

GENERALLY RECOGNIZED AS SAFE?: ANALYZING FLAWS IN THE FDA'S APPROACH TO GRAS ADDITIVES

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*"But that's the challenge—to change the system
more than it changes you."*¹

INTRODUCTION

As consumer demand for natural food products with fewer ingredients grows, so does curiosity and concern about the many food additives approved for use in the United States. In the broadest sense, an additive is any substance that "may reasonably be expected to result, directly or indirectly, in its becoming a component or otherwise affecting the characteristics of any food," and not all of them are worthy of concern.² While additives have long held an important place in the food supply, due largely to their preservative and other beneficial functions,³ the legitimate concerns of advocates and consumers regarding the Food and Drug Administration's (FDA) safety assessment and treatment of additives appear to be falling on deaf ears.⁴

Currently, there are more than 3,000 substances that fall under the FDA's designation of "Everything Added to Food in the United States"

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† This Article is dedicated in loving memory to Grace Beyranevand.

1. MICHAEL POLLAN, *THE OMNIVORE'S DILEMMA: A NATURAL HISTORY OF FOUR MEALS* 162 (2006).

2. 21 U.S.C. § 321(s) (2006); 21 C.F.R. § 170.3(e) (2012).

3. Thomas G. Neltner et al., *Navigating the U.S. Food Additive Regulatory Program*, 10 *COMPREHENSIVE REVIEWS IN FOOD SCI. AND FOOD SAFETY* 342, 342 (2011), available at <http://onlinelibrary.wiley.com/doi/10.1111/j.1541-4337.2011.00166.x/pdf> ("[F]ood additives are added to food to cultivate it, preserve it, process it, contain it, make it more appealing, and enhance its flavor, texture, and color; these substances serve a crucial role in meeting consumers' expectations and needs.").

4. See e.g., Michael Jacobsen, *FDA Is Not Protecting Consumers from Unsafe Food Additives*, HUFFINGTON POST (Jul. 11, 2012, 6:40 PM), http://www.huffingtonpost.com/michael-f-jacobson/food-additives-_b_1654034.html ("The bottom line is that FDA officials just don't act as if they are the protectors of health that the public expects them to be. Instead, time and time again, they have shoved problems under the carpet, perhaps hoping the problems will be forgotten or solved through voluntary action."); Barry Estabrook, *The FDA is Out to Lunch*, ON EARTH (Nov. 30, 2012), <http://www.onearth.org/article/out-to-lunch?page=1> (claiming that the FDA has been a "miserable failure"); INST. OF MEDICINE, *ENHANCING THE REGULATORY DECISION-MAKING PROCESS FOR DIRECT FOOD INGREDIENT TECHNOLOGIES 1* (1999), available at http://www.nap.edu/openbook.php?record_id=9453 ("Consumer groups are reluctant to praise FDA, and are not convinced that the public has been adequately served by the food additive petition process.").

(EAFUS),⁵ which includes all “ingredients added directly to food that FDA has either approved as food additives or listed or affirmed as GRAS [(generally recognized as safe)].”⁶ However, this list has been criticized for its failure to include more than “half of all substances allowed by FDA and less than 10% of the substances allowed by the Agency in the past 10 y[ears].”⁷ Given the amount of substances permitted for use in food, it should come as no surprise that the average person in the United States consumes approximately 150 pounds of additives per year.⁸ Many of these added substances are seemingly innocuous, such as common cooking spices.⁹ However, a great number of approved additives that are frequently used in American foods, including aspartame and partially hydrogenated oils (trans fats), raise serious health and safety concerns.¹⁰ From a safety perspective, two of the most commonly added substances—salt and sugar—present perhaps the most challenging issues for the FDA. Although both substances have been consumed for decades in safe quantities, they nevertheless present a host of health problems that the Agency appears either ill-equipped or yet unwilling to address.

The American public has been concerned about the number of additives in our food supply since the passage of the Food, Drug, and Cosmetic Act in 1938.¹¹ While it took almost two decades for Congress to enact legislation giving the FDA authority to regulate food additives, it finally passed the Food Additives Amendment of 1958.¹² Under this amendment, all additives are presumed unsafe¹³ and must receive pre-market approval by the Agency¹⁴ unless they are exempted as prior

5. *Everything Added to Food in the United States (EAFUS)*, FDA, <http://www.fda.gov/food/ingredientspackaginglabeling/ucm115326.htm> (last updated Nov. 17, 2011) [hereinafter *EAFUS*].

6. *Id.*

7. Neltner, *supra* note 3.

8. HARVEY BLATT, *AMERICA’S FOOD: WHAT YOU DON’T KNOW ABOUT WHAT YOU EAT* 199 (2008).

9. *EAFUS*, *supra* note 5.

10. *See, e.g.*, U.S. GOV’T ACCOUNTABILITY OFFICE, GAO-87-46, *FOOD AND DRUG ADMINISTRATION: FOOD ADDITIVE APPROVAL PROCESS FOLLOWED FOR ASPARTAME 2* (1987), available at <http://archive.gao.gov/d28t5/133460.pdf> (explaining that concerns about the safety of aspartame have existed since the FDA’s approval of it as an additive in 1981); Thomas J. Lueck & Kim Severson, *New York Bans Most Trans Fats in Restaurants*, N.Y. TIMES (Dec. 6, 2006), http://www.nytimes.com/2006/12/06/nyregion/06fat.html?_r=0 (explaining that, because of link to heart disease, the New York City Board of Health adopted a municipal ban “on the use of all but tiny amounts of artificial trans fats in restaurant cooking”).

11. 21 U.S.C. §§ 301–399 (2006).

12. Pub. L. No. 85-929, 72 Stat. 1784 (1958) (codified as amended at 21 U.S.C. §§ 301–399 (2006)).

13. 21 U.S.C. § 348(a).

14. *Id.* § 348(b).

approved¹⁵ or GRAS substances.¹⁶ For a substance to be considered GRAS, and thereby excluded from regulation as a food additive, it must be “recognized, among experts qualified by scientific training and experience to evaluate its safety, as having been adequately shown through scientific procedures . . . to be safe under the conditions of its intended use.”¹⁷ General recognition of safety can be established through either “scientific procedures”¹⁸ or, for those substances used prior to the passage of the Food Additives Amendment in 1958, “experience based on common use in food.”¹⁹ Practically speaking, these standards have not prevented many substances from being either affirmed as GRAS or delisted due to evolving science.

Many of the substances considered GRAS by the Agency may not be considered unsafe *per se* because they have been used for generations and are not unhealthy in the sense that they are not toxic and do not cause cancer. Yet, the statutory and regulatory provisions addressing the safety of these substances are incredibly broad. To determine a product’s safety, the Agency is required to consider whether “there is a reasonable certainty in the minds of competent scientists that the substance is not harmful under the intended conditions of use.”²⁰ There is no corresponding definition of what may be considered “harmful.” Arguably, Congress included this broad statutory language to provide the FDA with discretion to remove substances considered harmful in any manner from the marketplace. However, because these substances are largely unregulated by the Agency, they have been included in large quantities in many food products, such that they could become harmful or unsafe due to the unhealthy conditions that result from their consumption. Both sugar and salt are examples of GRAS substances that can be included in limitless quantities in any food product. However, both substances have been shown to increase risks of certain chronic diseases and other conditions when consumed in larger than recommended amounts.²¹ Despite the overwhelming evidence to demonstrate the relative

15. A list of prior approved substances is included in Food and Drugs, 21 C.F.R. §§ 181.1–181.34 (2012).

16. 21 U.S.C. § 321(s) (2006).

17. *Id.*

18. *Id.*; 21 C.F.R. § 130.70(a) (2012).

19. 21 U.S.C. § 321(s); 21 C.F.R. § 130.70(c)(1).

20. 21 C.F.R. § 170.3(i).

21. *See, e.g.*, INST. OF MEDICINE, DIETARY REFERENCE INTAKES FOR ENERGY, CARBOHYDRATE, FIBER, FAT, FATTY ACIDS, CHOLESTEROL, PROTEIN, AND AMINO ACIDS 295–321 (2005), available at http://www.nap.edu/catalog.php?record_id=10490 (explaining that overconsumption of sugar is responsible for adverse health conditions such as high cholesterol, diabetes, obesity, and cancer); INST. OF MEDICINE, STRATEGIES TO REDUCE SODIUM INTAKE IN THE UNITED STATES 39 (2010), available at http://books.nap.edu/openbook.php?record_id=12818&page=39

harm of these substances, the FDA has taken no steps toward significant regulation of either of them.

This Article argues that the FDA needs to reconsider its approach to the regulation, or perhaps more appropriately, the non-regulation of GRAS substances, using sugar by way of analysis. Further, the FDA should interpret its mandate to consider the “safety” of these substances in the broadest sense to more adequately protect consumers from the harms they pose. Part I of this Article provides a brief overview of the history of food additive regulation in the United States leading to the adoption of the Food Additives Amendment in 1958.²² Part II addresses GRAS substances and the FDA’s approach to evaluating the safety of new and already approved GRAS substances. Part III examines one of the most common GRAS substances—sugar—as an example of how the current regulatory system fails to address the harms posed by this so-called “safe” substance. Finally, Part III considers the potential solution of removing sugar from the GRAS list while recognizing the challenges of this regulatory approach.

I. A BRIEF HISTORY OF FOOD ADDITIVE REGULATION IN THE UNITED STATES

A. *The Food, Drug, and Cosmetic Act of 1938*

In response to overwhelming concern over issues of food safety and adulteration in the late 1800s—made public by muckraking journalists like Upton Sinclair²³—Congress passed the Pure Foods and Drugs Act of 1906.²⁴ The major purpose of the law was to prevent the adulteration of food, which led many representatives from agricultural states to provide

(explaining that overconsumption of salt is linked to high blood pressure, heart disease, and heart attacks); *What are Food Additives?*, INTL. FOOD ADDITIVES COUNCIL, http://www.foodadditives.org/pdf/Food_Additives_Booklet.pdf (last visited Apr. 10, 2013) (“The controlling factor in determining the safety of substances in our diet is quantity. Anything consumed in excessive amounts will be toxic, even those substances with which we are most familiar and in daily contact. There are no exceptions; anything from vitamins to water, if consumed in large enough quantities, will cause illness, and sometimes fatal effects. The age-old adage, ‘solo dosis facit venenum’ or ‘Only the dose makes the poison’ is well worth noting here.”).

22. Pub. L. No. 85-929, 72 Stat. 1784 (1958) (codified as amended at 21 U.S.C. §§ 301–399 (2006)).

23. *FDA History—Part I*, FDA, <http://www.fda.gov/AboutFDA/WhatWeDo/History/Origin/ucm054819.htm> (“In fact, the nauseating condition of the meat-packing industry that Upton Sinclair captured in *The Jungle* was the final precipitating force behind both a meat inspection law and a comprehensive food and drug law.”) (last visited Apr. 26, 2012).

