Government Repudiation of Americans' Safety: A Call for Reformulation of FDA's GRAS Notification Program

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ABSTRACT

This Article examines a seemingly benign exemption from the legal definition of "food additive." This exemption allows manufacturers to add substances to food without notice to FDA or the public. The so-called "GRAS exemption" has burgeoned into a black hole through which substances can go to market, inadequately tested and unbeknownst to consumers. This Article proposes changes to the Final GRAS Rule and assesses the likely outcome of pending litigation brought against FDA by a coalition of stakeholders.

INTRODUCTION

Mine was a childhood filled with longing for colorful sugary breakfast cereals. Born of immigrant parents who were suspect of America's rainbow sprinkles and prepackaged lunch meats, I was often denied in my childhood the foods enjoyed by my playground peers. By the time I reached near-adulthood, however, my parents' reservations about processed foods had long been instilled in me. Now, I always read the nutrition panel and the ingredients list of every box or can that I pick up at the supermarket. And I steer clear of things like hydrogenated soybean oil, enriched flour, and red #40. So naturally it was with great indignation that I learned the foods I so scrupulously select to place in my shopping cart may very well contain secret ingredients—secret in the sense that neither I as the consumer, nor the government as the supposed guardian of the food supply, has any way of knowing that these substances are present.

This Article examines the food additives regime that the Food and Drug Administration (FDA) has been charged with overseeing. A seemingly small and benign exemption from the legal definition of "food additive" has allowed manufacturers to add substances to food products without giving any notice to either FDA or the consuming public. As originally conceived by Congress, the so-called "GRAS exemption" was intended to apply to long-used traditional food ingredients like salt and vinegar. However, the GRAS exemption has become a gaping black hole through which substances can go to market, inadequately tested and unbeknownst to consumers. Part I of this Article addresses how food additives occur in the American

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diet, how food additives are regulated currently, and the science that suggests regulators should do more to verify the safety of food additives before they are made available to the public. Part II describes the history of food additives regulation and analyzes the deficiencies that plague the current regime as it exists under the Final GRAS Rule. Part III discusses recent litigation brought by public interest groups against FDA's promulgation of the Final GRAS Rule and the likely fate of that litigation pursuant to the administrative law that the courts will apply. Part IV proposes much-needed reforms to the Final GRAS Rule in consideration of prevailing trends in food science and the conflicts of interest inherent in a system of industry self-policing.

I. LET'S ADD IT UP: FOOD ADDITIVES IN THE AMERICAN DIET

A. What Are Food Additives?

Food additives are regulated pursuant to the Federal Food, Drug, and Cosmetic Act (FDCA).[1] Under the FDCA, the term "food additive" is broadly defined as a 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.[2] The FDCA distinguishes between "direct" food additives and "indirect" food additives.[3] Direct food additives are those intentionally added directly to food;[4] indirect food additives are those that may reasonably be expected to become a component of food.[5] Indirect food additives include substances present in food packaging or processing equipment that could migrate into the food product for which they are used.[6]

B. Food Additives Regulation in the United States: Food Additives Amendment

As noted above, food additives entering the American food supply are governed by the FDCA, specifically a 1958 amendment to the FDCA called the Food Additives

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[1] Federal Food, Drug, and Cosmetic Act, 21 U.S.C. §§ 301–399 (2018).

[2] The complete definition of "food additive," including the GRAS exemption from the definition, is as follows:

> The term "food additive" means 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 substance intended for use in producing, manufacturing, packing, processing, preparing, treating, packaging, transporting, or holding food; and including any source of radiation intended for any such use), if 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. 21 U.S.C. § 321(s) (2018).

[3] *Id.*

[4] 21 C.F.R. § 172 (2020).

[5] *Id.* § 174.

[6] 21 C.F.R. § 174.6 (2020).

Amendment (FAA).[7] When introduced, the FAA turned the prevailing food additives regime on its head.[8] It shifted the burden of proof with respect to food additive safety from FDA squarely onto the shoulders of industry.[9] Prior to the 1958 FAA, food additives, by default, had been deemed safe unless FDA produced evidence to the contrary.[10] The FAA instead provides that a food additive is to be deemed not safe unless either: (a) the manufacturer submits evidence sufficient to demonstrate the safety of the additive's proposed use; or (b) the additive is subject of an express exemption.[11] Pursuant to the FAA, FDA is no longer responsible for demonstrating that a food additive is unsafe. Rather, manufacturers are required to demonstrate that a food additive is safe by conducting tests and collecting data, which FDA then evaluates.[12]

At the time the FAA was introduced, public concern about food safety was on the rise.[13] Indeed, contemporaneous statements made to members of Congress reflect that the FAA was spurred by concern about the "danger from the daily intake of small amounts of chemical substances . . . ."[14] In other words, government officials had begun to ascribe potential harm to the incremental ingestion of additives over a long period of time.[15] To address this concern, the FAA provides for pre-market review of new food additives such that their safety must be adequately demonstrated before they can be used in the products that line our supermarket shelves.[16] The FAA provides for pre-market review by way of the "food additive petition process," which is still in effect today.[17] To participate in the food additive petition process, a manufacturer collects evidence demonstrating that a food additive is safe for a particular use. The manufacturer then submits a food additive petition for FDA review. If it approves the food additive petition, FDA then formally issues a federal regulation setting forth the conditions under which that food additive is deemed safe for use.[18] Notably, FDA does not grant blanket approval with respect to any given substance.[19] Rather, FDA approves one or more particular uses of a substance, taking into consideration a

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7 21 U.S.C. § 348 (2018).

