

Licensing Innovative Food Additives and Ingredients by FDA**

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Summary: The current system for ensuring the safety of innovative food additives and ingredients was developed by Congress in 1958. It is inadequate in today's marketplace where supply chains are more complex, dynamic, and global, and our understanding of health risks has greatly advanced. The food supply is at risk for allowing unsafe substances to threaten serious long-term health effects as long as the Food and Drug Administration (FDA) allows companies to self-certify that a substance's use is Generally Recognized As Safe (GRAS*) without the agency's or the public's knowledge. Rather than embracing innovation, consumers increasingly recognize the risk, and most see substances added to food as their most important food-safety issue. Congress needs to modernize the mechanisms that ensure safety in a way that supports innovators who develop safe substances through a process that consumers can trust. To be successful, the dynamic needs to change from a race to the bottom with respect to safety research to one which strongly incentivizes companies to invest in robust safety studies by protecting them from "copycat" competitors who rely on the innovator's research and granting a longer license from FDA when the evidence is compelling.

Current realities: In 1958, Congress created a groundbreaking system intended to ensure the safety of food additives, (which includes food ingredients) by requiring the FDA's pre-market approval of a substance's use unless it was GRAS or was covered by another approval process (e.g., pesticides and color additives). New substances and uses were presumed unsafe unless "there is a reasonable certainty in the minds of competent scientists that the substance is not harmful under the intended conditions of use" (21 CFR §170.3). When the law was passed, it generally worked because food processing was regional, the scientific understanding of safety was more limited, and the FDA could move quickly through a rulemaking process.

Today's reality is fundamentally different: innovative food ingredients dominate the marketplace; supply chains are more complex, dynamic, and global; and the scientific understanding of the impact of chemicals on human health has greatly advanced. Innovators, in a rush to get their products to the marketplace, are likely to bypass FDA review and self-certify a substance's use as GRAS to avoid risk of delays and uncertainties. As a result, unsafe products that threaten consumers' health enter the food supply without the FDA's or public's knowledge. The public recognizes the risk: In a 2019 survey, 50% of consumers rated substances added to food (i.e., chemicals in food, carcinogens in food, food additives and ingredients, allergens, and biotechnology products) as their most important food safety issue.

Figure 1 describes the two paths to market for companies producing innovative food ingredients pursuant to the Food Additives Amendment of 1958 to the Federal Food, Drug, and Cosmetic Act. Once a food's use is allowed by either path, there is no effective and systematic reassessment of its safety, even when questions are raised. The two paths are:

- For a food additive petition, a company can secure the FDA's pre-market approval by filing a petition pursuant to 21 CFR Part 171 asking the agency to issue a regulation expressly approving a substance's use. The substance may not be used until the process is completed, which typically takes more than a year and often involves many iterations. Once the FDA approves the product, competitors can develop "copycat" products without seeking agency approval if the specifications and manufacturing process are equivalent.
- For self-certified GRAS, the FDA allows a company to make its own determination that a substance's use is safe and that its safety is considered GRAS by "competent experts"

*The Environmental Defense Fund maintains that FDA's GRAS program is contrary to the law and has challenged its GRAS rule in court. This proposal provides an alternative approach Congress could adopt.

pursuant to 21 CFR Part 170. The company may market and use the substance immediately based on its self-certification of GRAS status. To improve the substance's marketability to food manufacturers and retailers, a company may voluntarily seek to have the FDA review the decision. Competitors may rely on the notice to develop and self-certify copycat products without seeking agency concurrence.

Due to delays and uncertainties in marketing and using a substance in food, innovators rarely use the food additive petition path today. Almost all companies choose to self-certify a substance's use as GRAS. However, the GRAS program has come under intense criticism from the U.S. Government Accountability Office and public health advocates, including the American Academy of Pediatrics. The main concerns are: (i) conflicts of interest when a company makes a safety determination, especially when it does not voluntarily seek FDA review of the decision; and (ii) lack of transparency, which makes it impossible for the FDA and companies to ensure a substance's use is safe. Transparency is critical because no one can adequately consider, as required by law, the "cumulative effect of the substance in the diet, taking into account any chemically or pharmacologically related substance or substances in such diet" when the precise identities of ingredients and their uses in food are not publicly known.

Scientifically credible approaches and challenges: The self-certified GRAS program has created a "race to the bottom" when it comes to the quality and quantity of evidence needed to conduct a safety evaluation. To get their innovative substances to the market as soon as possible, companies have strong incentives to do only the minimum to assess a substance's safety. The threat of legal liability, consumer backlash, and FDA intervention are often too intangible to offset the benefits of conducting the minimal amount of research needed to pass muster. For its part, the agency has strived to set high standards but slipped to avoid discouraging companies from submitting voluntary notifications. This shift is evidenced by: (i) the failure to consistently consider all pharmacologically-related substances in the diet; and (ii) lack of a rigorous evaluation of substances using the agency's guidance on recommended toxicology studies that are based on the amount expected in the food supply.