24. Pure Food and Drugs Act, Pub. L. No. 59-384, 34 Stat. 768 (1906) (codified at 21 U.S.C. §§ 1–15 (1906), repealed by 21 U.S.C. § 329(a) (1938)).

tremendous support for its passage.²⁵ Under the Act, a food could be deemed adulterated if it contained an “added poisonous or other added deleterious ingredient which may render such article injurious to health.”²⁶ Prior to removing the product from the market, federal officials had the burden of demonstrating that the product actually possessed the ability to injure the consumer.²⁷ The language of the Act did not amount to an outright ban on these ingredients and specifically included language that permitted producers and manufacturers to include “poisonous or other added deleterious ingredient[s]”²⁸ to their products so long as they were not injurious to the public health.²⁹

Despite the tremendous success of the 1906 Act, it left the Agency with little enforcement authority to address emerging risks to the food supply, which led to passage of the Federal Food, Drug, and Cosmetic Act of 1938 (FFDCA).³⁰ The 1938 version of the law provided the Agency with greater enforcement authority and also expressly permitted the Agency to set standards of identity and quality for food products.³¹ The law created enforceable, legal standards the Agency could use in misbranding and adulteration cases.³² While these changes represented substantial improvements, the amended version of the law failed to develop a modified system to address potential adulterants in food and retained the same after-market enforcement mechanisms.³³ However, section 406 of the 1938 Act required the Agency to set tolerance limits as necessary for the “protection of public health” for “[a]ny poisonous or deleterious substance added to any

25. John P. Swann, *FDA's Origin*, FDA, <http://www.fda.gov/AboutFDA/WhatWeDo/History/Origin/ucm124403.htm> (last updated June 18, 2009) (adapted from GEORGE KURIAN, *A HISTORICAL GUIDE TO THE U.S. GOVERNMENT* (1998)). Harvey Washington Wiley, the architect behind the 1906 Act to prohibit adulteration and misbranding of food and drugs, also unified support from “state chemists and food and drug inspectors, the General Federation of Women’s Clubs, and national associations of physicians and pharmacists.” KURIAN, *supra* note 25, at 249.

26. Pure Food and Drugs Act § 7, Pub. L. No. 59-384, 34 Stat. 768 (1906).

27. *United States v. Lexington Mill & Elevator Co.*, 232 U.S. 399, 411 (1914) (“If it cannot by any possibility, when the facts are reasonably considered, injure the health of any consumer, such flour, though having a small addition of poisonous or deleterious ingredients, may not be condemned under the act.”).

28. *Id.* at 410.

29. *Id.* at 410–11.

30. 21 U.S.C. §§ 301–399 (2006).

31. See *Developments in the Law: The Federal, Food, Drug, and Cosmetic Act*, 67 HARV. L. REV. 632, 636 (1954) (“[S]tates might place reasonable restrictions on food and drugs produced or sold within their borders, even though these restrictions affected interstate commerce, provided that they were not in conflict with federal laws.”).

32. See *id.* (“[W]here Congress has provided a system of thorough regulation of a particular commodity, such as the labeling of coal-tar hair dyes, it . . . [was] . . . held that federal law preempted the field.”).

33. Lars Noah & Richard A. Merrill, *Starting from Scratch?: Reinventing the Food Additive Approval Process*, 78 B.U. L. REV. 329, 331 (1998).

food” that is unavoidable or required to be added to food.³⁴ In a somewhat conflicting section, the language of section 402(a)(2) appeared to suggest that if a substance contained “any added poisonous or added deleterious substance” found to exceed the tolerance limits set under section 406, then the Agency could institute enforcement action and declare the food adulterated, regardless of whether the food might be injurious to health.³⁵ Consequently, even though the Agency retained the burden of demonstrating that the “poisonous or deleterious substance”³⁶ might render it “injurious to health,”³⁷ section 402(a) appeared to lower the FDA’s burden when taking enforcement action. So long as the Agency could demonstrate the substance exceeded the tolerance limit set under section 406, the FDA “would have difficulty allowing use [of the substance] at lower levels” that might be considered safe based on the language in section 402(a)(2).³⁸ Ultimately, the FFDCCA left the FDA in the precarious position of attempting to implement and administer a statute with an inconsistent and difficult set of safety standards for food additives while these potentially unsafe substances were simultaneously being marketed to the public.³⁹

B. *The Food Additives Amendment of 1958*

In the 1940s and 1950s, following the passage of the FFDCCA, changes in food technology, coupled with population migration from farms to cities, led to the development and production of new food additives, such as preservatives.⁴⁰ To address these newly emerging and potentially harmful substances, on June 20, 1950, the House of Representatives created a committee chaired by Representative James Delaney of New York to

34. 21 U.S.C. § 346 (2006).

35. *Id.* § 342(a)(2).

36. *Id.*

37. *Id.*

38. Noah & Merrill, *supra* note 33, at 335.

39. Kenneth E. Mulford, *The Food Additives Amendment of 1958*, 17 FOOD DRUG COSM. L.J. 292, 293 (1962) (“Sections 402 and 406 of the 1938 Act provided that a food shall be deemed to be adulterated if it contains any added poisonous or deleterious substance unless the added substance was required, could not be avoided by good manufacturing practice and was permitted by regulation under Section 406 limiting the quantity used to a safe amount. Because it was practically impossible to establish new added substance to be ‘required’ or ‘unavoidable’ and further by reason of the fact that Section 406 involved cumbersome hearing procedures, few, if any, regulations were issued under Section 406.”).

40. NEIL D. FORTIN, FOOD REGULATION: LAW, SCIENCE, POLICY, AND PRACTICE 261 (2009).

investigate chemicals in food.⁴¹ The hearings of the Delaney Committee ultimately prompted Congress to pass the Food Additives Amendment of 1958.⁴²

During the hearings, committee members were presented with conflicting testimony that was often highly technical in nature, leaving the Agency confused about the appropriate safety standards for additives.⁴³ The Agency responded to this uncertainty by employing a very strict interpretation of the “added poisonous or added deleterious” substances provision in section 402 of the FFDCA, which became known as the “absolute safety” or “poisonous per se doctrine.”⁴⁴ This approach discouraged advances in food technology even though the newly developed substances were effectively safe for human consumption and beneficial for food production.⁴⁵ However, food safety advocates argue that the approach taken by the FDA at this juncture, pending the approval of food additive legislation, was appropriate given the broad safety mandate under the FFDCA.

The committee filed its report on June 30, 1952 and advised amending the FFDCA to require that chemicals used in foods be subject to the same safety standards as those required for new drugs.⁴⁶ The Delaney Committee investigations revealed that only about half of the 840 chemicals used in the food supply during the 1950s were considered safe.⁴⁷ Ultimately, the report concluded that existing legislation failed to provide adequate safety assurances for food additives in the same manner as it did for new drugs, which required premarket approval by the Agency.⁴⁸ The Agency’s inability to regulate additives prior to their market entry presented problems for industry as well, due to the restrictive wording of section 406. Section 406 prohibited the use of chemicals found toxic at high levels, even in concentrations that were safe at low levels, unless the chemical was “required” or unavoidable.⁴⁹ While this issue lacked the same degree of urgency as others involving products regulated by the FDA, by 1958,

41. *Guide to The Records of The U.S. House of Representatives at The National Archives 1789–1989*, NATIONAL ARCHIVES, <http://www.archives.gov/legislative/guide/house/chapter-22-select-food-and-cosmetics.html> (last visited Apr. 10, 2013).

42. Pub. L. No. 85-929, 72 Stat. 1784 (1958) (codified, as amended at 21 U.S.C. §§ 301–399 (2006)).

43. Mulford, *supra* note 39, at 294.

44. *Id.*

45. *Id.*

46. Frederk H. Degnan, *Rethinking the Applicability and Usefulness of the GRAS Concept*, 46 FOOD DRUG COSM. L.J. 553, 554 (1991) (citing H.R. REP. NO. 82-2356 (1952)).

47. *Id.* (citing H.R. REP. NO. 82-2356 (1952)).

48. *Id.*

49. *Id.*; 21 U.S.C. § 342(a)(2) (2006).

industry, government, scientists, and Congress agreed that an amendment was necessary to specifically address the regulation of food additives.⁵⁰

Prior to the passage of the Food Additives Amendment (FAA) in 1958, Congress passed an amendment to the FFDCFA in 1954. This amendment required the setting of tolerances for any pesticide chemicals that were intended for use on raw agricultural commodities and created a system for premarket approval for pesticide residues on food.⁵¹ Four years later, after taking into account the many perspectives of industry, advocates, and the FDA, among others, Congress passed the FAA, stating that the purpose of the amendment was “to prohibit the use in food of additives which have not been adequately tested to establish their safety.”⁵² Specifically, the amendment was passed “in response to public concern about the increased use of chemicals in foods and food processing and with the support of the food industry.”⁵³

Under the amendment, food additives were defined broadly to include “any substance the intended use of which results or may reasonably be expected to result, directly or indirectly, in its becoming a component or otherwise affecting the characteristics of any food,” including any substances used in packaging, transport, processing, preparation, and other processes that might either affect or migrate into food.⁵⁴ Specifically excluded from the definition were substances that the Agency considered “prior sanction[ed]”⁵⁵ or deemed “generally recognized as safe.”⁵⁶ Prior to passage of the FAA, the House subcommittee members who drafted the legislation agreed that the bill could not include a “blanket grandfather clause” that exempted all substances currently used in foods, as this would

50. INST. OF MEDICINE, *supra* note 4, at 17.

51. *Id.* (citing Pub. L. No. 83-518, § 3 (408(a)), 68 Stat. 511 (1954)) (codified at 21 U.S.C. § 346a(a) (1994)), repealed and replaced by the Food Quality Protection Act of 1996, Pub. L. No. 104-170, § 405, 110 Stat. 1514).

52. Pub. L. No. 85-929, 72 Stat. 1784 (1958) (codified at 21 U.S.C. § 348 (2006)).

53. Substances Generally Recognized as Safe, 62 Fed. Reg. 18938, 18939 (Apr. 17, 1997).

54. 21 U.S.C. § 321(s) (2006).

55. 21 C.F.R. § 181.1 (2012).

56. 21 U.S.C. § 321(s) (“[I]f such substance is not generally recognized, among experts qualified by scientific training and experience to evaluate its safety, as having been adequately shown through scientific procedures (or, in the case of a substance used in food prior to January 1, 1958, through either scientific procedures or experience based on common use in food) to be safe under the conditions of its intended use; except that such term does not include—(1) a pesticide chemical residue in or on a raw agricultural commodity or processed food; or (2) a pesticide chemical; or (3) a color additive; or (4) any substance used in accordance with a sanction or approval granted prior to September 6, 1958, pursuant to this chapter, the Poultry Products Inspection Act [21 U.S.C. 451 et seq.] or the Meat Inspection Act of March 4, 1907, as amended and extended [21 U.S.C. 601 et seq.]; (5) a new animal drug; or (6) an ingredient described in paragraph (ff) in, or intended for use in, a dietary supplement.”).

defeat the food safety purposes of the legislation.⁵⁷ In other words, allowing the grandfathering of all substances that were in current use at the time of passage would not achieve the purpose of ensuring the safety of all additives used in foods. Yet, the members of the subcommittee also recognized that from a practical perspective, certain substances had been used for so long in foods that—despite not having been scientifically evaluated—their history of use arguably established their safety, thereby accomplishing the purposes of the Act without hampering innovation by consuming unnecessary agency resources to evaluate them.⁵⁸

Congress carved out the exception for prior sanctioned substances, which were those that either the FDA or the United States Department of Agriculture (USDA) explicitly approved for use in food prior to September 6, 1958, to grandfather in certain substances that the agencies had already formally deemed safe.⁵⁹ Any prior sanctioned substance was required to be the subject of a regulation specifying “whatever limitation(s) or condition(s) may be necessary for the safe use of the ingredient.”⁶⁰ Perhaps the most recognized examples of prior sanctioned substances are sodium nitrate and potassium nitrate, which are used in the curing of red meat and poultry.⁶¹ These substances went through testing and evaluation prior to passage of the FAA and had been formally approved for use in foods.