8 *See generally* INST. OF MED., ENHANCING THE REGULATORY DECISION-MAKING APPROVAL PROCESS FOR DIRECT FOOD INGREDIENT TECHNOLOGIES 17–18 (1999).

9 *Id.*

10 *Id.* at 15.

11 21 U.S.C. § 348 (a)(1), (b)(2) (2018).

12 *Id.*

13 *See* John L. Harvey, *Report from the Food and Drug Administration*, 12 FOOD DRUG COSMETIC L.J. 71, 75 (1957) (discussing growing public concern for food safety at the time the FAA was introduced).

14 *Food Additives: Hearings Before a Subcomm. of the House Comm. on Interstate and Foreign Commerce*, 85th Cong., 1st Sess. 421 (1957) (statement of Elliot Richardson, Assistant Sec'y, Dep't of Health, Educ., and Welfare).

15 *Id.*

16 TOM NELTNER & MARICEL MAFFINI, NAT. RESOURCES DEF. COUNCIL, GENERALLY RECOGNIZED AS SECRET: CHEMICALS ADDED TO FOOD IN THE UNITED STATES 3 (2014), https://www.nrdc.org/sites/default/files/safety-loophole-for-chemicals-in-food-report.pdf [https://perma.cc/XW3B-67UB] [hereinafter NRDC REPORT].

17 21 U.S.C. § 348(b) (2018).

18 *Id.* § 348(b)–(c).

19 *Id.* § 348(c)(1)(A).

number of variables, including the amount of the substance to be used and the purpose of such use.[20]

C. The GRAS Exemption: An Overview

Pursuant to the FAA, the food additive petition process serves as the pre-market review mechanism by which the safety of a food additive is assessed prior to entry into the food supply.[21] However, the legislative record indicates that "[t]he [FAA] was not . . . motivated exclusively by safety concerns. Congress [also] sought to promote continued innovation in food technology by giving FDA greater flexibility to authorize limited use of a substance in food even if shown in animal tests to be poisonous at higher levels."[22] As a result, the FAA charges FDA with the task of balancing two interests: (a) food safety and (b) innovation in food technology.[23] In fulfilling these two purposes, FDA has the discretion to approve the innovative use of a food additive in small amounts because the benefit of such use outweighs the little harm it may have been shown to pose when consumed at high levels.[24]

In furtherance of this bipartite motivation, Congress included in the FAA certain exemptions from the definition of "food additive."[25] Substances so exempted are not required to undergo pre-market review via the food additive petition process.[26] One such exemption is the "GRAS exemption," which applies to substances "generally recognized as safe" (GRAS).[27] If, pursuant to the FAA, use of a substance in a particular manner is generally recognized as safe, then such use is not subject to the food additive petition process.[28] Under the FAA, GRAS status is obtained in one of two ways: either (a) the substance was in common use in food before 1958; or (b) it is common knowledge among qualified experts, based on generally available scientific evidence, that the substance is safe for its intended use.[29] Supporters of the GRAS exemption contend that it promotes innovation by streamlining the regulatory process for all parties involved.[30] Manufacturers and FDA need not dedicate time and money to pre-market review of food additives that are already known to be safe based on long-time common use or generally available scientific evidence. Proponents of the GRAS exemption in its current form argue that it supports the FAA's interests in both advancement of food technology and safety by allowing FDA to direct its limited resources toward evaluation of the more cutting-edge developments in food science,

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[20] *Id.*

[21] *Id.*

[22] INST. OF MED., *supra* note 8, at 18.

[23] H.R. REP. NO. 2284, 85th Cong., 2d Sess. 1 (1958).

[24] INST. OF MED., *supra* note 8, at 34.

[25] 21 U.S.C. § 321(s) (2018).

[26] *Id. See generally* NRDC REPORT, *supra* note 16, at 3–4.

[27] 21 U.S.C. § 321(s) (2018).

[28] *Id.*

[29] *Id. See also* Martha Dragich, *GRAS-Fed Americans: Sick of Lax Regulation of Food Additives*, 49 IND. L. REV. 305, 316 (2016) (describing the "two paths to establishing GRAS status").

