



According to the U.S. Food and Drug Administration (FDA), under sections 201(s) and 409 of the Federal Food, Drug, and Cosmetic Act (the Act), any substance that is intentionally added to food is a food additive, that is subject to pre-market review and approval by the FDA, unless the substance is generally recognized, among qualified experts, as having been adequately shown to be safe under the conditions of its intended use, or unless the use of the substance is otherwise excluded from the definition of a food additive.

Under sections 201(s) and 409 of the Act, and FDA's implementing regulations in 21 CFR 170.3 and 21 CFR 170.30, the use of a food substance may be GRAS (generally recognized as safe) either through scientific procedures or, for a substance used in food before 1958, through experience based on common use in food.

"Prior to 1997, the FDA had to be petitioned to 'affirm' that a substance is GRAS, and was getting backed up with reviewing GRAS petitions," said John R. Endres, ND, CSO with AIBMR Life Sciences, Inc. (Puyallup, WA), a consulting firm that has been working with the natural products industry since its founding in 1978, and significantly increased its services to the functional foods industry in 2007. "On April 17, 1997, the FDA proposed a voluntary procedure whereby the Agency could be notified of a determination (the self-affirmation) that a substance is GRAS." While this proposed rule is yet to be finalized, all ingredients added to foods must have GRAS or Food Additive status.

Self-Affirmed GRAS

GRAS notification to the FDA is a voluntary process and not required, according to Endres. "Self-affirmation is accomplished according to the aforementioned FDA proposal. Companies hire a firm, such as AIBMR Life Sciences, to prepare a safety dossier generally based upon scientific procedures and corroborated by a history of human exposure. Finally, a panel of experts is assembled," he said, adding that AIBMR usually has two to three staff physician scientists as panel members, and the chair being a PhD toxicologist retired with 40 years experience with the FDA and EPA. "The expert panel must be qualified by training and experience to evaluate the safety of food ingredients, and must agree with the basis of the determination that the intended use of the ingredient is GRAS."

This was a route began in earnest in 2009 by Trace Minerals Resources

International, Inc. (TMR, Ogden, UT).

"We wanted to continue gathering scientific data giving validity to our trace mineral ingredient, ConcenTrace Trace Mineral Drops," said Ryan Fisher, the company's general manager. "As our company has grown over the last decade, we have had more international interest as well as larger food companies inquire about our minerals as a method to improve their products and add significant mineral claims to their products supplement facts. GRAS affirmation was required by some of them and encouraged by all of them. We wanted to make our product available to new markets and increase the availability of our product throughout the world."

TMR first looked at working individually with the required experts, but later decided to use the services of AIBMR. The estimated cost for GRAS affirmation is \$75,000 and the time frame was approximately two years to complete, which was a completely worthwhile investment, according to Fisher.

"We saw an immediate impact with our potential client list after the process was complete," he said. "Companies who had interest in our products before but had held off purchasing from us began to bring our products in. Other current customers expanded the amount of business they were doing with us because of the extra level of confidence that they gained with us."

Another company that has seen markets open up after securing self-affirmed GRAS in late summer 2011 for its patented cognitive health ingredient Magtein™ is City of Industry, CA-based AIDP, Inc. "This compound has large market potential for a broad number of conditions," said Kathy Lund, director of business development. "By securing self-affirmed GRAS, AIDP can assure customers of Magtein's safety. It indicates an investment behind the product and a commitment to market development. GRAS helps to open several market channels that would not otherwise consider a non-GRAS ingredient, such as beverages, which require a GRAS status."

Suzanne McNeary, president of NutraGenesis LLC (Brattleboro, VT), shared that her company's choice, as with many companies, for self-affirmed GRAS was deliberate. "Our company has always preferred self-affirmed GRAS and we are not alone—the majority of GRAS determinations are self-GRAS in order to protect the proprietary information of an ingredient from competitors," she said, adding that NutraGenesis has worked with RS McQuate & Associates and GRAS

tration was that it took a long time; longer than it should."

Beyond the consultants and direct interaction with the FDA, Sokoloski said that having the right internal resources didn't hurt. "Because of Healthco's access to NOW Foods' technical staff with their testing and regulatory expertise, as well as some of the most sophisticated labs in the business, we had a good understanding of what was required and the capacity to do it," he said.

"Although there are two different pathways for GRAS—self-affirmation and FDA no objection—and both pathways end up in an ingredient legal for food use, many food manufacturers will not accept a self-affirmation; they want an opinion from the FDA," added Michael Lelah, technical manager with NOW Foods. "This further protects them from the FDA disagreeing with a self-affirmation at some future date, which could happen."

AIBMR's Endres acknowledged this line of thinking, but offered another side. "There is the perception that the FDA 'no objection letter' is the best that can be obtained," he said. "GRAS self-affirmations, if properly prepared and reviewed, should be thorough enough to cause the FDA to not question the basis of the GRAS determination."

One company confidently banking on

this is Kemin Health L.C. (Des Moines, IA), which began its GRAS self-affirmation review in October 2010 for AssuriTEA Wellbeing™ and worked steadily on the review up through the time the Expert Panel was convened in September 2011.

"If a company makes a self-determination, FDA may challenge that determination on the basis that the product is an illegal food additive," said Debbie Trinker, Esq., vice president of regulatory and legal affairs with Kemin.

"However, Kemin is not aware of any situation where FDA has challenged the GRAS status of a substance that has been self-affirmed after a thorough, documented scientific finding of GRAS status was confirmed by an qualified and independent scientific experts, such as was done for AssuriTEA."

The company's confidence is well placed, according to Trinker, as Kemin has carefully followed FDA regulations at 21 CFR 170.30 on GRAS status that require "common knowledge about the substance throughout the scientific community knowledgeable about the safety of substances directly or indirectly added to food ..." "The GRAS determination of the proposed uses of AssuriTEA Wellbeing was based upon 'scientific procedures' as described in the regulation, as corroborated by history of safe

use of green and black teas," Trinker explained. "Kemin was able to rely upon the history of safe use of tea, because its ingredient is a water extract that qualitatively and quantitatively compares compositionally to brewed tea. Unlike some commercial tea ingredients, AssuriTEA Wellbeing is not extracted with alcohol and its green tea component is not concentrated to EGCG or any other constituent, making reliance upon the history of safe use of tea appropriate."

Kemin's AssuriTEA Wellbeing review has taken a year and cost tens of thousands of dollars in external consulting fees, as well as required extensive use of the company's internal resources. Other discussions on the GRAS process estimate \$75,000 in fees from external consultants, and six months of review time. "The amount of time and money a company will spend will depend on the ingredient, the proposed food applications and usage levels," said Trinker. "Based on Kemin's experience with a number of ingredients, companies can easily expect to pay in the six figures and for the GRAS review process to take considerably longer than six months."

GRAS and NDIs

With the door closing on the FDA's acceptance of comments regarding its

(Continued on page 39)



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