Unlike prior sanctioned substances, GRAS substances were not explicitly sanctioned for use prior to September 6, 1958. However, many of these substances were commonly used in food for decades without any known health hazards. Despite the differences between the two exemptions, the purpose was the same. The FDA needed mechanisms by which it could address substances that were either proven to be or commonly recognized as safe without having to perform resource-intensive testing and extensive evaluation. The GRAS exemption was intended to provide additional flexibility so the Agency could quickly and efficiently approve additives that were not sanctioned prior but were “generally recognized” to be safe under their intended conditions of use.⁶²

57. Degan, *supra* note 46, at 556 (citing *Chemical Additives in Food: Hearings on H.R. 4475 Before the Subcomm. On Health and Sci. of the House Comm. On Interstate and Foreign Commerce*, 84th Cong., 2d Sess. 28 (1956) (statement of Rep. Delaney)).

58. *Id.*

59. 21 C.F.R. § 181.5(a).

60. *Id.* § 181.5(c).

61. *Id.* § 181.33.

62. Noah & Merrill, *supra* note 33, at 350–51 & nn.16, 91, 92; Charles Wesley Dunn, *Initial Comments—for Food Law Institute*, 13 FOOD DRUG COSM. L.J. 743, 744 (1958) (“Hence it may be said that the amendment will deal mostly with new additives and more occasionally with old ones.”).

While recognizing the need to provide a streamlined process for the Agency, some were troubled by the fact that the phrase “generally recognized” lacked specificity. As Congressman Dies of Texas stated, “It is very, very vague and indefinite. I do not see how anyone could tell whether you came within the law or not.”⁶³ The vagueness of the language, however, did not prevent its inclusion as part of the FAA since most of the witnesses in the hearings advocated for it nonetheless.⁶⁴ The FDA favored the imprecise standard because it allowed the Agency to exclude many chemicals that were already being used, as well as take action against substances it considered unsafe.⁶⁵ In addition, industry supported the “general recognition” language since there had been no discussion during the hearings indicating that the FDA was the only party permitted to determine whether a substance fell within the exemption.⁶⁶ Finally, the language did not prove problematic to Congress, which had many opportunities to draft a less ambiguous standard or at least provide a definition for the phrase.⁶⁷ The exemption for GRAS substances allowed the Agency to determine their status based on “the current state of scientific knowledge and expert opinion,” a standard that provided a necessary degree of discretion.⁶⁸

All other additives not exempted are presumed unsafe unless proven otherwise and require premarket approval by the Agency, which can be obtained only upon a showing that the additive will be safe under the proposed conditions of use.⁶⁹ While this Article is meant to address GRAS substances, a brief overview of the review process for food additives is useful. The procedure for premarket review commences when any person seeking the FDA’s approval of a new additive files a petition.⁷⁰ The petition must include the identity of the additive, the proposed use, the intended technical effect, the method of analysis in food, and full reports of all safety studies.⁷¹ In addition, upon request of the Agency, the petitioner must describe the “methods used in, and the facilities and controls used for, the

63. Roger D. Middlekauff, *Food Safety Review—New Concepts for GRAS*, 30 FOOD DRUG COSM. L.J. 288, 289 (1975) (citing *Hearings Before a Subcommittee of the Committee on Interstate and Foreign Commerce on H.R. 4475 et al.*, 84th Cong., 2d Sess. 152 (1956)).

64. Degnan, *supra* note 46, at 559.

65. *Id.*

66. *Id.* at 559–60 (“On the contrary, industry and agency witnesses alike assumed that a manufacturer had the opportunity to make its own GRAS determinations.”).

67. *Id.* at 560.

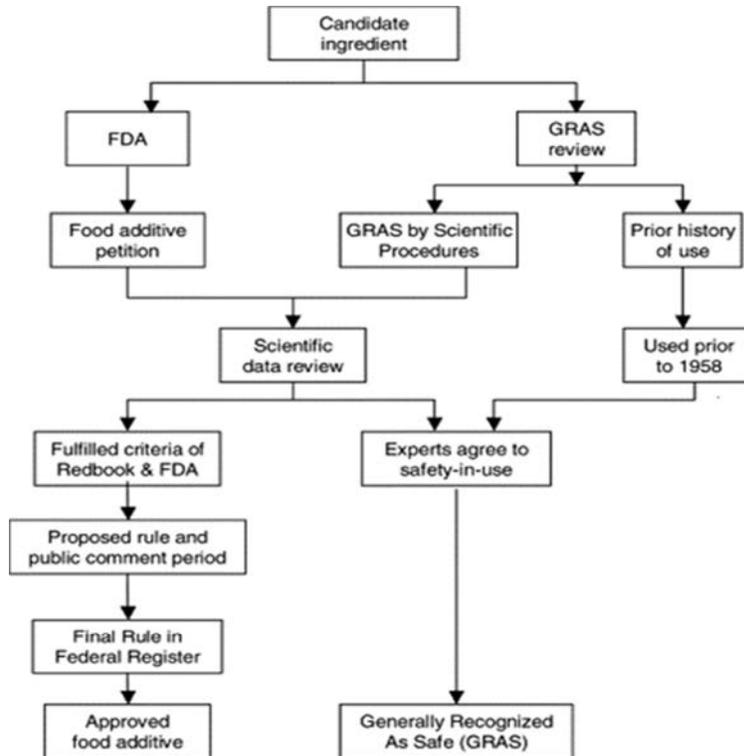
68. *Id.*

69. 21 U.S.C. § 348(b) (2006).

70. *Id.* § 348(b).

71. *Id.* § 348(b)(2).

production of such additive,”⁷² as well as samples of the additive.⁷³ If the Agency determines that the petitioner has adequately established the additive’s safety, the Agency will draft a regulation prescribing the specific manner in which the additive may be used.⁷⁴ The following chart explains the difference in procedure for food additives and GRAS substances.⁷⁵



Ultimately, the FAA was intended to accomplish two functions: (1) to ensure the safety of food additives and added substances for consumption; and (2) to aid in the approval of safe food additives.⁷⁶ However, some

72. *Id.* § 348(b)(3).

73. *Id.* § 348(b)(4).

74. *Id.* § 348(b).

75. George A Burdock & Ioana G Carabin, *Generally Recognized as Safe (GRAS): History and Description*, 150 TOXICOLOGY LETTERS, Jul. 22, 2003, at 6.

76. Stuart M. Pape, *Food Industry Initiatives to Improve the FDA’s Food Ingredient Review Processes*, 51 FOOD & DRUG L.J. 413, 416 (1996) (“[T]he scope of review and the resources and time allocated to review must be commensurate with the nature of the substance under review and the potential safety issues that it presents.”).

suggest that the Agency has failed to accomplish either goal since passage of the amendment. In part, this failure stems from the fact that the FDA lacks the funding to adequately and fully address substances added to food. However, the Agency also lacks the appropriate procedures to efficiently address petitions for new food additives.⁷⁷ Because the amendment was meant as a protective measure, any questions regarding safety or scientific evidence should be resolved in favor of that policy.⁷⁸ While the Agency may find it difficult to address new additive petitions in a timely manner, the issue of added substances in the food supply that have the potential to cause harm to consumers deserves far more attention and resources.

II. GRAS SUBSTANCES AND THE STANDARD OF SAFETY

A. History of the GRAS Exemption

Specifically exempt from the definition of “food additive” under section 321(s) of the FFDCFA, GRAS substances are defined as “generally recognized, among experts qualified by scientific training and experience to evaluate [their] safety . . . to be safe under the conditions of [their] intended use.”⁷⁹ Because these substances are excluded from the definition of “food additive,” they are also exempted from the statutory requirements that apply to new food additive petitions.⁸⁰ Largely, the GRAS exemption applies to what were commonly considered “safe additives” used before passage of the FAA—for example, salt, sugar, and other substances that had been used in foods without evidence of harm.⁸¹ Following passage of the FAA, the FDA created a “list of food substances that, when used for the purposes indicated and in accordance with current good manufacturing

77. *Id.*

78. Dunn, *supra* note 62.

79. 21 U.S.C. § 321(s) (2006).

80. *Id.*

81. *See* Substances Generally Recognized as Safe, 62 Fed. Reg. 18,938, 18,939 (Apr. 17, 1997) (“It is on the basis of the GRAS exemption to the food additive definition that many substances (such as vinegar, vegetable oil, baking powder, and many salts, spices, flavors, gums, and preservatives) are lawfully marketed today without a food additive regulation.”); 21 C.F.R. § 182.1 (2012) (as amended at 21 C.F.R. §§ 152, 182) (“It is impracticable to list all substances that are generally recognized as safe for their intended use. However, by way of illustration, the Commissioner regards such common food ingredients as salt, pepper, sugar, vinegar, baking powder, and monosodium glutamate as safe for their intended use.”); *California Cannery & Growers Ass’n v. United States*, 9 Cl. Ct. 774, 776 (Cl. Ct. 1986) (“By exempting GRAS substances from the definition of food additive, Congress allowed the marketing of GRAS substances without the pre-market safety testing and prior government approval required for food additives. This established that ingredients which had long been used in foods without apparent harmful effects, such as salt, sugar and other familiar substances, would not have to undergo extensive new testing to be used in food products.”).

practice, are GRAS.”⁸² Once listed, a GRAS substance could effectively be used without restriction subject only to “good manufacturing practices,” which address the quantity of the substance used in and its effects on the food, as well as the grade and quality.⁸³

Following its creation, the FDA updated the original GRAS list over the years. While the list was relatively broad, many substances that manufacturers considered GRAS did not make their way onto the list.⁸⁴ As discussed, the FAA did not require pre-market approval of GRAS substances. Yet, as a matter of practice, manufacturers often sought informal review by the Agency in the form of an “opinion letter” before placing their products into the market.⁸⁵ These opinion letters were not binding on the Agency, and ultimately the process was formally revoked in 1970 in favor of a more formal set of procedures.⁸⁶ The opinion letter process was also voluntary, meaning that the FDA learned of a manufacturer’s GRAS determination only if the manufacturer notified the Agency.⁸⁷ Soon thereafter, the Agency published notice in the Federal Register to announce the FDA’s comprehensive review of the individual substances included on the GRAS list.⁸⁸ This announcement came in direct response to President Nixon’s directive to the Agency to reconsider the safety of GRAS substances after a group of cyclamate salts had been found to cause bladder tumors in rodents.⁸⁹

82. Substances Generally Recognized as Safe, 62 Fed. Reg. at 18,939 (“This list was incorporated into the Agency’s regulations as §121.101(d) (now parts 182 and 582 (21 CFR parts 182 and 582)) (24 FR 9368, November 20, 1959.”).