[30] INST. OF MED., *supra* note 8, at 27.

which likely pose graver health risks or at least more unknowns that require assessment.[31]

Importantly, the FAA does not specify explicitly what role FDA should play in determining GRAS status, or if it should play any role at all.[32] At present, FDA maintains its long-held position that GRAS determinations are to be made by manufacturers independently without FDA oversight. Given the language of the FAA, FDA asserts that it does not have the statutory authority to require FDA review of independent GRAS determinations or even to require that a manufacturer disclose to FDA that a GRAS determination has been made.[33] Having rendered a GRAS determination, a manufacturer can either: (a) take the substance directly to market; or (b) voluntarily notify FDA of its determination.[34] The choice belongs to the manufacturer.[35] With an understanding of this framework, readers may ask why they should care about food additives. Simply, because food additives are everywhere,[36] and science has not yet adequately confirmed whether or not the prevalence of food additives in our diets has any cumulative or chronic impact on human health.[37]

D. Why Should Consumers Care About Additives?

1. Additives Are Everywhere

In post-WWII America, with demographics shifting from farm to city, additives became increasingly prevalent in food consumed by Americans, a trend that continues today in full force.[38] Additives perform various functions, namely improving or maintaining freshness, adding nutritional value, and enhancing taste, texture, and appearance.[39] As the Congressional Record for the FAA reflects, legislators certainly appreciated that, among other benefits, additives can enhance food appeal and

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[31] *See generally* Ricardo Carvajal & Nisha P. Shah, *On FDA and Food Ingredient Safety: Is the "GRAS" Henhouse at Risk?* 25 LEGAL BACKGROUNDERS (Dec. 3, 2010) at 1, https://www.wlf.org/2010/12/03/publishing/on-fda-and-food-ingredient-safety-is-the-gras-henhouse-atrisk/ [https://perma.cc/T55D-AKWL] (arguing in support of FDA's administration of the GRAS exemption).

[32] Substances Generally Recognized as Safe, 81 Fed. Reg. 54,960, 54,971 (Aug. 17, 2016), https://www.gpo.gov/fdsys/pkg/FR-2016-08-17/html/2016-19164.htm [https://perma.cc/J2L7-D567] ("Although the FD&C Act specifically provides for our [FDA's] review of food additives, it is silent with respect to industry submissions to us [FDA] on the use of GRAS substances.") [hereinafter *Final GRAS Rule*].

[33] *Id.* at 54,981.

[34] *See id.* at 55,019 ("A GRAS notice presents an opportunity [but not the obligation] for you to inform us [FDA] about your conclusion of GRAS status rather than for you to test a hypothesis that there is a sufficient basis to reach a conclusion of GRAS status. If we [FDA] send you an 'insufficient basis letter,' we [FDA] advise you to carefully consider whether marketing the notified substance would be lawful.").

[35] *See id.* at 54,966 (indicating that industry has the discretion to choose whether FDA is to be involved in independent GRAS determinations: "We strongly encourage any company considering addition of a substance to any food on the basis of a conclusion of GRAS status to contact us and follow the available procedure for FDA oversight of such decisions.").

[36] *See* Dragich, *supra* note 29, at 307 (discussing the "plethora" of products in which additives are used).

[37] *Id.*

[38] NEAL D. FORTIN, FOOD REGULATION: LAW, SCIENCE, POLICY, AND PRACTICE 261 (2d ed. 2016).

[39] U.S. GOV'T ACCOUNTABILITY OFF., GAO-10-246, FDA SHOULD STRENGTHEN ITS OVERSIGHT OF FOOD INGREDIENTS DETERMINED TO BE GENERALLY RECOGNIZED AS SAFE (GRAS) 1 (2010) [hereinafter *GAO Report*].

accessibility.[40] But Congress also recognized that additives can operate more perniciously.[41] Occurring in tiny increments, additives might not present immediate acute effects on human health. It remains largely unknown whether additives have a cumulative, long-term impact on human health.[42] As discussed above, this was a central concern that motivated the FAA in the first place.[43] In the absence of advanced concerted research efforts by stakeholders, this question will persist unanswered.[44] As explored below, FDA's current administration of the GRAS exemption severely undermines any attempts by the scientific community to gather the information needed to address this concern.

2. FDA Testing Requirements

Recent FDA guidance emphasizes that food additive petitions and GRAS determinations must meet the same safety standard: reasonable certainty of no harm based on a substance's intended use.[45] For a substance to qualify as GRAS, the reasonable certainty of no harm as to such substance's intended use must, in addition, be common knowledge among qualified experts.[46] Thus, GRAS status attaches only if both requirements are met: the "reasonable certainty of no harm" requirement and the "common knowledge" requirement.[47]

How should evaluators determine that there is "reasonable certainty of no harm"? As guidance for industry, FDA's Redbook sets forth "toxicological principles for the safety assessment of food ingredients," including food and color additives.[48] The Redbook prescribes increasingly rigorous testing based on the "level of concern" assigned to a particular additive, Concern Level I requiring the least rigorous testing and Concern Level III the most.[49] Pursuant to the Redbook, the longest minimum testing period for Concern Level III substances is two years, and in no case does the Redbook call for testing of multiple substances in combination.[50] Certain stakeholders,

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[40] *Id.*

[41] H.R. REP. NO. 2356, 82d Cong., 2d Sess. 3–4 (1952).

[42] *Id.*

[43] *See supra* Section I.B.

