

The best blend for greatest profits combines innovation and safety

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ABSTRACT: To market an ingredient in the United States (U.S.), safety must first be demonstrated at the proposed levels of use. Plants may contain minor constituents that, through the extraction process, are concentrated to levels that could pose health risks. The U.S. Food and Drug Administration (FDA) has two ways of determining if a food ingredient is safe:

1. Food Additive Petition submitted to the FDA
2. Determination of Generally Recognized As Safe (GRAS) status

This article focuses on the GRAS determination. A GRAS determination of an ingredient is based on views of experts qualified by scientific training and experience to evaluate a substance's safety when directly or indirectly added to food.

The development of a new food ingredient can be both an exciting and chaotic process. Take, for example, a fractionated extract of the leaf of a plant not typically consumed as a food. It becomes apparent from initial bench-top testing that this fraction contains potent antioxidant capabilities useful for a variety of food products, unlike anything else seen on the market. However, even at this early stage, critical questions need to be answered before moving forward:

- Will this ingredient enhance the high-quality characteristics of a variety of products?
- Does this ingredient provide added value over existing antioxidant ingredients?

Ingredient formulators know that ingredients require a tailored approach to satisfy customers' need to complement the quality and characteristics of their existing or anticipated consumer food products. To take this example further, many hours are spent in the initial phases of ingredient development analyzing the novel extract to identify the constituent(s) providing the antioxidative properties, so the product can be standardized and consistently reproduced. Even more time is allocated toward analyzing industry need for an antioxidant with the specific characteristics of the extract, when compared to similar products already on the market. To continue the above example, assume that after a determination that this new antioxidant has the right properties to add value to food products, a company wants to move forward to develop this extract for a variety of food uses. Typically, from a business perspective, a project timeline is then planned, analyzing costs, time-to-market, and potential marketing capabilities, with the overall analysis of potential revenue. At the same time, additional technical information

must be determined as you formulate this antioxidant for commercial production, including any additives/stabilizers that must be included in the ingredient to increase shelf-life, the food chemistry interactions between this ingredient and planned final food products, and the cost of the required raw materials to produce this antioxidant. Integral to this process should be an analysis of the safety regulations that pertain to bringing a new ingredient into the marketplace.

PUTTING SAFETY FIRST

To market a new ingredient in the United States (U.S.), safety must first be demonstrated at the proposed levels of use. Plants may contain minor constituents that, through the extraction process, are concentrated to levels that could pose significant health risks. The U.S. Food and Drug Administration (FDA) has two ways of determining if a food ingredient is safe:

1. Food Additive Petition submitted to the FDA
2. Determination of Generally Recognized As Safe (GRAS) status

This article will focus on the GRAS determination. A GRAS determination of a food ingredient is based on the views of experts qualified by scientific training and experience to evaluate the safety of substances directly or indirectly added to food (1). This general recognition of safety requires common knowledge within the scientific community knowledgeable about the safety of substances. Too often, the safety and regulatory process is treated as an afterthought and only initiated at the last minute, which could cost the company significant financial losses in delayed timelines and missed opportunities. The project plan must incorporate the determination of safety to have an accurate view of probable timelines, costs and marketing plans. Many ingredient manufacturers will work with a third party, having food toxicologists on staff, that has the right resources and infrastructure to efficiently guide the manufacturing company through the appropriate stages and possible studies to show FDA that the novel ingredient is safe when used as intended.

SETTING SPECIFICATIONS

A part of the safety process includes the setting of specifications. A GRAS determination must include the



ingredient specifications, as well as the manufacturing process, to verify that the ingredient can be manufactured in a consistent manner, and that the manufacturing process does not introduce any potentially toxic substances into the ingredient.

Specifications define the composition of an ingredient, and this is true from both food manufacturing and regulatory standpoints. The specifications of an ingredient help food toxicologists determine if the ingredient is substantially similar to other ingredients on the market or if it is unique and must be viewed as a novel entity.