83. *Id.*, see also 21 C.F.R. § 582.1 (2012) (“[G]ood manufacturing or feeding practice shall be defined to include the following restrictions: (1) The quantity of a substance added to food does not exceed the amount reasonably required to accomplish its intended physical, nutritional, or other technical effect in food; and (2) The quantity of a substance that becomes a component of food as a result of its use in the manufacturing, processing, or packaging of food, and which is not intended to accomplish any physical or other technical effect in the food itself, shall be reduced to the extent reasonably possible. (3) The substance is of appropriate grade and is prepared and handled as a food ingredient. Upon request the Commissioner will offer an opinion, based on specifications and intended use, as to whether or not a particular grade or lot of the substance is of suitable purity for use in food and would generally be regarded as safe for the purpose intended, by experts qualified to evaluate its safety.”).

84. Substances Generally Recognized as Safe, 62 Fed. Reg. at 18,939.

85. Food Additive Status Opinion Letters: Statement of Policy, 35 Fed. Reg. 5810, 5810 (Apr. 9, 1970).

86. *Id.* at 5810–11; Substances Generally Recognized as Safe, 62 Fed. Reg. at 18,939.

87. U.S. GOV’T ACCOUNTABILITY OFFICE, GAO-10-246, FOOD SAFETY: THE FDA SHOULD STRENGTHEN ITS OVERSIGHT OF FOOD INGREDIENTS DETERMINED TO BE GENERALLY RECOGNIZED AS SAFE (GRAS) 5 (2010), available at <http://www.gao.gov/products/GAO-10-246>.

88. *Id.*

89. Substances Generally Recognized as Safe, 62 Fed. Reg. at 18,939. The FDA’s decision to remove cyclamates from the GRAS list was not without controversy, as researchers were unable to replicate the findings of the original study. The FDA later determined that cyclamate was non-carcinogenic and asked the National Academy of Sciences to re-evaluate the scientific information

The stated purpose of the Agency's comprehensive study was to evaluate each substance on the GRAS list using what were then "contemporary standards" and "to issue each item in a new (i.e., affirmed) GRAS list, a food additive regulation, or in an interim food additive regulation pending completion of additional [toxicity] studies."⁹⁰ Many in industry hoped the comprehensive review would answer the remaining questions regarding the convoluted GRAS process.⁹¹ The review generated a tremendous amount of information through the use of surveys, which encouraged the National Academy of Sciences to develop data providing an estimate of the individual daily intake of GRAS substances.⁹² To conduct this review, the Agency worked with the Federation of American Societies for Experimental Biology, an independent scientific organization, and asked it to recommend restrictions for any of the reviewed substances.⁹³

From 1972 to 1982, the committee reviewed 422 substances that were directly added to food, finding issues with thirty five of those.⁹⁴ For thirty of those substances, the committee anticipated revocation of GRAS status unless the FDA was provided with additional evidence demonstrating the substance's safety.⁹⁵ "For the remaining [five] substances," the committee determined the substances were not harmful at the current levels of consumption, but did question the safety of the substances.⁹⁶ One of these substances was sodium chloride, or salt, for which the committee suggested that the FDA draft guidelines to limit its use in processed foods.⁹⁷ As of 2009, the FDA had affirmed the GRAS status of seventeen of these substances and issued regulations to that effect, while taking no action on the remaining eighteen substances.⁹⁸ After engaging in its comprehensive review and requesting assistance and guidance from an independent scientific organization, the Agency essentially ignored all of the recommendations without explaining its reasons for doing so.⁹⁹

regarding the substance's cancer causing properties. While the National Academy of Sciences did find that cyclamate likely does not cause cancer on its own, it "may trigger the disease earlier or increase the number of tumors when used in combination with known carcinogens." Marlene Cimons, *Cyclamate Fails to Win Clearance in Cancer Study*, L.A. TIMES, June 11, 1985, http://articles.latimes.com/1985-06-11/news/mn-10329_1_bladder-cancer.

90. Substances Generally Recognized as Safe, 62 Fed. Reg. at 18,939.

91. Middlekauff, *supra* note 63, at 293.

92. *Id.*

93. U.S. GOV'T ACCOUNTABILITY OFFICE, *supra* note 87, at 20.

94. *Id.*

95. *Id.* at 20–21.

96. *Id.* at 21.

97. *Id.*

98. *Id.*

99. *Id.*

In addition, the Agency's 1970 notice proposed revising the existing regulations regarding safety to state that "[s]afe' must be understood to connote that the Food and Drug Administration, after reviewing all available evidence, can conclude there is no significant risk of harm from using the substance as intended."¹⁰⁰ For substances that the FDA had not included on the GRAS list, GRAS affirmation could be sought by submitting the relevant data and information to the Agency.¹⁰¹ With regard to substances whose status might change as a result of the promulgation of new regulations, the FDA made clear that, although new testing establishing harm could not be considered definitive proof of potential harm, it would establish that the substance should be removed from the GRAS list.¹⁰²

Following the Agency's 1970 notice, the FDA revised its regulations "to establish the general administrative plan for classifying substances as GRAS,"¹⁰³ which some argue demonstrated the Agency's determination that certain GRAS substances were "more GRAS than others."¹⁰⁴ Specifically, the Agency singled out a small group of substances that would be considered GRAS without any further evidence or studies.¹⁰⁵ These substances were of "natural biological origin that [have] been widely consumed for [their] nutrient properties in the United States prior to January 1, 1958, without detrimental effect when used under reasonably anticipated patterns of consumption."¹⁰⁶ This exemption also included substances that fell under this category but had been modified through conventional processing techniques prior to January 1, 1958.¹⁰⁷ For all other GRAS substances, the Agency sought advice from experts regarding their safety through notice and comment in the Federal Register.¹⁰⁸

100. Eligibility of Substances for Classification as Generally Recognized as Safe In Food, 35 Fed. Reg. 18,623, 18,624 (Dec. 8, 1970) (codified at 21 CFR § 121.3).

101. *Id.*

102. *Id.* ("Newly reported information must be carefully evaluated along with the total available knowledge to determine whether or not there has been significant increase in the risk of harm from using the substance as intended. No status change will be made until the Food and Drug Administration has had an opportunity to evaluate the new findings.")

103. Eligibility of Substances for Classification as Generally Recognized as Safe In Food, 36 Fed. Reg. 12,093, 12,093 (June 25, 1971) (codified at 21 CFR § 121.3).

104. Middlekauff, *supra* note 63, at 290.

105. *Id.*; Eligibility of Substances for Classification as Generally Recognized as Safe In Food, 36 Fed. Reg. at 12,093 ("The GRAS status of *particular* substances will not be changed by the proposed revision of § 121.3.") (emphasis added).

106. Eligibility of Substances for Classification as Generally Recognized as Safe In Food, 36 Fed. Reg. at 12,093; 21 C.F.R. § 121.3 (as amended at 21 C.F.R. § 170.30).

107. Eligibility of Substances for Classification as Generally Recognized as Safe In Food, 36 Fed. Reg. at 12,093.

108. *Id.*

Because the Agency's review did not encompass every GRAS substance—namely, those that had been marketed after a manufacturer's independent determination of GRAS status—the FDA developed a process by which individuals could petition the Agency to consider the GRAS status of substances not included in its review.¹⁰⁹ The Agency's decisions regarding these issues were highly criticized, as they provided no definition or guidance regarding what specific factors should go into the consideration of general recognition of safety, except to say that certain substances would be excluded and no longer considered GRAS.¹¹⁰ According to critics, the Agency was making it incredibly difficult for new substances to receive GRAS affirmation, while simultaneously making it increasingly challenging for those already affirmed by the Agency to remain on the list.¹¹¹ In other words, it appeared that the FDA determined that the only substances that would be affirmed as GRAS—excluding those of “natural biological origin” that were consumed for their nutritional properties prior to January 1, 1958—were the substances that had not yet been affirmed as GRAS, but would be subsequently listed.¹¹² Any substances that did not fall into this category, regardless of their prior GRAS status, would be removed from the list. Because neither the FFDCRA nor the FAA explicitly granted the FDA the authority to make final GRAS determinations, many saw this decision as within the province of the courts, which was also problematic given the degree of uncertainty.¹¹³ Unlike the provisions for new food additive petitions—where the Agency clearly had the final say regarding the petition's status—in the realm of GRAS substances, it was unclear whether the Agency's decisions in this regard were final and authoritative.¹¹⁴

Finally, in 1974, the Agency attempted to specify the criteria for GRAS status, explain the difference between GRAS status and food additive petitions, and provide some guidance regarding the procedures used in the review of GRAS substances.¹¹⁵ For a substance to be considered GRAS,

109. Substances Generally Recognized as Safe, 62 Fed. Reg. 18938, 18940 (Apr. 1997).

110. Alan H. Kaplan, *Safety and Gras Status or Has the GRAS List Gone to Pot?*, 27 FOOD DRUG COSM. L.J. 98, 99 (1972).

111. *Id.*

112. *Id.* at 102.

113. *Id.* at 101; *California Cannery & Growers Ass'n v. United States*, 9 Cl. Ct. 774, 776 (Cl. Ct. 1986) (“The new legislation required the courts, rather than the FDA, to determine if a substance is GRAS.”).

114. Under 21 U.S.C. § 348(b) (2006), the Secretary of the FDA is required, upon receipt of a petition for the approval of a new food additive petition, to either issue a regulation approving the additive and specifying the conditions of use, or issue an order denying the petition. No similar provision exists for GRAS substances.

115. General Recognition of Safety and Prior Sanction for Food Ingredients, 39 Fed. Reg. 34,194, 34,194 (Sept. 23, 1974) (codified at 21 CFR § 121).

“general recognition of safety” must be demonstrated in one of two ways.¹¹⁶ First, safety can be established through scientific procedures.¹¹⁷ Second, safety can be established through experience based on common use in food prior to January 1, 1958.¹¹⁸ Prior to the FDA’s issuance of its 1974 notice in the Federal Register, there was a fair amount of confusion over what the Agency intended to require when affirming a GRAS substance through scientific procedures. In 1974, the Agency clearly expressed its interpretation of the Act, stating that “Congress intended the phrase ‘scientific procedures’ as used in section 201(s) of the act to have the same dimensions as the full reports of investigations required to prove the safety of a food additive under section 409 of the act.”¹¹⁹

In other words, the FDA determined that “scientific procedures” would “require the same quantity and quality of scientific evidence as is required to obtain approval of a food additive regulation for the ingredient.”¹²⁰ The Agency based this interpretation on two Supreme Court decisions—*Weinberger v. Hynson, Westcott & Dunning, Inc.* and *Weinberger v. Bentex Pharmaceuticals, Inc.*—that addressed GRAS affirmation in the context of drugs and required the same standard of scientific evidence for GRAS drugs as for new drug applications.¹²¹ Comparing the provisions addressing drugs to those addressing food in the Act, the Agency determined that Congress must have also intended for the same degree of scientific evidence to apply for GRAS substances as for new additive petitions.¹²² With this notice, the FDA completely changed the landscape for affirmation of GRAS substances. The issue was no longer simply whether experts recognized the GRAS substance as safe; rather, the issue was now whether the substance met the criteria required for a food additive.¹²³

The FDA also stated that the scientific procedures relied upon “shall ordinarily be based upon published studies which may be corroborated by unpublished studies and other data and information.”¹²⁴ This decision was also based on the *Bentex* case, which held that “whether a particular drug is a ‘new drug’ depends in part on the expert knowledge and experience of

116. 21 C.F.R. § 170.30(a) (2012).