[44] *See* Center for Science in the Public Interest, Comment Letter on the Proposed Rule to Use Voluntary Notification Process to Designate GRAS Substances under the Food Additives Amendment of 1958 75–77 (Apr. 15, 2015), https://cspinet.org/sites/default/files/attachment/GRAS%20Comment%20FINAL_0.pdf [https://perma.cc/E64T-ZS9V] (discussing the need for ongoing exposure studies of substances accorded GRAS status) [hereinafter *CSPI Comment Letter*].

[45] *Final GRAS Rule*, *supra* note 32, at 54,961.

[46] *Id.*

[47] *Id.*

[48] *See generally Guidance for Industry and Other Stakeholders: Toxicological Principles for the Safety Assessment of Food Ingredients (Redbook 2000)*, FOOD & DRUG ADMIN. (updated July 2007), http://www.fda.gov/downloads/Food/GuidanceRegulation/UCM222779.pdf [https://perma.cc/A5BM-5AQD] [hereinafter *Redbook*].

[49] *Id.* at 194. *See also* Thomas G. Neltner et al., *Data Gaps in Toxicity Testing of Chemicals Allowed in Food in the United States*, 42 REPROD. TOXICOLOGY 85, 86 (2013) (describing the three concern levels established by FDA) [hereinafter *Data Gaps*].

[50] NAT'L RESEARCH COUNCIL, TOXICITY TESTING FOR ASSESSMENT OF ENVIRONMENTAL AGENTS: INTERIM REPORT 96–99 (2006) (describing FDA testing strategies for food additives). *See generally* Peter Pressman et al., *Food Additive Safety: A Review of Toxicologic and Regulatory Issues*, 1 TOXICOLOGY RES. & APPLICATION 1–22 (2017) (examining safety approaches and procedures pertaining to food additives).

including international regulatory agencies and academic researchers, urge that the methods used to assess the safety of food additives must be reformed to capture the cumulative chronic impact of additives on human health.[51] While short-term testing may indicate that an additive poses little to no harm, minimal information exists about harm resulting from long-term intake or ingestion in combination with other additive and non-additive substances.[52]

3. How Food Additives Occur in Our Bodies: The Cocktail Effect

Scientific developments, particularly studies of the so-called "cocktail effect," suggest that FDA's testing requirements for food additives are inadequate. FDA requires only that each substance be tested in isolation, not in combination with other substances.[53] The "cocktail" or "combination" effect is a phenomenon thought by scientists to result in some cases when substances occur in combination with one another, as they often do in our bodies.[54] Importantly, scientists observe cocktail effects even when each one of multiple substances tested in combination with each other occurs at a level deemed "safe" pursuant to testing currently prescribed by regulators.[55] Early studies of the cocktail effect have shown that, when so combined, substances may interact synergistically to produce magnified toxicity.[56] This synergistic relationship—where the whole is greater than the sum of the parts—suggests that the manner in which regulators have long evaluated the safety of additives, each in isolation, does not reflect how chemicals actually interact in our bodies.[57]

A 2005 University of Liverpool study on the combined effects of certain food additives notes that, while safety of individual food additives is tested widely, "combined adverse effects of [food additives] are unclear and have not been widely studied."[58] The Liverpool study observes that "food additives are typically used in combination within processed foods."[59] That is, in our daily lives, a food additive does

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[51] *See, e.g.*, Andreas Kortenkamp, *Low Dose Mixture Effects of Endocrine Disrupters: Implications for Risk Assessment and Epidemiology*, 31 INT'L J. ANDROLOGY 233 (2007) [hereinafter Kortenkamp, *Mixture Effects*]; Denisa Margina et al., *Overview of the Effects of Chemical Mixtures with Endocrine Disrupting Activity in the Context of Real-Life Risk Simulation*, 1 WORLD ACAD. SCI. J. 157, 157 (2019).

[52] Karen Lau et al., *Synergistic Interactions between Commonly Used Food Additives in a Developmental Neurotoxicity Test,* 90(1) TOXICOLOGICAL SCI. 178, 185 (2006), https://doi.org/10.1093/toxsci/kfj073 [https://perma.cc/JE9E-PMLV] ("Very few long-term experiments have been attempted, and cumulative toxic effects have hardly been explored at all.").

[53] *See generally* Maricel V. Maffini & Thomas G. Neltner, *Brain Drain: The Cost of Neglected Responsibilities in Evaluating Cumulative Effects of Environmental Chemicals*, 69 J. EPIDEMIOLOGY & COMMUNITY HEALTH 496–99 (2015) (discussing the need for cumulative risk assessment of food additives).

[54] *See generally* U.K. COMMITTEE ON TOXICITY, STATEMENT ON FOOD STANDARDS AGENCY-FUNDED RESEARCH ON HEALTH EFFECTS OF MIXTURES OF FOOD ADDITIVES (Dec. 2008), https://cot.food.gov.uk/sites/default/files/cot/cotstatementmixtures200809.pdf [https://perma.cc/FZN3-C5H].

[55] *See generally* Lau, *supra* note 52.

[56] *Id.* at 182 ("[T]he results indicate that both combinations are potentially more toxic than might be predicted from the sum of their individual compounds.").

