Present-day U.S. food-ingredient safety considerations can be traced to 1958, when Congress passed the Food Additives Amendment to the Food, Drug, and Cosmetic Act. This legislation established the requirement that new food ingredients had to undergo premarket safety approvals by FDA before such substances could be legally added to foods. It also specifically allowed that substances that were generally recognized as safe (GRAS) were exempt from FDA’s premarket approval requirements.

Furthermore, GRAS status could be established either by FDA regulatory actions or by companies independently making such safety assessments—so-called self-affirmed GRAS determinations—as long as the GRAS conclusion resulted from actions taken by individuals who were qualified by training and experience to issue valid food-ingredient safety determinations.(1)

Over the course of the past fifty-plus years, the use of substances considered to be GRAS by FDA, or self-affirmed GRAS as determined independently, has been a mainstay of the regulated food industry’s new product innovations. The regulatory procedures that were in place under the purview of FDA immediately following the passage of the 1958 Food Additives Amendment were modified in 1997, when FDA issued proposed regulations to implement a voluntary GRAS notification program.(2) Although not officially finalized as regulations, the voluntary GRAS notification procedures have been operational since 1997, with general satisfaction and acceptance by affected parties.

In 2006, at the request of Senator Tom Harkin and Representative Rosa DeLauro, the U.S. Government Accountability Office (GAO) initiated a review of FDA actions, procedures, and oversight,
as well as pertinent laws and regulations, applicable to GRAS substances and their associated food uses. Particular focus was directed toward FDA’s voluntary GRAS notification program, spanning the time period 1998 through 2008. In February last year, GAO issued its comprehensive findings in a report titled “FDA Should Strengthen Its Oversight of Food Ingredients Determined to Be Generally Recognized as Safe (GRAS).”(3)

GAO’s report addressed multiple aspects of establishing GRAS status for defined uses of the subject ingredients. GAO acknowledged the importance of openness and transparency in the GRAS safety-evaluation processes, while encouraging FDA to finalize the proposal that is governing the voluntary GRAS notification program.

Among the substantive concerns with GRAS safety determinations GAO highlighted was the potential public health vulnerabilities stemming from current practices that involve the safety of new GRAS substances. In particular, the fact that FDA only reviews the safety of substances that are voluntarily submitted for agency evaluation triggered GAO concern, since many self-affirmed GRAS notifications are not submitted for FDA review and therefore may escape FDA oversight. It is feared that some self-affirmed GRAS determinations may be of inadequate depth and scope, thereby fueling concerns regarding health vulnerabilities. GAO explicitly commented that these safety concerns extend to engineered nanomaterials, which may raise unique safety questions due to the smaller particle sizes and associated increased surface areas.

In light of what GAO considers to be potential public health vulnerabilities linked to GRAS assessments for new ingredients, GAO recommended that FDA develop a strategy to require firms conducting self-affirmed GRAS evaluations to provide FDA with the documentation to support their GRAS conclusions. In effect, GAO advocated that it should be mandatory and not voluntary for firms making independent GRAS determinations to notify FDA. FDA reviewed the GAO draft report and provided detailed written feedback that was incorporated in the final GAO report. FDA acknowledged that an increasing number of independent GRAS determinations are being made that escape FDA oversight, and that this absence of agency oversight can increase the possibilities of adverse health consequences stemming from flawed or casual independent GRAS determinations. However, FDA recognizes the limits of its authority regarding GRAS evaluations, noting that the 1958 legislation does not grant the agency the authority on its own initiative to require the submission of safety documentation in support of independent GRAS determinations.

**What Lies Ahead**

While FDA concurred that expanded agency oversight of independent GRAS determinations should be strengthened, it commented in the final GAO report that it would pursue refinements to its food-ingredient safety program following internal deliberations and said it intended to implement changes in GRAS processes and procedures under current law.

FDA’s intent to address the GRAS substances concerns as described above has been illustrated by two very recent developments:

- While the topic of food safety was under consideration during the recently concluded Congress, there were no apparent FDA-initiated actions seeking expanded legislative authority for mandatory FDA notifications of all independent GRAS evaluations. The recently enacted Food Safety Modernization Act (FSMA) seems to be silent on the topic of GRAS substances, despite the prominent role that Senator Harkin played in obtaining passage of the subject legislation and his previous interest in the safety of GRAS substances that prompted the GAO investigation and the 2010 GAO report. Instead, FSMA addresses several other important food-safety aspects that focus on prevention-based controls, responding in large measure to the serious outbreaks of food poisoning experienced in recent years in the United States involving eggs, peanuts, and selected fresh produce.

- In seeking to enhance the safety considerations for GRAS substances under current law, while also responding to GAO’s recommendation that FDA finalize the proposed 1997 regulations regarding voluntary GRAS notification procedures, FDA published a notice in the Federal Register on December 28, 2010,(4) announcing the reopening of the comment period. The agency has requested feedback by March 28 on various aspects presented in the original proposal and possibly as refined by the collective experiences of implementing these
procedures since 1997. FDA is also seeking feedback on some—but not all—GAO recommendations. Feedback was specifically requested, 1) To obtain more information on the use of engineered nanomaterials, 2) To minimize potential conflicts of interest for those involved in making GRAS determinations, and 3) To issue meaningful guidance on how to document GRAS determinations.

Without any legislative actions that expand FDA’s authority to regulate GRAS substances, and with the agency’s interest in finalizing the proposed voluntary GRAS notification program following receipt and review of submitted comments, it seems highly unlikely that filing independent or self-affirmed GRAS determinations with FDA will become mandatory. Instead, the program will remain voluntary. Some ingredient suppliers and food manufacturers will continue to participate in the voluntary notification program as administered by FDA. Others who undertake independent GRAS determinations will forego the notification option and will not seek FDA’s concurrence with their safety determinations. Barring any serious adverse public health events linked to the consumption of GRAS ingredients, the independent GRAS determinations will undoubtedly remain a part of the food regulatory landscape in the immediate future. Marketplace influences will have a direct bearing as to whether or not a given independent GRAS evaluation will be submitted for FDA review. Those ingredient manufacturers and suppliers who elect not to submit their GRAS determinations to FDA may want to consider requiring their appropriately qualified GRAS expert panels to adhere closely to FDA GRAS criteria and standards for their self-affirmations, thereby elevating their accountability in ensuring ingredient safety. Finished-food manufacturers similarly may want to consider requiring their ingredient suppliers to document the quality of their self-affirmed GRAS determinations as a condition of purchase. As an alternative to submitting the GRAS evaluations to FDA for review, such actions associated with self-affirmed GRAS assessments would provide further safeguards for the consuming public.

References
1. Section 201(s) of the Food, Drug, and Cosmetic Act provides the definition of the term food additive, while also providing foundational information on GRAS substances.
2. See the Federal Register of April 17, 1997 (62 FR 18938).
4. See the Federal Register of December 28, 2010 (75 FR 81536)

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