117. *Id.*; 21 U.S.C. § 321(s) (2006).

118. 21 U.S.C. § 321(s); 21 C.F.R. § 170.30(a).

119. General Recognition of Safety and Prior Sanction for Food Ingredients, 39 Fed. Reg. at 34194.

120. 21 U.S.C. § 321(s); 21 C.F.R. § 170.30(b).

121. General Recognition of Safety and Prior Sanction for Food Ingredients, 39 Fed. Reg. at 34194 (citing *Weinberger v. Hynson, Westcott & Dunning, Inc.*, 412 U.S. 609 (1973); *Weinberger v. Benetex Pharm., Inc.*, 412 U.S. 645 (1973)).

122. Middlekauff, *supra* note 63 at 294.

123. *Id.*

124. 21 C.F.R. § 170.30(b).

scientists based on controlled clinical experimentation and backed by 'substantial support in scientific literature.'"¹²⁵ Equating the legal issues involving drugs to the issues regarding GRAS substances and food additives, the Agency determined that the scientific evidence required for GRAS status must be "widely disseminated" such that it becomes "common knowledge among such scientists."¹²⁶ Critics of this provision noted that the evidentiary requirements were above and beyond what the statute seemed to require.¹²⁷ Moreover, they claimed that requiring the evidence be not only published, but also common knowledge, was impractical because it meant scientists had to take the extra step of considering and absorbing the literature.¹²⁸

The Agency noted that, unlike applications for new drugs, substances could be GRAS based on common use in food so long as it was marketed prior to January 1, 1958.¹²⁹ For these substances, there was no requirement that scientific procedures establish the safety for GRAS status.¹³⁰ The FDA defined "[c]ommon use in food" as requiring a substantial history of consumption of a substance by a significant number of consumers in the United States.¹³¹ Arguably, the Agency developed a rigid standard for GRAS substances marketed and developed after 1958 that did not exist for those marketed prior to 1958. While justifying the need to "grandfather" in certain substances that most people would consider safe based on their long history of use as reasonable, the Agency created a seemingly objective standard for some substances, which have ill effects in the quantities in which they are now being consumed. Consequently, even though the same requirements for a food additive petition need not necessarily be included for GRAS affirmation, when attempting to establish "general recognition of safety" through scientific procedures, it is clear that the same requirements

125. General Recognition of Safety and Prior Sanction for Food Ingredients, 39 Fed. Reg. at 34,194 (quoting *Bentex*, 412 U.S. at 652)).

126. *Id.*

127. *Id.* ("Accordingly, there will be at least some gap between the gathering of the scientific knowledge necessary to provide the toxicological underpinning for general recognition of safety and the dissemination to and assimilation by the scientific community of this material that *is* necessary for general recognition of safety to exist."); Degnan, *supra* note 46, at 571 ("the Agency's change in approach to the regulation of GRAS substances was dramatic . . . [The regulations'] effect was to further limit the applicability of the GRAS exemption and to further formalize the GRAS affirmation process.").

128. Middlekauff, *supra* note 63, at 294.

129. *Id.*

130. *Id.*

131. *Id.* at 294-95. In addition, the FDA required "any expert, who considers whether or not a substance is safe, had to consider the same quantity and quality of scientific evidence as is required for proof of safety," thereby dramatically changing "the ground rules for determination of safety of GRAS substances." *Id.*

should be considered.¹³² To address substances that might be considered safe now—but might not be later upon new information—the Agency developed a de-GRAS provision, which allowed for the removal of GRAS status upon reevaluation.¹³³ These regulations constituted the FDA’s final set of regulations on the matter, and have remained relatively unchanged.¹³⁴

In 1997, the FDA proposed a GRAS notification program to replace the petition process developed in 1972.¹³⁵ The Agency’s rationale for the proposed change was based on its belief that the petition process was simply too onerous and, despite being voluntary, it worked to discourage individuals from requesting the FDA’s affirmation of their self-determined GRAS status.¹³⁶ Specifically, the petition process formerly used by the Agency required notice and comment rulemaking—meaning that the Agency was required to publish notice in the Federal Register; review and respond to public comments on the petition; evaluate the information submitted with the petition, as well as any data received through the public comment process to determine whether the evidence establishes the substance’s GRAS status; draft a detailed response to the petition explaining the rationale behind the Agency’s determination that the substance is GRAS; and publish notice of that determination in the Federal Register.¹³⁷ Ironically, the burdens cited by the Agency that would prevent an individual from filing a petition fell largely on the Agency. The data and information submitted with the petition needed to be collected for an independent determination of GRAS status regardless of whether the information was submitted to the FDA.¹³⁸ Put simply, the only part of this “resource-intensive process” that placed a burden on industry was the actual filing of the petition.¹³⁹

For a more streamlined process, and to receive more information about independent GRAS determinations from industry, the FDA proposed a notification program whereby a person simply notifies the Agency of its GRAS determination.¹⁴⁰ Like the petition process, the notification

132. 21 C.F.R. § 171.1(c) (2012).

133. *General Recognition of Safety and Prior Sanction for Food Ingredients*, 39 Fed. Reg. at 34,196 (“New information may at any time require reconsideration of the GRAS status of a food ingredient. Any change in §§ 121.101, 121.104, or 121.105 shall be accomplished pursuant to § 121.41.”).

134. *Substances Generally Recognized as Safe*, 62 Fed. Reg. 18,938, 18,940 (Apr. 17, 1997).

135. *Id.* at 18,941.

136. *Id.*

137. *Id.*

138. *Id.*

139. *Id.*

140. *Id.*

procedure was also completely voluntary.¹⁴¹ Each notification had to include “a succinct description of the ‘notified substance’ (i.e., the substance that is the subject of the notice), the applicable conditions of use, and the basis for the GRAS determination (i.e., through scientific procedures or through experience based on common use in food),” as well as the notifier’s signature and date.¹⁴²

Upon receipt of the notification, the Agency evaluates the information and responds by letter in one of three ways. First, the Agency can determine that it has no issue with the basis for the GRAS determination.¹⁴³ Second, the Agency may conclude the notification does not provide a sufficient basis for determining GRAS status because it either fails to include the appropriate data or the data raises questions about the safety of the substance.¹⁴⁴ Finally, the Agency can respond by informing the notifier that it has ceased its review upon the notifier’s request.¹⁴⁵

While the “FDA did not formally terminate the petition . . . process,” it has stated that it no longer devotes resources to the reviews of individually submitted petitions.¹⁴⁶ The FDA has never promulgated a final rule regarding the procedures for the notification program and the procedure remains voluntary. Not surprisingly, from 1998 to 2008, companies submitted just 274 GRAS determination notifications to the FDA.¹⁴⁷ For all other GRAS determinations, the Agency usually does not possess information about these substances as companies are not required to comply with the notification procedure.¹⁴⁸ Once the substance becomes marketed, the FDA would be hard-pressed to determine that it presents a food safety problem since the Agency is typically unaware of the GRAS determination.¹⁴⁹

B. Standard of Safety as Applied by the FDA

A determination that a substance is GRAS requires “both technical evidence of safety and a basis to conclude that this technical evidence of safety is generally known and accepted”—a different standard than that

141. *Id.*

142. *Id.*

143. Office of Food Additive Safety, *About the GRAS Notification Program*, FDA (March 2009), <http://www.fda.gov/Food/FoodIngredientsPackaging/GenerallyRecognizedasSafeGRAS/GRASNotificationProgram/default.htm>.

144. *Id.*

145. *Id.*

146. U.S. GOV’T ACCOUNTABILITY OFFICE, *supra* note 87, at 6.

147. *Id.* at 8.

148. *Id.* at 12.

149. *Id.*

required to prove the safety of a food additive, which requires only technical evidence of safety.¹⁵⁰ Consequently, GRAS substances have the additional requirement of “common knowledge about the safety of the substance for its intended use” in addition to scientific evidence about what the substance actually is or the specific data that is considered or evaluated to determine the substance’s safety.¹⁵¹ In this context, the FDA has defined “safe” or “safety” to mean that “there is a reasonable certainty in the minds of competent scientists that the substance is not harmful under the intended conditions of use.”¹⁵² As part of this definition, the Agency recognizes that it is impossible to establish safety with “complete certainty [regarding] the absolute harmlessness of the use of any substance.”¹⁵³ Yet, safety can be established through either “scientific procedures” or “general recognition of safety.”¹⁵⁴

When assessing safety, certain factors must be considered:

- (1) The probable consumption of the substance and of any substance formed in or on food because of its use[;]
- (2) The cumulative effect of the substance in the diet[;] . . .
- (3) Safety factors which, in the opinion of experts qualified by scientific training and experience to evaluate the safety of food and food ingredients, are generally recognized as appropriate.¹⁵⁵

The language of the statute¹⁵⁶ suggests that the experts evaluating this data must be qualified to evaluate the safety of the particular food substance at issue rather than food additives or substances more generally.¹⁵⁷

As previously discussed, general recognition of safety through scientific procedures requires the same degree of scientific evidence

150. Substances Generally Recognized as Safe, 62 Fed. Reg. 18,938, 18,940 (Apr. 17, 1997).

151. *Id.*

152. 21 C.F.R. § 170.3(i) (2012).

153. *Id.*

154. *Id.*

155. *Id.*

156. 21 U.S.C. § 321(s) (2006) (explaining the term “food additive” to include those substances “not generally recognized, among experts qualified by scientific training and experience to evaluate its safety, as having been adequately shown through scientific procedures . . . to be safe under the conditions of its intended use”).

157. Joseph D. Becker, *The GRAS Clause of the Food Additives Amendment*, 15 FOOD DRUG COSM. L.J. 444, 445 (1960) (“A class of experts qualified to evaluate ‘its’ safety is a much more restricted circle than a class qualified to evaluate the safety of food additives generically. Assuming, *arguendo*, that the qualification of an expert under any interpretation of the clause will require that he have done actual toxicological research (a less exacting standard may in fact suffice) it follows that, while any toxicologist who has done research on any food additive may be qualified to evaluate the safety of ‘food additives,’ only those toxicologists who have studied the particular additive in question or the class of additives to which the particular additive belongs are qualified to evaluate ‘its’ safety.”).

required for food additives.¹⁵⁸ In contrast, “general recognition of safety through experience based on common use in food prior to January 1, 1958” may be determined without the same volume of scientific evidence but “[must] be based solely on food use of the substance prior to [that date].”¹⁵⁹ Specifically, the “common knowledge” aspect requires two elements. First, the data and information necessary to establish the scientific evidence has to be “generally available.”¹⁶⁰ Second, there must be a basis for consensus in the scientific community regarding the safety of the substance.¹⁶¹

According to the FDA, the “usual mechanism” to demonstrate that scientific and technical information is widely available or disseminated is through publication in a peer reviewed scientific journal.¹⁶² Yet, the Agency has been clear that this is not the only means of showing general availability of the scientific and technical information.¹⁶³ In some instances, this can be established through other means including “secondary scientific literature,” documentation through an “expert panel,” or opinions from organizations such as the National Academy of Sciences on either a “broad or specific issue” related to a GRAS determination.¹⁶⁴ With regard to the common knowledge element, the Agency uses the term “consensus” but acknowledges that this does not require “unanimity among qualified experts.”¹⁶⁵ Therefore, if the FDA received a single report regarding the safety of a substance, it would not automatically determine that the substance cannot meet the GRAS standard, but would instead evaluate the report along with other published studies.¹⁶⁶

Practically speaking, safety in this context is defined “broadly” and does not apply solely to “acute risks,” but rather the term must be considered in the broadest sense.¹⁶⁷ To do so provides the only means of accomplishing the expansive protective purposes of the Federal Food, Drug, and Cosmetic Act and the Food Additives Amendment. While both Congress and the FDA recognized that science can never ultimately provide

158. 21 C.F.R. § 170.30(b).