[57] *Id.* at 185 ("Humans are . . . exposed to . . . complex mixtures of chemicals rather than to individual chemicals, yet they continue to be tested for toxicity in isolation from each other.").

[58] *Id.* at 178.

[59] *Id.*

not occur in isolation.[60] The typical Western diet comprises countless processed additive-laden foods.[61] It might be expected that, when occurring together, chemicals interact in an "additive" manner, or such that the chemicals "are no more and no less effective in combination than they are separately."[62] However, chemicals can also interact synergistically or antagonistically, such that their effectiveness is increased or decreased, respectively, when occurring in combination.[63] In a number of studies, two of which are described below, food additives occurring together or with other non-additive substances have been shown to interact synergistically, suggesting that testing any one additive on its own does not accurately represent the effects of that additive as part of a typical diet.[64]

1. Endocrine Disrupting Chemicals

A 2007 journal article cites that "95% of the resources in toxicological research are devoted to the study of single chemicals, with an almost complete neglect of mixture studies."[65] The author goes on to note that such a pattern of research also applies to endocrine disrupting chemicals (EDCs).[66] EDCs, in great part synthetic, occur in various materials, including additives.[67] As reported by the World Health Organization, EDCs are linked with altered reproductive function, increased incidence of breast cancer, abnormal growth patterns and neurodevelopmental delays in children, and changes in immune function.[68] Propyl gallate[69] and butylated hydroxyanisole,[70] two substances that have received much attention for their potential endocrine disrupting effects,[71] have been deemed GRAS. As a result, they are not subject to pre-

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[60] *Id.* at 185.

[61] *See id.* ("It has been estimated that we have in our bodies between 300 and 500 chemicals that did not exist 50 years ago.").

[62] *Id.* at 179.

[63] *Id.*

[64] *See, e.g.*, *id.* ("Although the use of single food additives at their regulated concentrations is believed to be relatively safe in terms of neuronal development, their combined effects remain unclear.").

[65] Andreas Kortenkamp, *Ten Years of Mixing Cocktails: A Review of Combination Effects of Endocrine-Disrupting Chemicals*, 115 ENVTL. HEALTH PERSP. 98, 98 (2007). *See also* Supratik Kar & Jerzy Leszczynski, *Exploration of Computational Approaches to Predict the Toxicity of Chemical Mixtures*, 7 TOXICS 1, 1–2 (2019).

[66] *Id.*

[67] WORLD HEALTH ORG., STATE OF THE SCIENCE OF ENDOCRINE DISRUPTING CHEMICALS 189 (Åke Bergman et al. eds., 2012), http://www.who.int/ceh/risks/cehemerging2/en/ [https://perma.cc/R9CW-JZAT].

[68] *Id.*

[69] 21 C.F.R. § 184.1660 (2020). Propyl gallate was deemed GRAS pursuant to the GRAS affirmation process, precursor to the GRAS notification process currently in place. The former GRAS affirmation process, like today's GRAS notification process, is one in which manufacturers were not required to participate. See *infra* Section II.B. for more detailed discussion on FDA's administration of the GRAS exemption.

[70] Butylated hydroxyanisole was included on the so-called "GRAS List," an initiative by the Nixon administration to assemble a list of substances in common use before 1958 that were considered GRAS. *Id.* § 182.3169.

[71] Jacque Wilson & Jen Christensen, *7 Other Chemicals in Your Food*, CNN (Feb. 10, 2014), https://www.cnn.com/2014/02/10/health/chemical-food-additives/index.html [https://perma.cc/GYB3-H4HS] (discussing the concern of some scientists about propyl gallate's endocrine disrupting effects). On a list of potential endocrine disruptors released by the European Union, butylated hydroxyanisole is designated

market review by FDA.[72] This is in spite of research conducted on EDCs suggesting that they can cause combination effects.[73] Even where EDCs have been combined at doses below their respective no-observable-adverse-effect levels (NOAELs), together they demonstrate significant synergies.[74] Granted, conflicting studies do exist.[75] But FDA, like the regulatory bodies of other developed countries dedicated to food safety, would be well advised to devote resources to cumulative risk assessment of EDCs, as well as other food additives, so that a definitive conclusion can be had either way.[76]

2. Amplified Effects: Toxicity in Children

The Liverpool study referenced above[77] "examined the neurotoxic effects of two common food additives, each in combination with a common color additive"[78]: (a) L-glutamic acid with Brilliant Blue; and (b) aspartame with Quinoline Yellow.[79] The purpose was to gauge how and to what extent these food-and-color-additive combinations affect the development of neurons, particularly the development that occurs in humans from the sixth month of gestation to several years after birth.[80] Specifically, the authors of the study sought to determine whether these pairs of substances interacted synergistically.[81] The results of the study indicate that the toxicity of the additives may indeed be magnified when they occur together.[82] At the levels tested, which reflect "concentrations . . . theoretically achievable in plasma by

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a "Category 1" substance to be "given the highest priority for further studies." DANISH ENVTL. PROT. AGENCY, THE EU LIST OF POTENTIAL ENDOCRINE DISRUPTORS, https://eng.mst.dk/chemicals/chemicals-in-products/focus-on-specific-substances/endocrine-disruptors/the-eu-list-of-potential-endocrine-disruptors/ [https://perma.cc/C28T-MCL6].

