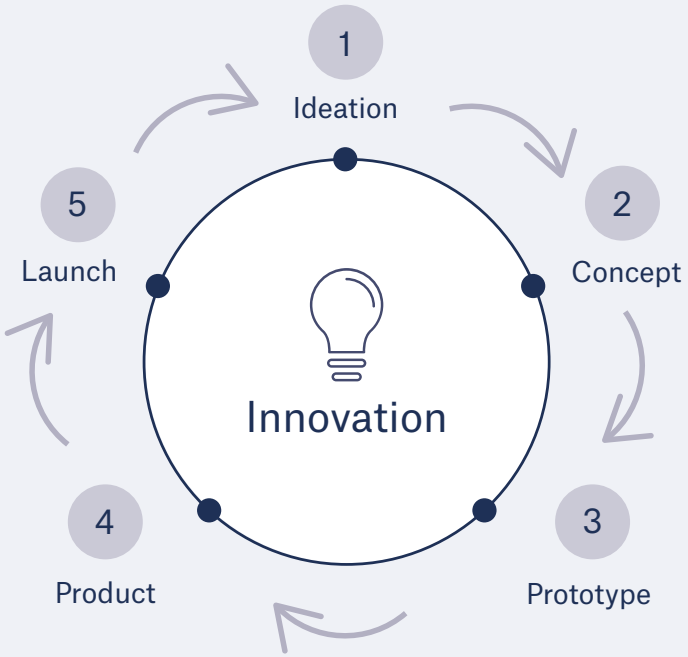


Figure 2. The product development lifecycle

When developing products that use functional ingredients to impart health benefits, there are three important factors that should be considered during the ideation phase (1):

- Are the ingredients permissible in target markets?
- Is the processing technology acceptable?
- Can Health, Nutrition or Marketing claims can be used on products?

1. Will the functional ingredients be permitted in target markets?

Understanding which functional ingredients can be used in different target markets is fundamental when formulating food and beverage products with health properties. This is a complex area, and a product's categorisation ('supplement' vs. 'food and beverage') has an impact on which national and regional regulations or guidelines apply. This influences everything from labelling and logos to taxation.

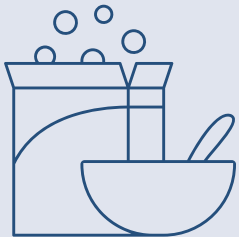
In the EU, ingredients which weren't extensively consumed before 15 May 1997 are considered 'novel' and require pre-market authorisation. This may cover foods which have a long history of consumption outside the EU, such as baobab fruit pulp. Australia on the other hand tends to accept the use of any foods which have traditionally been consumed in other parts of the world.

Requirements for functional ingredients with physiological effects vary between different markets. It may be necessary to profile safety, dosage, bioavailability and toxicological features. Depending on the dosage, some products may be classified as 'medicinal' in some markets. Product development also needs to verify that the presence of other ingredients does not modify the behaviour of the functional ingredients.

For products targeting multiple markets, it's important to be aware of the different regulatory requirements at an early stage so decisions about functional ingredients are fully informed.

Ingredient spotlight

Chia seeds are a traditional food in South America but not in the EU, so their use required pre-market safety approval. This ingredient is now approved for use in bakery and cereal products as a new source of omega 3 fatty acids.



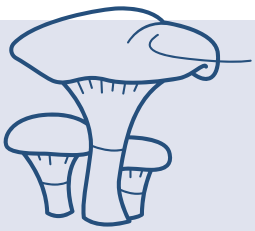
2. Is the processing technology acceptable?

On-shelf stability and *in vivo* bioavailability profiles are critical quality markers for pharmafood products. It follows that new technologies which reduce or eliminate degradation of functional compounds are of great interest to manufacturers. Enzymes and UV treatment as well as extraction, microwave and plant-breeding technologies are among the approaches being considered. They may enable pure extractions of functional ingredients, as well as delivery of intact functional compounds.

With this rapid technical progress, businesses need to be mindful of how emerging technologies relate to existing regulatory frameworks. Before implementing a new approach at scale, it is prudent to check its compliance with the national regulations of target markets. There have been instances where a technology that comes under the Generally Recognized as Safe (GRAS) classification in the US is deemed 'novel' in the EU. Detailed upfront assessment helps reduce risk and avoids complications later.

3. Can health, nutrition or marketing claims be used on products?

At the point of inception, it is vital to determine any claims that will be central to product positioning, then work towards their substantiation. Claims for pharmafoods fall into two categories 'Nutrition and Health claims' and 'Marketing claims'. Requirements vary between different markets which can complicate matters for products sold globally.