159. *Id.* § 170.30(c)(1).

160. Substances Generally Recognized as Safe, 62 Fed. Reg. 18,938, 18,940 (Apr. 17, 1997).

161. *Id.*

162. *Id.*

163. *Id.*

164. *Id.* at 18,940–41.

165. *Id.* at 18,941.

166. *Id.* (citing *United States v. Articles of Food & Drug Consisting of Coli-Trol 80*, 518 F.2d 743, 745 (5th Cir. 1975)).

167. Rebecca L. Goldberg, *Administering Real Food: How the Eat–Food Movement Should-and Should Not–Approach Government Regulation*, 39 *ECOLOGY L.Q.* 773, 794 (2012) (“For example, it is clear that a substance will not be found safe at a level that, over time, has been shown to increase the risk of a deadly disease such as cancer.”). *Id.* at 794 n.102.

a definitive answer regarding a substance's safety, they never questioned the assumption that science should guide these decisions, as the "reasonable certainty" standard depends on the determinations of "competent scientists."¹⁶⁸ It has also been difficult to determine what "role, if any, a consideration of benefits should play in applying the general safety standard."¹⁶⁹ However, it is clear from the FDA's perspective that "[t]he key determinant in the safety evaluation of a substance found in or added to the diet is the relation of its probable human intake to the level at which adverse effects are observed in toxicological studies."¹⁷⁰ The Agency cites the old adage "the dose makes the poison" to demonstrate that a substance that may be GRAS for one use may not be GRAS for all, depending on the amount consumed.¹⁷¹

Both the courts and the Agency have struggled to apply the GRAS exemption, ultimately concluding it requires "a fairly high level of scientific agreement."¹⁷² The cases considering the "general recognition of safety" language, largely involving drugs for use in either humans or animals, interpreted the phrase to require consideration of whether safety for the intended uses is "generally recognized" by qualified experts, making the consideration in those cases similar to the one at hand.¹⁷³ Specifically, the cases bolstered the approach used by the FDA, holding that consensus among experts does not require unanimity.¹⁷⁴ Rather, to determine the substance's general recognition of safety, the issue should not be "to determine [actual] safety . . . but to ascertain the . . . [product's] general reputation in the scientific community for such characteristics."¹⁷⁵ In other words, when the Agency can demonstrate that a "genuine dispute . . . exist[s]" among experts regarding "general recognition," courts

168. *Id.* at 796 (citing 21 C.F.R. § 170.3(i) (2012)).

169. INST. OF MEDICINE, *supra* note 4, at 34.

170. *Guidance for Industry: Estimating Dietary Intake of Substances in Food*, FDA (Aug. 2006), <http://www.fda.gov/Food/GuidanceComplianceRegulatoryInformation/GuidanceDocuments/FoodIngredientsandPackaging/ucm074725.htm> ("Generally, animal studies are used to determine an acceptable daily intake (ADI), that has to be greater than the estimated daily intake (EDI) to ensure safety.").

171. *Id.* (citing Paracelsus, 16th century).

172. INST. OF MEDICINE, *supra* note 4, at 22 & nn.109, 110 (citing Degnan, *supra* note 46, at 570–80).

173. Degnan, *supra* note 46, at 575 n.95 (citing *United States v. Articles of Food & Drug Consisting of Coli-Trol 80*, 372 F. Supp. 915 (N.D. Ga. 1974), *aff'd* 518 F.2d 743, 745 (5th Cir. 1975)).

174. *See e.g.*, *Articles of Food & Drug Consisting of Coli-Trol 80*, 518 F.2d at 746 (explaining that because even properly conducted studies may cause disagreement, unanimity is required).

175. Degnan, *supra* note 46, at 574 (citing *United States v. Articles of Food & Drug Consisting of Coli-Trol 80*, 518 F.2d 743 (5th Cir. 1975)).

will typically find that general recognition of safety has not been established.¹⁷⁶

Unfortunately, the Agency has a long history of failing to attract appropriately trained scientists to make such safety determinations for GRAS substances.¹⁷⁷ Because the FDA is an organization based in science, as opposed to a scientific research organization, critics argue that it should rely on science research organizations that have access to needed information when making determinations requiring scientific evidence.¹⁷⁸ To date, the FDA has failed to meet a number of safety directives. Specifically, the Agency has not yet completed the comprehensive review of GRAS substances it began in the 1970s and, in fact, stopped the program due to limited resources.¹⁷⁹ Currently, the Agency reviews the safety of marketed GRAS substances only when specific issues are raised.¹⁸⁰

Perhaps more disconcerting is the fact that the Agency has failed to issue guidance to industry regarding conflicts of interest among employees examining GRAS substances and their scientific determinations to ensure the independent safety of these substances.¹⁸¹ While the FDA has created policies preventing its staff that may have a financial conflict of interest from serving on either the GRAS Notice Review Teams or the scientific and advisory panels reviewing GRAS substances, the Agency has failed to develop similar guidelines for private companies making independent GRAS determinations.¹⁸²

To establish scientific consensus, industry can use any of the methods discussed above, including expert panels convened for the purpose of reviewing the substance. This approach of not using FDA experts to make the determination about the substance's safety was contemplated back in 1957 during the hearings on the FAA.¹⁸³ According to the FDA, "it is not

176. *Id.* "Numerous courts have held that even where some experts testify unequivocally that a product is generally recognized as safe, the product is nevertheless not GRAS if other qualified experts disagree and there is a genuine difference of opinion among experts regarding the product's reputation." *Id.* at n.98.

177. Peter Barton Hutt, *The State of Science at the Food and Drug Administration*, 60 ADMIN. L. REV. 431, 436 (2008) ("Without congressional appropriations for increased scientific personnel and funds to support participation in professional scientific meetings and to maintain cutting-edge educational programs within the Agency, the FDA staff become increasingly isolated and fall behind their counterparts in academia and the regulated industry.").

178. *Id.* at 444.

179. *Id.* at 448 (citing Peter Barton Hutt, *Regulation of Food Additives in the United States*, Food Additives 199, 205 (A. Larry Branen et al. eds., 2d ed. 2001)).

180. *Id.*

181. U.S. GOV'T ACCOUNTABILITY OFFICE, *supra* note 87, at 14.

182. *Id.*

183. INST. OF MEDICINE, *supra* note 4, at 22 (citing *Food Additives: Hearings Before a Subcomm. of the H. Comm. on Interstate and Foreign Commerce*, 85th Cong., 1st Sess. 94-95 (1957)).

uncommon” for companies to use expert panels that may include members of the company’s own staff or individuals “hired by the company or by a consulting firm.”¹⁸⁴ There is, however, no requirement that the panel members remain free from bias or conflicts of interest.¹⁸⁵ In addition, the FDA has neither provided industry with guidance regarding how to accomplish non-biased review, nor provided any check to ensure these decisions are independent.¹⁸⁶

Finally, despite recognizing that the status of a GRAS substance may change over time—as additional information is discovered about the substance’s safety¹⁸⁷—the FDA has not comprehensively reconsidered the safety of GRAS substances since 1982.¹⁸⁸ The Agency justifies its failure based on a database called the “Priority Based Assessment of Food Additives,” which it suggests helps prioritize substances for reassessment using “administrative, chemical, and toxicological information.”¹⁸⁹ Relying on this database to demonstrate measures that it is taking to reevaluate the safety of existing GRAS substances, the Agency has yet to provide an example of a reconsideration made pursuant to the information generated from the database.¹⁹⁰

The Agency also cites media reports, individual complaints from the public, citizen petitions, or reports published by groups the Agency considers “authoritative” as sources of information to help prioritize reassessments.¹⁹¹ Yet, even after receiving eleven citizen petitions from both individuals and consumer groups, the Agency has, for the most part, failed to respond meaningfully to these concerns.¹⁹² Indeed, the Agency has neither revoked the GRAS status of any substances that have been affirmed since 1972, nor retracted its “no questions” position for any substance about which it received a notification letter since 1997.¹⁹³ In addition to cyclamate salts, the FDA has completely prohibited the use of only one other GRAS

(statement of Robert B. Smith, Jr., President of the Medical College of Virginia) (“At least one witness at the 1957 congressional hearings . . . suggest[ed] that a company could seek the advice of private or academic consultants on the question of whether there was general recognition of safety based on existing data.”)).

184. U.S. GOV’T ACCOUNTABILITY OFFICE, *supra* note 87, at 15.

185. *Id.*

186. *Id.*

187. 21 C.F.R. § 170.30(k)(1) (2012) (“New information may at any time require reconsideration of the GRAS status of a food ingredient. Any change in part 182, part 184, or § 186.1 of this chapter shall be accomplished pursuant to § 170.38.”).

188. U.S. GOV’T ACCOUNTABILITY OFFICE, *supra* note 87, at 21.

189. *Id.*

190. *Id.*

191. *Id.*

192. *Id.* at 22.

193. *Id.*

substance—cinnamyl anthranilate, a flavoring agent known to cause cancer in mice.¹⁹⁴ The Agency also prohibited the use of sulfites on raw fruits and vegetables due to severe allergic reactions in a portion of the population.¹⁹⁵ This limited agency action—tantamount to inaction—fails to address the myriad of concerns regarding many GRAS substances presently on the market. While the Agency cites either limited resources as the reason it has yet failed to respond or the need for additional information and studies before revoking or amending the substance’s GRAS status, the time has come for the FDA to respond.

III. THE FAILURES OF THE FDA’S APPROACH TO GRAS SUBSTANCES

A. *The Not-so-Sweet Effects of Sugar*

As early as the 1950s, Dr. William Coda Martin classified refined sugar as a poison because of its interference with integral bodily functions.¹⁹⁶ The idea that sugar is detrimental to our health is not a new one, although it has been receiving increasing attention in the past few years.

In February 2012, a group of doctors and scientists wrote a highly publicized article in *Nature* calling for the removal of sugar from the GRAS list because of its potential for abuse and “deadly effect[s].”¹⁹⁷ The article followed a lecture by one of its authors, Dr. Robert Lustig, given in 2009, entitled “Sugar: The Bitter Truth.”¹⁹⁸ The lecture received a great deal of attention on YouTube.¹⁹⁹ Dr. Lustig, a specialist in pediatric hormone disorders and an expert on childhood obesity, made the argument that sugar is a “toxin” or “poison,” and that people abuse it in the same manner they do drugs and alcohol.²⁰⁰ By sugar, Lustig refers not only to sucrose, but also to high fructose corn syrup—making no real distinction between the two, as he considers them equally dangerous.²⁰¹

The traditional argument about the dangers of sugar consumption has centered on the substance’s non-nutritive properties and the fact that, when

194. *Id.*

195. *Id.*

196. BLATT, *supra* note 8, at 237.

197. Robert H. Lustig, Laura A. Schmidt & Claire D. Brindis, *The Toxic Truth About Sugar*, 482 NATURE, Feb. 2, 2012, at 28.