[72] *See supra* Section I.C.

[73] *See* Edna Ribeiro et al., *EDCs Mixtures: A Stealthy Hazard for Human Health?* 5 TOXICS 1, 10 (2017), https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5606671/pdf/toxics-05-00005.pdf [https://perma.cc/GLC7-6BXT].

[74] Kortenkamp, *Mixture Effects*, *supra* note 51, at 98.

[75] *See, e.g.*, COMM. ON TOXICITY OF CHEMICALS IN FOOD, CONSUMER PROD. AND THE ENV'T, ANNUAL REPORT 32–34 (2004), https://cot.food.gov.uk/sites/default/files/cot/cotsection.pdf (discussing the lack of conclusive evidence that EDCs could harm male reproductive health) [https://perma.cc/6GCE-DUVM].

[76] Margina, *supra* note 51, at 160 (discussing the inadequacy of current testing methods in capturing the real-life combination effects of EDCs in humans).

[77] *See supra* Section I.D.iii.1.

[78] Under the FDCA, color additives are governed not by the FAA but rather by a separate Color Additives Amendment (CAA). Unlike the FAA, the CAA contains no GRAS exemption from the definition of "color additive." FOOD & DRUG ADMIN., GUIDANCE FOR INDUSTRY: ASSESSING THE EFFECTS OF SIGNIFICANT MANUFACTURING PROCESS CHANGES, INCLUDING EMERGING TECHNOLOGIES, ON THE SAFETY AND REGULATORY STATUS OF FOOD INGREDIENTS AND FOOD CONTACT SUBSTANCES, INCLUDING FOOD INGREDIENTS THAT ARE COLOR ADDITIVES 10 (June 2014), https://www.fda.gov/media/115075/download [https://perma.cc/5SUZ-2D75] [hereinafter FDA NEW TECHNOLOGIES GUIDANCE].

[79] Lau, *supra* note 52, at 178.

[80] *Id.*

[81] *Id.* at 179.

[82] *Id.* at 178.

ingestion of a typical snack and drink,"[83] the study showed that food additives could very well "interfere with brain development and subsequent function" in children.[84]

The above studies demonstrate how additives, as consumed in the Western diet, may very well be harming human health. When they occur together or with other non-additive substances, food additives may interact synergistically pursuant to the phenomenon referred to as the cocktail effect, whereby additives' harmful properties are amplified beyond what is observed when each additive is tested in isolation.[85] Given this potential for cocktail effect synergies, food additives demand greater scrutiny and must be evaluated to account for the risk they may pose in combination and over a period of years. Under the voluntary GRAS notification system, such food additives may not only skirt pre-market review by FDA, but may also enter the food supply without any notice to the consuming public.[86]

II. GRAS COULD BE GREENER

A. GRAS Roots: How Industry Self-Determination Replaced FDA Oversight

Since the FAA was enacted in 1958, FDA's approach to the GRAS exemption has undergone multiple iterations.[87] As noted previously, the statute itself does not explicitly assign to FDA an active role in the GRAS determination process.[88] Instead, it simply provides that GRAS substances are exempt from the definition of "food additive" and are thus not subject to the food additive petition process, failing to specify who is responsible for determining that a substance is indeed GRAS. Despite the FAA's silence as to who is responsible for making GRAS determinations, the degree to which FDA has chosen to engage in the GRAS determination process has become increasingly tenuous over the decades since the GRAS exemption was first introduced. Initially, FDA began assembling its own list of GRAS substances. Subsequently, FDA adopted a process by which to affirm (or disaffirm) manufacturers' GRAS determinations. Now, FDA simply reviews notifications from manufacturers that GRAS determinations have been made.[89]

In the aftermath of the FAA's enactment, FDA endeavored at the direction of President Nixon[90] to re-assess and document pre-1958 common-use substances considered GRAS in what is referred to as the "GRAS List."[91] In the early 1970s, FDA

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[83] *Id.* at 186.

[84] *Id.* at 185–86.

[85] *Id.* at 182 (describing synergism as occurring when combinations are "more toxic than might be predicted from the sum of their individual compounds").

[86] *CSPI Comment Letter*, *supra* note 44, at 74.

[87] Paulette M. Gaynor, *FDA's Approach to the GRAS Provision: A History of Processes*, Poster Presentation at FDA Science Forum (2006), https://www.fda.gov/Food/IngredientsPackagingLabeling/GRAS/ucm094040.htm (describing FDA's successive approaches to the GRAS provision) [https://perma.cc/WH2Q-VMM9].

[88] *See supra* Section I.C.

[89] *See* Gaynor, *supra* note 87.

[90] *Final GRAS Rule*, *supra* note 32, at 54,963 (discussing the Nixon directive to assemble the GRAS List).

