



## **GRAS: Generally Recognised As The Gateway To A New Market**

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*Many companies mistakenly think that dietary supplement status under DSHEA is the same as GRAS status for conventional foods. It is not. **Loren Israelsen** explains.*

What is GRAS, and why is it important to dietary supplement companies who wish to expand their sales opportunities into the food arena? The answer is surprisingly simple yet widely misunderstood.

GRAS means Generally Recognised As Safe. The US Congress established this concept and regulatory policy in 1958 as part of food safety legislation. As a result of this law, a wide range of foods and food ingredients were "grandfathered" as safe for their intended use and listed at Section 182 of the Code of Federal Regulations (CFR). This list of substances, ranging from alfalfa to zedoary, are GRAS, meaning that qualified experts agree that these ingredients are safe when used in foods at levels to accomplish their technical or nutritional purposes.

Any substance proposed for use in food not included on this GRAS list must go through a pre-market safety evaluation/ affirmation process. This can be done as a food additive petition or GRAS self-affirmation (GRAS/SA). Food additive petitions are of little interest to the dietary supplements and functional foods market, as the purpose of food additives are highly technical (emulsifiers, stabilisers, sequestrates, etc.) and serve virtually no value-added nutritional or functional foods ingredient benefit. (See CFR 182 Subparts c, d, e, g, h for listing details.)

GRAS status, on the other hand, has quite suddenly taken on great importance for the dietary supplements and functional foods industries as a gateway to use dietary ingredients as valued additions to conventional foods. The commercial incentive is obvious. Imagine having your dietary supplement ingredient, such as lutein, Co-Q10, DHA, grape seed extract, soy isoflavones, or oat fibre extract, in one of the leading energy bars, breakfast cereals or ready-to-drink beverages. The sales and volume potential far exceeds that for most dietary supplement categories.

Unfortunately many US and foreign dietary supplements and functional foods

companies mistakenly think that dietary supplement status under DSHEA is the same as GRAS status for conventional foods. It is not. DSHEA created a special safety standard and its own special "grandfather" list (known as the Old Dietary Ingredient List) for ingredients sold in the US as dietary supplements prior to October 15, 1994. These dietary ingredients are considered safe when used in dietary supplements, but are not allowed as conventional food ingredients unless they appear on the GRAS list (CFR 182) or are affirmed as GRAS.

Notwithstanding, some dietary supplement and conventional food companies have crossed this regulatory wall. Examples include St. John's wort in soups and potato chips, Ginkgo biloba in breakfast cereals and kava kava corn chips. More recently, several popular beverages added these and other non-GRAS ingredients to their products, prompting the US Food and Drug Administration to issue warnings against this practice and threatening action against those who fail to remove these ingredients from offending conventional food products.

Many executives, marketers and ingredient producers are puzzled that well-known dietary ingredients can be freely sold at any potency level or quantity in dietary supplements in the US, but the very same dietary ingredient is banned from use in conventional foods at any level. This is due to the different legal standard set out in the Food, Drug & Cosmetic Act, the 1958 Food Additive Amendments and DSHEA.

### **Determine GRAS Status**

How then does a dietary supplement ingredient become a GRAS food ingredient? In 1997, FDA issued a rule setting out a notification process for GRAS/SA. This rule sets requirements for determining GRAS status that involve two core principles: An assessment of the ingredient's safety; and that the basis for reaching the conclusion of safety is "generally recognised" (publicly available and generally accepted) by experts in the fields. There are two ways to demonstrate this:

- A current scientific assessment done by an expert review panel, or
- Showing that the food ingredient was sold in commerce in foods prior to January 1, 1958. This latter approach is seldom used for most dietary ingredients presently sold.

Unlike that of many other countries (which have either a positive list or a government approval system), an unusual feature of GRAS/SA in the US is the use of a private expert review panel organised by the company seeking GRAS/SA. Reputable companies go to great lengths to engage highly respected experts whose scientific and personal integrity are beyond doubt. FDA may challenge the adequacy of the expert panel's conclusions or underlying safety data, which could result in serious regulatory problems and create a strong incentive to exercise the necessary scientific rigor to achieve GRAS/SA status acceptable to FDA.

FDA also provided for a voluntary notification process if a company wishes to

advise FDA of its GRAS/SA findings. On balance, notification is preferred because it minimises the risk of FDA disagreeing with the GRAS/SA and throwing a new or improved food product launch (using your ingredient) into chaos. Should you consider a GRAS/SA affirmation? The answer is both a technical and economic one and requires a careful assessment of your ingredient's current safety profile, including:

- Toxicology in humans and animals;
- A costing analysis of how your ingredient would affect the retail price of the conventional foods using the ingredient;
- The potential benefit and claims allowed or possible to enhance the value of the conventional food; and
- Any supply or production limitations, which cause concern among big food companies.

The average GRAS/SA will take four to six months if the safety data is reasonably sound. The cost to develop a GRAS dossier necessary for affirmation, which includes engaging an expert review panel, and all other related costs, can often run between \$40,000 and \$70,000.

The rewards of GRAS affirmation can be well worth the time and expense. A growing number of companies have announced GRAS/SA for ingredients, including grape seed extract, lutein, DHA, concentrated soy isoflavones, L-Carnitine crystalline, L-Carnitine L-tartrate and tuna oil. A significant number of other ingredients are at varying stages of the GRAS/SA process.

A commonly asked question is whether a GRAS/SA is exclusive and proprietary to the sponsor or can a competitor rely on another GRAS/SA dossier as the basis to assert GRAS for their own product? The answer to the latter is almost always no. Each GRAS/SA must detail manufacturing processes, intended uses and usage levels and other safety data that are not usually identical among competitive products. It would be unwise and risky to "borrow" GRAS/SA status of a competitor as the basis for the safety of another product.

The decision to be or not to be GRAS requires a carefully thought-out plan, particularly to assess the chance of leveraging US GRAS affirmation in foreign markets, which also require some form of safety assessment for ingredients sold in novel foods as dietary supplements or as natural health products.

The concept of GRAS is well understood in most industrial countries, but the US procedure of a private GRAS/SA is uniquely American. Nevertheless, a rigorous and thoroughly conducted GRAS/SA would carry significant weight in achieving status as a novel food ingredient or a food supplement ingredient under EU's directives or as a FOSHU ingredient in Japan.

For many, GRAS may be greener!

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