198. Dr. Robert Lustig, *Sugar: The Bitter Truth*, Remarks Given at the University of San Francisco (May 26, 2009), available at <http://www.youtube.com/watch?v=dBnniua6-oM>.

199. Gary Taubes, *Is Sugar Toxic?*, N.Y. TIMES, Apr. 13, 2011, <http://www.nytimes.com/2011/04/17/magazine/mag-17Sugar-t.html?pagewanted=all>.

200. *Id.*

201. *Id.*

individuals consume sugar, they are essentially consuming empty calories.²⁰² However, Lustig's concern, which has been echoed by other biochemists, centers on the manner in which the human body metabolizes the fructose in sugar when consumed in certain amounts.²⁰³ Specifically, scientific evidence suggests that "fructose can trigger processes that lead to liver toxicity and a host of other chronic diseases."²⁰⁴ Sugar creates the same set of concerns that led to the regulation of alcohol in our society—"unavoidability (or pervasiveness throughout society), toxicity, and potential for abuse and negative impact on society."²⁰⁵ The toxicity of sugar is evidenced by its responsibility for metabolic diseases including hypertension, high triglycerides, and diabetes, as well as its toxic effects on the liver.²⁰⁶ Moreover, sugar has the potential for abuse because its effects on the brain encourage more intake.²⁰⁷

Despite the connections between sugar and obesity, as well as other chronic and deadly conditions, the federal government remains of the opinion that there is simply not enough evidence to regulate sugar in the manner demanded by advocates. In a 2010 report prepared by the Institute of Medicine (IOM) to address what information should be included on front of package labeling to curb obesity, the IOM stated with regard to "total sugars":

There is a lack of scientific agreement about the amount of sugars that can be consumed in a healthy diet and about potential adverse health effects of sugars beyond an effect on dental caries. Thus, it is difficult to conclude that total sugars intake is of sufficient public health concern to be included in [Front of Package] rating systems.²⁰⁸

202. *Id.*

203. *Id.*

204. Lustig, *supra* note 197, at 28 (quoting Robert Lustig, *Fructose: Metabolic, Hedonic, and Societal Parallels with Ethanol*, 110 AM. DIET. ASSOC. 1307, 1307–21 (2010), available at <http://podcast.uctv.tv/webdocuments/Fructose-and-Ethanol.pdf>).

205. *Id.* (citing THOMAS BABOR, ET AL., ALCOHOL: NO ORDINARY COMMODITY: RESEARCH AND PUBLIC POLICY (2003)).

206. *Id.* (citing Robert Lustig, *Fructose: Metabolic, Hedonic, and Societal Parallels with Ethanol*, 110 AM. DIET. ASSOC. 1307, 1307–21 (2010), available at <http://podcast.uctv.tv/webdocuments/Fructose-and-Ethanol.pdf>); Luc. Tappy, Kim A. Le, Christel Tran, and Nicolas Paquot, *Fructose and Metabolic Diseases: New Findings, New Questions*, 26 NUTRITION 1044, 1044–49 (2010)).

207. *Id.*

208. INST. OF MEDICINE, EXAMINATION OF FRONT-OF-PACKAGE NUTRITION RATING SYSTEMS AND SYMBOLS: PHASE I REPORT 12 (2010), available at http://books.nap.edu/openbook.php?record_id=12957&page=12.

In addition, the IOM concluded that, although “added sugars” contribute an “overall increase in calories” to the “American diet . . . evidence and agreement are lacking about adverse health effects of added sugars”—with the exception being the additional calories they add to an individual’s diet and the “dilution of essential nutrient intake.”²⁰⁹

Although the Agency has not spoken to the issue since 1986, the FDA’s conclusion on the matter, not surprisingly, was the same. After reviewing over 1,000 scientific papers, the Agency concluded that “[o]ther than the contribution to dental caries, there is no conclusive evidence on sugars that demonstrates a hazard to the general public when sugars are consumed at the levels that are now current and in the manner now practiced.”²¹⁰ While many in the sugar industry viewed this finding as an “exoneration” of added sugars, the FDA’s conclusions were premised on the consumption of sugars at their 1986 levels. This suggests that perhaps the time has come for the FDA to reconsider the conclusions in this report in light of more recent scientific evidence such as that cited by Lustig.

The principal author of the FDA’s study, who is now an advisor for the Corn Refiner’s Association, agrees that sugars may be toxic. Yet he argues that any substance has the potential to be toxic if consumed in unnatural doses or quantities—in other words, the dose makes the poison.²¹¹ Yet, when the FDA drafted its report in 1986, the levels of added sugars consumed were estimated at forty pounds per individual each year, which is the equivalent of just 200 calories or less than the amount in one and one-half cans of Coca-Cola.²¹² However, a more reliable estimate from the USDA suggested that Americans were consuming seventy-five pounds per year, a number that increased by the early 2000s to more than ninety pounds each year.²¹³ Recent estimates from the USDA suggest that this number is closer to 142 pounds per year presently.²¹⁴

209. *Id.*

210. Walter H. Glinsmann, Hiltje Irausquin, & Youngmee K. Park, *Evaluation of Health Aspects of Sugars Contained in Carbohydrate Sweeteners: Report of Sugars Task Force*, J. NUTR. 1986, at S117, available at http://jn.nutrition.org/content/116/11_Suppl.toc.

211. Taubes, *supra* note 199.

212. *Id.*

213. *Id.*

214. HODAN FARAH WELLS & JEAN C. BUZBY, USDA, DIETARY ASSESSMENT OF MAJOR TRENDS IN U.S. FOOD CONSUMPTION, 1970-2005, at iv (2008), available at http://www.ers.usda.gov/media/210681/eib33_1_.pdf (“According to the loss-adjusted food availability data, Americans consumed 30 teaspoons per person per day of added sugars and sweeteners in 2005. This finding suggests that Americans, on average, need to scale back on added sugars and sweeteners.”).

B. FDA's Review of Sugar

Sugar has an interesting history and, some might suggest, a sordid relationship with the FDA. When the FDA began its comprehensive review of GRAS substances in the 1970s, sugar was one of the substances under review. As mentioned above, to complete its Herculean task of comprehensively reviewing all of the substances on the GRAS list, the Agency subcontracted with the Federation of American Societies for Experimental Biology. This organization was headed by a biochemist named George W. Irving Jr., whose previous position was chairman of the scientific advisory board of the International Sugar Research Foundation.²¹⁵ Another member of the panel, Samuel Fomon, also had ties to the sugar industry, as he had received funding from the industry for three of the five years prior to the GRAS review process.²¹⁶

In its review of sugar, the panel relied heavily on a publication entitled “Sugar in the Diet of Man,” which was produced by Frederick Stare, founder and chairman of the Harvard School of Public Health’s Department of Nutrition.²¹⁷ Stare had a long history with the sugar industry, which provided a significant amount of funding for many of the institution’s papers as well as a new building.²¹⁸

The “Sugar in the Diet of Man” report was a detailed white paper—funded by the sugar industry—which was meant to include the “scientific facts” about sugar to counter the evidence presented by others regarding the substance’s harm.²¹⁹ The section of the panel’s report considering the potential risks of heart disease from sugar noted that there were fourteen conflicting reports, but then cited to sections from “Sugar in the Diet of Man” to support its inconclusive determination.²²⁰ Similarly, the section on diabetes acknowledged that “long term consumption of sucrose can result in a functional change in the capacity to metabolize carbohydrates and thus lead to diabetes mellitus,” but again cited five reports with contradicting conclusions—including “Sugar in the Diet of Man” and four others with industry ties—leading the Agency to conclude the links to diabetes were inconclusive.²²¹ While many scientists agreed with this determination, there

215. Gary Taubes & Cristin Kearns Couzens, *Big Sugar's Sweet Little Lies*, MOTHER JONES (Oct. 31, 2012), <http://www.motherjones.com/environment/2012/10/sugar-industry-lies-campaign?page=1>.

216. *Id.*

217. *Id.*

218. *Id.*

219. *Id.*

220. *Id.*

221. *Id.*

were also many that did not. Specifically, the USDA's Carbohydrate Nutrition Laboratory submitted evidence in response to the FDA's review to establish the link between sugar consumption and obesity, diabetes, and heart disease.²²²

In 1988, the FDA stood firm on its findings and promulgated a final rule formally affirming certain sugars (corn sugar, corn syrup, invert sugar, and sucrose) as GRAS substances after a comprehensive review of their safety.²²³ The Agency based this rule on the safety evaluations of the Select Committee on GRAS Substances, which in 1976 determined that, beyond its contribution to dental caries, "there is no clear evidence in the available information on sucrose that demonstrates a hazard to the public when used at the levels that are now current and in the manner now prescribed."²²⁴ In other words, the Select Committee made the identical determination to that of the FDA and the Institute of Medicine, using almost exactly the same language. However, the Select Committee specifically acknowledged that its finding might change, should consumption dramatically increase, as the Committee had no means of determining whether different consumption rates might present a "dietary hazard."²²⁵

Because the Select Committee determined "that the safety of possible expanded consumption of these ingredients could not be ascertained," the FDA noted that it would "ordinarily" set limitations on the use of these substances in food.²²⁶ However, the Agency decided that it would be imprudent to do so at that time "because they would be impractical to enforce" and would fail to "prevent an expansion in total dietary sugars consumption" due to the availability of high-sugar-content foods that can be freely purchased by the consumer.²²⁷ The Agency did note that it would continue to monitor the consumption of these substances, suggesting that "it would undertake a new evaluation of the safety of the use of sweeteners if total dietary consumption would increase significantly."²²⁸

In its notice, the Agency recounted the many comments it received regarding the negative health effects associated with overconsumption of sugars, ultimately finding that they failed to provide a basis on which to question the Select Committee's determination of safety and consequently,

222. *Id.*

223. GRAS Status of Corn Sugar, Corn Syrup, Invert Sugar, and Sucrose, 53 Fed. Reg. 44,862, 44,862 (Nov. 7, 1988) (codified at 21 CFR §§ 182, 184).

224. *Id.* at 44,862-63.

225. *Id.* at 44,863.

226. *Id.*

227. *Id.*

228. *Id.*

to amend the substances' GRAS status.²²⁹ In addition, while some of the comments presented additional data and information previously unavailable to the Select Committee and subsequent Task Force, the Agency considered this new data and still concluded that "these data did not provide sufficient evidence of any health concerns from sugars consumption."²³⁰ In its final rules, none of these substances were subject to any limitation beyond good manufacturing practices.