Processing spotlight

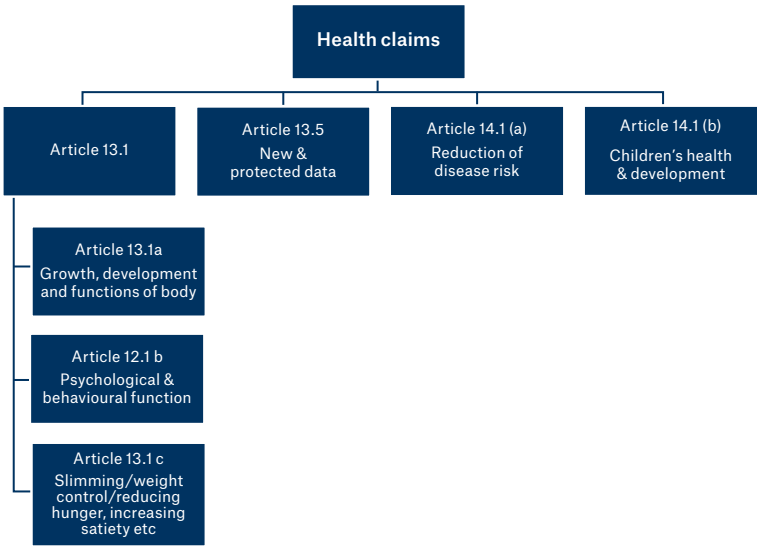
Controlled UV irradiation is used to enhance the concentration of vitamin D2 in mushrooms. Commercially grown UV-treated *Agaricus bisporus* mushrooms have been approved in the EU market as a novel food since 2016 (Novel Union list, Regulation EU 2017/2470, as amended).

Nutrition & Health claims

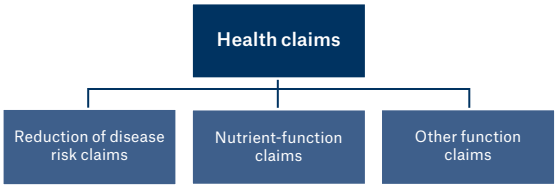
It is important to distinguish between 'Nutrition claims' which relate to beneficial nutritional properties and 'Health claims' which imply a particular ingredient confers a health benefit.

The regulatory situation for Nutrition claims is fairly consistent across different markets, focusing on the level of nutrients present in a product. Any divergence tends to revolve around criteria and wording. The same is true of comparative claims, which differentiate the product from others in the same category.

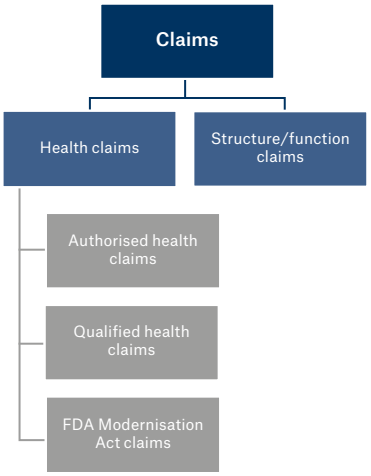
When it comes to Health claims, things are more complex. Regulatory definitions, requirements and processes can vary significantly, as the diagrams in Figure 3 illustrate. It is important to be aware of any differences which may impact the global positioning and labelling of products intended for multiple markets.



Structure for health claims in the EU



Structure for health claims in India



Structure for health claims in the USA

Figure 3. Approval of health claims in the EU, India and the USA

Regardless of market requirements, it is advisable to understand the weight of scientific evidence available for a functional ingredient-health benefit relationship. This can be used to steer fundamental aspects of concept design and progression.

It's important to acknowledge the need for consumer reassurance[6] that a given product works in delivering the health benefit it claims. Where there is a substantial weight of evidence, the concept is more likely to satisfy both consumers and enforcement authorities.

Manufacturers must also review and cross-reference recipe formulations with authorities' requirements. In some markets, official lists or registers exist for Nutrition or Health claims, but in others, the authorities need to be directly notified prior to market launch. The review also provides opportunities to identify alternative ingredients, such as different botanical sources or bioavailable forms or formats.

In most scenarios, dossiers containing scientific evidence of the relationship between the functional ingredient and the health benefit are advisable to support any claims made. They can also be used to counter any challenges from consumers, authorities or competitors.

Marketing claims

Terms such as 'clean label', 'natural' or 'sustainable' are considered Marketing claims.

Unlike Nutrition and Health claims, for which there are clear regulatory statements, there is a lack of regulatory definition for such terms. Instead, there are guidelines available. For instance, in the UK, the Food Standards Agency (FSA) specifies that a natural product is *"comprised of natural ingredients, e.g. ingredients produced by nature, not the work of man or interfered with by man"* as well as providing criteria for use of the term 'natural'[7].

To avoid or withstand potential challenges from consumers, competitors or authorities, it is best to assess the guidelines in different target markets and ensure any marketing claims can be qualified and quantified.

Key takeaways

- There is increasing consumer awareness of health benefits brought about by functional ingredients. Consumers therefore want healthy food and beverage products containing these functional ingredients, especially those from natural sources

- To maximise brand protection and reputation management, manufacturers need to prove the provenance and efficacy of products. New technologies are emerging to source and utilise functional ingredients within mainstream and niche product applications

- Functional ingredients for the management of cognitive, gut, skin and stress issues are being discovered and leveraged via new product development. It is important to validate these ingredients at the point of inception, to be sure that they are approved for food and beverage applications. It's also important to ensure that end-products will not fall into the medicinal domain

- When using Marketing or Nutrition and Health claims, it is vital that statements do not mislead consumers. The relationship between a functional ingredient and the product claim must be substantiated in line with the legal conditions of use. Failure to do so can result in costly product withdrawal and penalties

How can Leatherhead help?

The ‘Point of Inception’ rule

A regulatory review of a product concept is a prudent strategic move in circumstances where success or failure could have a significant impact on brand reputation. Leatherhead has the experience, knowledge and capability to provide an unbiased assessment of pharmafood product concepts, technologies and claim propositions. Applying this expertise during the inception phase of product development can de-risk the innovation process.

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