When the concept of determining the safety of the ingredient through third-party review is built into the project plan from the beginning, the completed specifications (along with the other aspects of the ingredient) can be quickly reviewed by the third party to provide the necessary steps to determine GRAS status for the ingredient. A GRAS determination is based either through scientific procedures (*i.e.*, safety studies confirming the safety of the ingredient at the desired level of daily consumption by the general population), or in the case of an ingredient used in food prior to January 1, 1958, through experience based on common use in food. A GRAS determination may be maintained in the company's files, or the company may notify FDA of the GRAS determination to ensure that the agency has no questions concerning the safety of the ingredient at the intended levels of use.

GRAS BEGINNINGS

The development of modern food law and regulation during the 1950s (due, in part, to the contamination of some foods by chemicals), brought about the Food Additives Amendment (FAA) of 1958, and with it the concept of GRAS. In the Act, Congress defined a food additive as "any substance the intended use of which results or may reasonably be expected to result, directly or indirectly, in its becoming a component or otherwise affecting the characteristics of any food [...] if such substance is not generally recognized among experts qualified by scientific training and experience to evaluate its safety...under the conditions of use". In this manner, Congress provided the legal terminology of a food additive, while also creating a new class of substances... those that are not food additives, but are "generally recognized" to be safe, under certain conditions of use. In this manner, GRAS substances are "exempt" from the food additive process. Later discussions within the FDA in 1997 clarified the knowledge of safety, when comparing GRAS status to a Food Additive Petition: "a GRAS substance is neither more safe nor less safe than an approved food additive. Rather, the distinction between a GRAS substance and an approved food additive is that, for a GRAS substance, there is common knowledge of safety within the scientific community" (2).

GETTING A HEAD START

Realistic expectations must be incorporated into any project timeline. Evaluating a novel ingredient for any safety issues at the onset is the best method of maximizing the time available, so that any safety-related issues can be addressed early to keep the project on time and under budget. An ingredient manufacturing company has to deal with the standardization of the ingredient, prototype development, scale-up from bench-top or pilot scale

production to commercial production scale, as well as marketing and commercial distribution. In considering a new ingredient, food manufacturers are more likely to want to know up-front that safety has been addressed. Furthermore, food manufacturers have shortened development timelines and thus are less likely to spend time exploring a new ingredient with unanswered safety questions.

A safety consulting company should be able to provide a "feasibility" report at the outset, laying out a step-by-step plan that indicates what is necessary for a GRAS determination, including specifications, manufacturing process and the potential need for any preclinical toxicology studies. Based on a critical review of the scientific literature of substances structurally similar to an ingredient (such as a novel extract, in the above example), there may be enough information to determine that an ingredient is GRAS without any further safety testing.

However, in other instances, such as extracts from plants that are not typically consumed, the ingredient (as in the case of the antioxidant extract above) may need toxicology studies to determine safe levels of use. A feasibility assessment will outline the studies necessary to determine this safe use level, and should provide timelines and approximate costs necessary to complete these experiments. Having an assessment of any potential safety-related issues early in the ingredient formulation process and integrated into the overall project plan will provide a true assessment of the costs and time required to obtain final product release.

TOP OF MIND: QUALITY AND SAFETY

The first priority of product developers is to create the best possible product for their customers. Certainly, there are general guidelines and standard protocols followed in developing a new product, and now more than ever safety is a top priority, both to product manufacturers and consumers. For this reason, many product developers have begun pre-qualifying ingredients prior to inclusion in their formulations. This precautionary step has evolved over the years and is now becoming status quo, instead of an added bonus. For food manufacturers concerned about vicarious liability and upholding brand image and integrity, this critical step early on in development cannot be overlooked, and has begun to incorporate the concept of safety. Food scientists have typically held a multifaceted and ever-changing role in the industry. They have had to gracefully balance both science and marketing to develop and execute profitable products that not only provide a benefit to consumers, but are safe and effective as well. For food products, ingredient selection and qualification has evolved from examining the quality, cost and availability of an ingredient to now placing safety as a top consideration with an examination of GRAS status as a necessary qualifier. Savvy food ingredient manufacturers have also seen this growing trend as an opportunity to be more competitive in the marketplace and streamline their ingredient production by incorporating the GRAS determination process early in a novel ingredient development plan.

REFERENCES AND NOTES

1. FDA Code of Federal Regulations, 21 CFR170.30 Eligibility for classification as generally recognized as safe (GRAS) (2008).
2. *Federal Register*, **62**, pp. 18937-18964 (1997).