C. Measures to Regulate Sugar Consumption and Removing Sugar from the GRAS List

The past few years have seen varied attempts at the regulation of sugar, although no one has yet filed a petition with the FDA requesting the removal of sugar from the GRAS list. In 1999, however, the Center for Science in the Public Interest (CSPI) filed a petition with the Agency requesting that it "establish a Daily Reference Value (DRV) for 'added sugars' of 40 grams and require a mandatory disclosure of added sugars in both grams per serving and % Daily Value, i.e., the percentage of that DRV."²³¹ In the petition, CSPI referenced the FDA's statement that it would reevaluate the safety of these substances if dietary consumption increased significantly.²³² As of 1999, according to the CSPI's estimates, the per capita consumption had increased by twenty-eight percent.²³³ In turn, the organization asked the FDA to meet its own mandate and undertake a new safety evaluation of these substances, citing the myriad of health problems scientists and health professionals attribute to the overconsumption of sugars.²³⁴

The Agency published notice of the petition in the Federal Register and sought comment upon receipt of the petition, yet only one comment is available in the docket, which succinctly stated its support of CSPI's request.²³⁵ The FDA responded to CSPI, stating that "[i]n accordance with 21 CFR 10.30(e)(2), this letter is to advise you that we have been unable to reach a decision on your petition within the first 180 days of its receipt

229. *Id.* at 44,872.

230. *Id.*

231. Letter from Center for Science in the Public Interest to FDA 3 (Aug. 3, 1999), *available at* <http://www.cspinet.org/reports/sugar/sugarpet1.pdf>

232. *Id.* at 1.

233. *Id.*

234. *Id.*

235. Letter from Public Health Services of San Joaquin County to Jane E. Henney, FDA Commissioner, Docket ID: FDA-1999-P-0158-0002 (Oct. 1, 1999), *available at* <http://www.regulations.gov#!documentDetail;D=FDA-1999-P-0158-0002>.

because of *other Agency priorities and the limited availability of resources*.²³⁶ Presently, there appear to be no attempts on the part of the Agency toward setting Daily Reference Values for added sugars. However, the Agency is presently considering information about consumer reactions to specific nutrition information on food labels—including information about added sugars—which may ultimately result in the setting of a DRV.²³⁷

Local municipalities have also attempted their own measures. Receiving a tremendous amount of criticism and support, Mayor Bloomberg's recent implementation of a "soda ban" in New York City is perhaps the most recognizable. The measure prohibits the sale of sugary drinks and sodas that are larger than sixteen ounces in size at restaurants and other public establishments that receive inspection grades from the health department—meaning convenience stores, some vending machines, and newsstands are exempted from the ordinance.²³⁸ The measure was taken in an attempt to curb obesity in New York City, where more than half of adults are either obese or overweight.²³⁹ Not surprisingly, the soda ban has been hotly contested, with one of the major criticisms being that it rests on faulty science.²⁴⁰

There have been numerous—if not countless—studies to determine the health effects of consuming sugary drinks. In 2011, a paper compiled all the existing research and data into a "meta meta-analysis" and found that the studies used only four of eleven best practices when making their conclusions.²⁴¹ In other words, "[r]esearch on sugar-sweetened beverages

236. Letter from Food and Drug Administration to Michael F. Jacobsen, CSPI, Docket ID: FDA-1999-P-0158-0001 (Jan. 27, 2000) (emphasis added), *available at* <http://www.regulations.gov/#!documentDetail;D=FDA-1999-P-0158-0001>.

237. Notice of Agency Information Collection, 77 Fed. Reg. 32,120, 32,121 (May 31, 2012) ("This study will also explore how declaring the added sugars content of foods might affect consumers' attention to and understanding of the sugars and calorie contents and other information on the Nutrition Facts label. FDA received numerous comments regarding the declaration of added sugars in response to the 2007 ANPRM even though the Agency did not ask any questions regarding the declaration of added sugars. the Agency is not aware of any existing consumer research that has examined this topic and is therefore interested in using this study to enhance understanding of how consumers would comprehend and use this new information.").

238. Michael Grynbaum, *Health Panel Approves Restriction on Sale of Large Sugary Drinks*, N.Y. TIMES, Sept. 13, 2012, <http://www.nytimes.com/2012/09/14/nyregion/health-board-approves-bloombergs-soda-ban.html>.

239. *Id.* ("This is the single biggest step any city, I think, has ever taken to curb obesity," Mr. Bloomberg said shortly after the vote. "It's certainly not the last step that lots of cities are going to take, and we believe that it will help save lives.").

240. Daniel Engber, *Fuzzy and Fizzy: The Contested Science Behind Bloomberg's Ban on Large Sized Sodas*, SLATE (Sep. 13, 2012, 1:15 PM), http://www.slate.com/articles/health_and_science/science/2012/06/bloomberg_bans_large_sized_soda_the_science_behind_the_decision_2.html.

241. *Id.*

has been so sloppy and vague as to be inconclusive.”²⁴² The meta analyses examined for the study—which reached the conclusion that there is simply not enough evidence to show a causal link between the consumption of sugary beverages and body weight—were either funded by, or received some support from, various food and beverage companies.²⁴³ Arguably, the science has also suffered from the influence of industry.

Regardless of this unsavory history, the fact remains that sugar is treated differently than a GRAS substance like trans fats, one variety of which is partially hydrogenated vegetable oils, which the FDA has agreed with the science establishing that they “raise[] the LDL (or “bad”) cholesterol that increases your risk for [coronary heart disease].”²⁴⁴ The Agency, therefore, required greater labeling measures to provide disclosures to consumers in the interests of public health. Currently, the Agency is in the process of reviewing the GRAS status of partially hydrogenated oils after receiving two citizen petitions on the issue.²⁴⁵

Similarly, the FDA has explicitly recognized that Americans consume unhealthy amounts of salt, which can present “a serious health hazard, because excess sodium consumption contributes to the development and escalation of high blood pressure, a leading cause of heart disease, kidney disease, and stroke.”²⁴⁶ The Agency has even indicated a willingness to reevaluate salt’s GRAS status, stating that it has the “legal authority to regulate the safe use of ingredients, including salt, added to food”²⁴⁷ The major difference between these substances and sugar is that the FDA has been willing to accept the science suggesting that these substances require further regulation and even removal from the GRAS list.

Somewhat unpredictably, the Agency has an article on its website discussing the role of sugar in food and drug history.²⁴⁸ The article references a study by the World Health Organization (WHO), which concluded that “aside from mere issues of weight loss, . . . the science did support the idea that there were demonstrable metabolic differences between simple sugars and complex carbohydrates in the daily diet.”²⁴⁹ The

242. *Id.*

243. *Id.*

244. *Trans Fat Now Listed with Saturated Fat and Cholesterol*, FDA, <http://www.fda.gov/Food/ResourcesForYou/Consumers/NFLPM/ucm274590.htm> (last visited Jan. 27, 2013).

245. U.S. GOV’T ACCOUNTABILITY OFFICE, *supra* note 87, at 48.

246. *Helping Consumers Reduce Sodium Intake*, FDA, <http://www.fda.gov/ForConsumers/ConsumerUpdates/ucm327369.htm> (last visited Jan. 27, 2013).

247. U.S. GOV’T ACCOUNTABILITY OFFICE, *supra* note 87, at 44–45.

248. Suzanne White Junod, *Sugar: A Cautionary Tale*, FDA, <http://www.fda.gov/AboutFDA/WhatWeDo/History/ProductRegulation/SelectionsFromFDLIUpdateSeriesonFDAHistory/ucm091680.htm> (last updated May 21, 2009).

249. *Id.*

article goes on to state that the Centers for Disease Control have determined that forty-seven million Americans suffer from “metabolic syndrome,” which encompasses a “cluster of medical conditions characterized by insulin resistance, obesity, abdominal fat, high blood sugar and triglycerides, high blood cholesterol, and high blood pressure.”²⁵⁰ The article concludes by suggesting that the WHO report represents the “opening volley in what promises to be a lively new chapter in the history of sugar.”²⁵¹ Arguably, this “opening volley” has been received and returned, as scientists are now starting to “accept that the primary risk factor for both heart disease and type 2 diabetes is . . . metabolic syndrome,” which researchers associated with sugar almost fifty years ago.²⁵² As Dr. Lustig would suggest, the science is clear regarding the connection, yet the FDA remains unconvinced.²⁵³

The question remains then: Exactly what evidence does the FDA need to remove sugar or any substance from the GRAS list? It seems likely that a case could be made demonstrating a “genuine dispute” among scientists regarding the harms posed by sugars as an added substance. Yet, the Agency must consider whether there “is a *lack of convincing evidence* that the substance is GRAS.”²⁵⁴ This determination occurs only after the Agency decides of its own accord, or upon the petition of an individual, to review the substance’s GRAS status, post notice in the Federal Register, and receive and review comments on the action.²⁵⁵ Because there are so few examples of instances where the FDA has taken the step of removing a substance from the GRAS list, it remains questionable what the Agency will deem a “lack of convincing evidence.”²⁵⁶ In other words, the Agency could decide that evidence demonstrating a genuine dispute among scientists, or the lack of consensus regarding the safety of added sugars, presents a real issue regarding the “general recognition of safety” standard.

However, this places the impetus on an individual to file a petition with the Agency and encourage scientists to submit current published studies describing the established connection between added sugars and metabolic syndrome, or any established harms. If these studies have not yet been developed or published, then scientists should consider making their data more widely available such that they become “generally recognized” by

250. *Id.*

251. *Id.*

252. Taubes, *supra* note 215.

253. *Id.*

254. 21 C.F.R. § 170.38(b)(3) (2012) (emphasis added).

255. *Id.* § 170.38(b)(1)–(3).

256. *Id.* §§ 170.35(b)(4), 170.35(c)(6), 170.38(b)(3).

other scientists. Yet, if the Agency continues to rely on the reports of expert panels such as the Institute of Medicine—which have not made a determination about the specific harms posed by sugar—then it appears unlikely that the Agency will remove sugar from the GRAS list.

Arguably, however, the language of the regulation and the consideration under the statute requires that the evidence of *safety* be convincing, not the evidence of harm. Given the broad purposes of the statute to protect human health from potential or known hazards, advocates could make the compelling case that the evidence establishing “a reasonable certainty of *no* harm” simply does not exist because there are studies establishing harm. Ultimately, the Agency cannot distinguish its regulatory policy decisions from the scientific questions. Yet, in the case of GRAS substances, the statutory and regulatory requirements make clear that the Agency must fully consider the scientific evidence.

CONCLUSION

Rather than revoking sugar’s GRAS status, which seems unlikely at present, the FDA could consider other regulatory options that may be less controversial and easier to implement. For example, it could define the conditions under which added sugars are GRAS and specify intended uses, as well as limits, in the same manner it has for other substances. Because sugar is one of the GRAS substances that can be added to foods with no restriction other than good manufacturing practices, the FDA could reconsider this policy and determine more precise requirements for GRAS use. Alternatively, the Agency could revoke sugar’s GRAS status for specific uses and at specific levels. This could accomplish the goal of reducing unnecessary added sugars in products that are not intended to be sweet. Finally, the Agency could consider labeling aimed at the target population of consumers for which it intends to reduce consumption. With this step, at least, the Agency would be utilizing its study regarding labeling information to address added sugars.

As some suggest, one of the best justifications for the presence of even a small amount of harmful substances in food “is the exceedingly high cost of removing them completely.”²⁵⁷ In the case of sugar—a valuable added substance that has a long history of use in the United States—whatever course the FDA chooses is likely to be marked by controversy, administrative headaches, and regulatory action for which the Agency lacks

257. Richard Zeckhauser, *Measuring Risks and Benefits of Food Safety Decisions*, 38 VAND. L. REV. 539, 553 (1985).

funding. Regardless, these challenges should not prevent the Agency from fulfilling its mission to continue to ensure the safety of added substances in the American food supply.