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United States Senate

April 26, 2016

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The Honorable Robert Califf, M.D.
Commissioner
Food and Drug Administration
10903 New Hampshire Avenue
Silver Spring, MD 20993

Dear Commissioner Califf:

I write to request information about the Food and Drug Administration's (FDA) ability to better address ingredients that are self-determined by food and beverage companies to be "generally recognized as safe," or GRAS.

The public assumes that the FDA plays a pivotal role in assessing the safety of new food ingredients by ensuring that any ingredient used in food has been thoroughly vetted and determined safe by the agency. Many would be shocked to learn that numerous ingredients are used in food and beverages without ever being evaluated by the FDA, and furthermore, in many circumstances the FDA is not even aware such chemicals are being used unless a company voluntarily discloses that information.

The Federal Food, Drug and Cosmetic Act directed the FDA to create a system of pre-market review for chemicals used in food and to periodically and systematically reassess the safety of these chemicals to address any new information that emerges. As noted in a report from the U.S. Government Accountability Office (GAO), GRAS substances are exempt from the prior approval requirement for food chemicals provided companies can, "[C]onclude there is common knowledge about the safety of the substance among experts qualified by scientific training and experience to evaluate its safety."¹ As a result, ingredient manufacturers have been permitted to secretly decide whether a new ingredient is "generally recognized as safe" and therefore able to bypass the requirement for premarket FDA review. Furthermore, because notification is voluntary, companies may include that new ingredient, which was self-determined to be safe, in their products without ever informing the FDA.

Even when the FDA is notified about a new ingredient that a company has self-determined to be GRAS and the agency's review of the substance reveals safety concerns, the substance can still end up in the food supply. For example, one company notified the FDA of their intent to use sweet lupin in several products including baked goods and candy.² However, the chemical was

¹ <http://www.gao.gov/new.items/d10246.pdf>

² <http://www.fda.gov/downloads/food/ingredientspackaginglabeling/gras/noticeinventory/ucm269154.pdf>

known to cause allergic reactions for individuals with sensitivity to peanuts. Following the FDA's expressed concern, the company withdrew their notice, halting further review by the FDA.³ Despite the GRAS notification process and review, an investigation still found sweet lupin in over 20 food products in the marketplace because other companies self-determined sweet lupin to be GRAS and chose not to voluntarily notify to the FDA.⁴

Due to this GRAS loophole, a study by the Pew Charitable Trusts estimated that 1,000 chemicals have entered the food supply without ever undergoing a safety review by FDA.⁵ Moreover, FDA typically does not know the identity of GRAS substances, the foods in which they are used, and how much they are used. This system challenges the statutory intent of FDA's assignment to protect the safety of the food supply, because there is no way to track the degree to which people have been exposed to these types of ingredients.

Given the loose structure of the voluntary notification program and the allowance for GRAS substances to be self-determined by the food industry, conflicts of interest have pervaded the system. Of the 451 GRAS notifications voluntarily made to FDA between 1997 and 2012, 22 percent were made by an employee of an additive manufacturer, 13 percent by an employee of a consulting firm to the manufacturer, and 64 percent by an expert panel selected directly or indirectly by a consulting firm and/or manufacturer.⁶ These statistics demonstrate that both the entities making GRAS determinations and those who are evaluating safety are inextricably linked by their vested interest in the perceived safety of the chemical.

Pew concluded that financial conflicts of interest are ubiquitous in GRAS determinations—even those submitted voluntarily to FDA. Existing regulations create an incentive for companies to shield the most hazardous substances from FDA's oversight, and such a process increases the possibility that GRAS determinations made in secret are less reliable than those sent to the agency, both in terms of the quality of the scientific evaluations being made and the self-interest that afflicts their conclusions about safety.

In order to better understand the current regulatory framework, its ability to reduce the number of unknown substances in food or beverages, and the extent to which any limitations to FDA's authority requires a legislative remedy, I request that you respond to the following questions by May 17, 2016.

1. There is a serious gap between public expectations of the FDA's role in reviewing ingredient safety, and the current industry-run safety determinations that are being made. Does the FDA have sufficient authority to require a special label on any foods or beverages containing ingredients that have been self-determined to be GRAS without an FDA review? If so, what could such a label look like? Could the FDA consider the use of a statement similar to the standard disclaimer on dietary supplements, but instead refers to the safety of the product's ingredient(s) for example: "The safety of some ingredients in this product has not been evaluated by the Food and Drug Administration."

³ <http://www.fda.gov/food/ingredientspackaginglabeling/gras/noticeinventory/ucm155004.htm>

⁴ <https://www.nrdc.org/sites/default/files/safety-loophole-for-chemicals-in-food-report.pdf>

⁵ http://www.pewtrusts.org/~/media/legacy/uploadedfiles/phg/content_level_pages/reports/foodadditivescapstonereportpdf.pdf

⁶ <http://www.reuters.com/article/us-food-additives-bias-idUSBRE9760Z820130807>

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2. The FDA has indicated it could develop guidance for convening expert panels as part of GRAS self-determinations to mitigate conflicts of interest.⁷ However, any such guidance would be nonbinding and completely voluntary. Does the FDA have the authority to promulgate rules that set parameters and minimize conflicts of interest for expert panels that are reviewing self-determined GRAS substances? If so, does FDA plan on promulgating such rules?

3. The GAO report encouraged the FDA to, “[D]evelop a strategy to monitor the appropriateness of companies’ GRAS determinations through random audits or some other means, including issuing guidance on how to document GRAS determinations.”⁸ Recognizing the limited information available for self-determined GRAS substances that are not voluntarily shared with the FDA, what steps has the agency planned to strengthen oversight of GRAS substances? Does the agency believe it needs additional authority to ensure the safety of GRAS substances? Please explain.

Thank you for your prompt response to these inquiries. If you have any questions, please have a member of your staff contact Elyssa Malin or Avenel Joseph at 202-224-2742.

Sincerely,



Edward J. Markey
United States Senator

⁷ <http://www.gao.gov/new.items/d10246.pdf>

⁸ *Id.*