[91] Dragich, *supra* note 29, at 314.

began overseeing a new mechanism, the GRAS affirmation process, pursuant to which a company could, at its election, submit a "GRAS affirmation petition" to FDA for review.[92] If the data provided in a petition supported affirmation of GRAS status, FDA would then engage in administrative rulemaking[93] to expressly provide for GRAS status for the proposed usage of that substance in the Code of Federal Regulation.[94]

The GRAS affirmation process, consisting as it did in notice-and-comment rulemaking, quickly became overly burdensome for FDA.[95] The agency was responsible for overseeing an increasingly complex food supply subject to a continual flow of new, largely synthetic, food and food-related substances.[96] Judging by the backlog in the petitions pipeline, the GRAS affirmation process was not one FDA could handle for long.[97] As a result, in 1997 FDA took tentative steps to replace the GRAS affirmation process with the GRAS notification process.[98] Under the new notification scheme, FDA would not wield notice-and-comment rulemaking procedure in response to GRAS affirmation petitions voluntarily submitted by industry.[99] Instead, FDA would respond by letter to GRAS notifications voluntarily submitted by industry.[100] The GRAS notification process is still in effect today, having formally become FDA policy with the agency's promulgation of the Final GRAS Rule in 2016.[101] At present, each time industry makes a GRAS determination, it has the opportunity—not the obligation—to notify FDA of the same.[102] The GRAS notification process culminates in one of three responses from FDA: (1) a "no questions" letter that in effect greenlights the petitioner's use of the substance; (2) an "insufficient basis" letter in which the agency explains deficiencies it finds in the basis for the petitioner's GRAS determination; or (3) a "cease to evaluate" letter confirming the petitioner's withdrawal of the notification.[103] As the latter suggests, petitioners retain the option, after having submitted a GRAS notification, to withdraw the

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92 *Id.* at 315.

93 In rendering a positive GRAS affirmation, FDA employed the notice-and-comment rulemaking mechanism pursuant to Section 553 of the Administrative Procedure Act, whereby FDA published notice of the given substance and the parameters of its use, solicited public comment, and issued in the Federal Register a final notice for or against GRAS status based on its evaluation of the comments received from the public. *See* 21 C.F.R. § 170.35 (2019).

94 *Id.*

95 *GAO Report*, *supra* note 39, at 5 (describing the GRAS affirmation petition process).

96 *Id.* at 6 (describing the "resource intensive" nature of the GRAS affirmation process).

97 Tom Neltner et al., *Navigating the U.S. Food Additive Regulatory Program*, 10 COMPREHENSIVE REV. FOOD SCI. & FOOD SAFETY 342, 347 (2011), https://onlinelibrary.wiley.com/doi/epdf/10.1111/j.1541-4337.2011.00166.x (discussing the FAA's definition of "food additive") [https://perma.cc/FE75-6PCV] [hereinafter *Navigating*].

98 *Id.*

99 For greater detail on the substantive differences between the GRAS affirmation and notification processes, see Maricel V. Maffini et al., *Looking Back to Look Forward: A Review of FDA's Food Additives Safety Assessment and Recommendations for Modernizing its Program*, 12 COMPREHENSIVE REV. FOOD SCI. & FOOD SAFETY 439, 449 (2013).

100 *Navigating*, *supra* note 97, at 347.

101 *Final GRAS Rule*, *supra* note 32.

102 *Navigating*, *supra* note 97, at 348.

103 *Final GRAS Rule*, *supra* note 32, at 54,967 (describing the categories of letters used to reply to GRAS notices and the typical text of each).

notification, whereupon FDA issues a letter confirming such withdrawal and terminates review.[104] Following receipt of either an "insufficient basis" letter or a "cease to evaluate" letter, a company may choose how to proceed, one choice being continued marketing of the product for use in food.[105] Importantly, both the former GRAS affirmation process and the now-prevailing GRAS notification process are voluntary. Manufacturers were not required to submit petitions for affirmation, nor are they now required to submit notifications of their GRAS determinations.[106]

B. Deficiencies of the Final GRAS Rule

The Final GRAS Rule reflects FDA's long-held position that it lacks the authority to mandate GRAS notification.[107] As noted above, participation in the GRAS notification process is entirely optional. Having made a GRAS determination internally, a manufacturer is free to use and sell the substance at issue without informing any authority.[108] To be clear, the GRAS exemption was included in the FAA because drafters recognized that not all uses of food additives should require pre-market review by FDA.[109] Supporters of the voluntary GRAS notification process point out that, given its limited resources,[110] FDA should not devote time, money, and manpower to assessing the usage of additives extensively evaluated by, and widely approved as safe among, experts. Instead, as is in the public interest, FDA should direct its attention toward the latest innovations in food science about which much less is known.[111] Nevertheless, stakeholders have taken issue with the voluntary GRAS notification process on the grounds that it renders FDA oversight of food additives virtually meaningless.[112]

1. Voluntary is Vacuous

As long as GRAS notification remains voluntary, gaps will continue to exist in the collective knowledge about the American food supply as a whole. As noted above, FDA has clarified that GRAS substances are to be held to the same safety standard as food additives governed by the formal food additive petition process over which FDA presides.[113] Thus, in theory, GRAS substances and food additives alike—irrespective

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[104] *Navigating*, *supra* note 97, at 348.