A credible framework to begin to address the concerns is the FDA's Food Contact Substance Notification (FCN) program established by Congress in 1997. Companies making innovative food contact substances for food packaging and handling equipment submit a notification to the same office that handles food ingredients. If the agency does not object within 120 days, the notice is deemed "effective." The FDA has consistently made timely decisions, although about 20% of the notices are withdrawn to avoid an objection. A company with an effective FCN essentially receives a "license" from the agency, which is critical because, unlike food additive petitions and GRAS determinations, competitors with copycat substances must either pursue their own license or make a self-certified GRAS determination.

Any approach must recognize that scientific knowledge evolves and so does our understanding of risk. Therefore, any system to ensure innovative food ingredients are safe requires periodic reassessment as new evidence emerges. Unfortunately, the FDA lacks any effective means to know what chemicals are actually used and in what quantities, and the agency typically intervenes only when the evidence is compelling or when it is forced to by public attention. As a result, harm that develops over time and is not obviously connected to a substance may go unaddressed. The best example is *trans* fatty acids in partially hydrogenated oils (PHOs). In 2015, FDA ruled the use of PHOs was no longer GRAS in response to a 1994 petition from the Center for Science in the Public Interest, a lawsuit from an academic researcher, and two Institute of Medicine panels citing serious risks. The agency estimates these substances contribute to as many as 58,000 cases of coronary heart disease and 23,000 deaths per year.

Evidence-based options and real-world opportunities: The objective should be a system that ensures ingredients are safe and is robust and credible enough that consumers can embrace innovative food ingredients for their potential sustainability benefits. While mandated FDA safety review and approval and improved transparency of that process are essential changes needed, they are unlikely to be sufficient on their own. The system needs to incentivize innovators to conduct the research necessary to ensure their products are safe—to move from a race to the bottom to a system in which new data and scientific evidence are valued. Two key incentives are: (i) protection from copycat competitors who rely on the innovator’s research to demonstrate safety and more quickly reach the market; and (ii) a longer license from FDA when the evidence is robust to reduce the uncertainties around license renewals and convey FDA’s confidence in the substance’s safety to food manufacturers.

To achieve this objective, Congress needs to substantially revise the framework it established in 1958 and build on—and improve upon—the FCN approach it created in 1997. The changes would only be prospective in order to address the challenge of innovative food ingredients. While it is critical to address the legacy of the thousands of substances already allowed in food, a framework moving forward for new substances is an important first step.

Figure 1 describes the new process and compares it to the current approach. Congress should:

- Eliminate GRAS for new substances so FDA review and approval is needed for all innovative food ingredients. FDA review will level the playing field among competitors and build credibility and transparency with the public.
- Expand the FCN process to include innovative food ingredients and make it a true license granted by FDA. The agency would vary the license from 3–10 years, based on the quantity and quality of the toxicology and exposure evidence. Competitors would need to pursue their own license for their copycat products and must secure the approval of the company that funded any pivotal research conducted in the past three years on which they rely.
- Improve the information in the notice so it is more transparent and useful to FDA, food manufacturers, and the public. The notice would have to: (i) identify all chemically and pharmacologically related substances in the diet; (ii) identify and evaluate all relevant health, safety, or exposure studies; and (iii) indicate which studies published in the past three years are pivotal while documenting that the notifier has secured approval to reference the study from the company that funded the research.
- Enhance the transparency and credibility of the review process by: (i) ensuring FDA has sufficient resources through application fees and other funding to enable the agency to conduct a thorough review in a timely manner; (ii) allowing 180 days instead of 120 days for the FDA to complete the review since it is likely to be more complex than food contact substances; (iii) directing the FDA to post receipt of the notice and, when the decision is made, both the notice and the decision on its website; (iv) providing the public and competitors a 60-day opportunity to file objections to the notice based on safety concerns or reliance on a pivotal study published in the previous three years without approval; and (v) if an objection is filed, giving the FDA 120 days to publish a decision regarding the objection.
- Authorize the FDA to require periodic reporting by licensees so the agency can identify issues.

Reference: International Food Information Council, 2019 Food and Health Survey, May 22, 2019, <http://foodinsight.org/thanks-for-your-interest-in-the-ific-2019-food-health-survey>.

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Figure 1 – Two existing paths to market for innovative food additives and ingredients and proposed replacement for self-certified GRAS