[105] NRDC REPORT, *supra* note 16, at 9 ("[W]hen a company withdraws a notice and asks FDA to stop further review, the agency issues a letter confirming the withdrawal without publicly explaining any of the concerns that could have prompted the withdrawal. The withdrawal does not prevent the company from continuing to market the product for use in food.").

[106] *How U.S. FDA's GRAS Notification Program Works*, FOOD & DRUG ADMIN. (2006), https://www.fda.gov/Food/IngredientsPackagingLabeling/GRAS/ucm083022.htm [https://perma.cc/2VY4-WJV4].

[107] *Final GRAS Rule*, *supra* note 32, at 54,981–82.

[108] *See generally* NRDC REPORT, *supra* note 16 (detailing the secret nature of GRAS determinations).

[109] Dragich, *supra* note 29, at 313.

[110] *Id.* at 364 (referring to FDA's "broad responsibilities and limited resources").

[111] *See Final GRAS Rule*, *supra* note 32, at 54,961 ("Experience also has shown that streamlining our evaluation of conclusions of GRAS status will enable us [FDA] to evaluate more, and higher priority, substances.").

[112] *See, e.g.*, *CSPI Comment Letter*, *supra* note 44, at 12.

[113] *See supra* Section I.D.2.

of the degree of FDA oversight—are expected to satisfy a common safety threshold.[114] Because industry is not required to notify FDA of its GRAS determinations, there is no way for FDA to certify that the safety standards are being met. Still, even presuming that all industry GRAS determinations do meet the applicable safety standard, the fact that many GRAS determinations are secreted in the coffers of private companies means stakeholders have an incomplete understanding of the food supply.[115] A 2014 report by the Natural Resources Defense Council (NRDC) indicates that "275 chemicals from 56 companies . . . appear to be marketed for use in food based on undisclosed GRAS safety determinations."[116] The report goes on to note that some other reports peg that number at as high as 1,000 undisclosed GRAS determinations.[117] Surely those figures will continue to rise as time goes on.

As the notion of food additives' cocktail effects gains more and more traction in the scientific community,[118] the tattered conception of the overall food supply with which the GRAS exemption leaves us becomes increasingly troubling. Not only do companies face zero accountability for any unfounded GRAS determinations they may make, but also voluntary notification robs stakeholders of the information they need to account for the combination effects of food additives.[119] If scientists do not know and have no way of gauging the full variety and incidence of food additives consumed by the average person over a lifetime, the long-term and combination effects of food additives on human health can never be properly evaluated.[120]

Furthermore, the voluntary GRAS notification process undermines the essential function of judicial and public oversight.[121] Because FDA no longer engages in formal rulemaking as it did pursuant to the GRAS affirmation process, there is no mechanism akin to public notice and comment by which stakeholders can challenge FDA findings before they are finalized. With FDA's formal rule-making having been replaced with informal letter responses, FDA GRAS "decisions" are no longer subject to judicial review as they would have been if embodied in a regulation. Section 704 of the Administrative Procedure Act (APA) provides that courts can only review "final" agency action.[122] If FDA responds to GRAS notifications only with informal letters,

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[114] 21 C.F.R. § 170.35 (2020).

[115] NRDC REPORT, *supra* note 16, at 2.

[116] *Id.* at 2.

[117] *Id.*

[118] Growing traction with respect to the cocktail effects of food additives is demonstrated by the European Commission's EuroMix project, a four-year research endeavor ended in 2019 aimed at uncovering "[t]he truth about our exposure to chemical cocktails [including food additives cocktails] and its impact on our health." Sophie Jensen, *The Truth About Our Exposure to Chemical Cocktails and its Impact on Our Health*, EUROMIX (Mar. 19, 2019), https://cordis.europa.eu/article/id/254166-the-truth-about-our-exposure-to-chemical-cocktails-and-its-impact-on-our-health [https://perma.cc/BK5R-D789].

[119] *CSPI Comment Letter*, *supra* note 44, at 4.

[120] *Id.*

[121] Pew Charitable Tr., *Fixing the Oversight of Chemicals Added to Our Food* (Nov. 7, 2013), http://www.pewtrusts.org/~/media/legacy/uploadedfiles/phg/content_level_pages/reports/foodadditivescapstonereportpdf.pdf [https://perma.cc/4EGR-CH38] (describing the lack of transparency in the GRAS notification system).

[122] *See* 5 U.S.C. § 704 (2018); Fund for Animals, Inc. v. U.S. Bureau of Land Mgmt., 460 F.3d 13, 18 (D.C. Cir. 2006) ("Whether there has been 'agency action' or 'final agency action' within the meaning of the APA are threshold questions; if these requirements are not met, the action is not reviewable.").

i.e., without FDA's attendant issuance of a regulation, then FDA's position on any given substance is not challengeable in court because it is not deemed final agency action.

2. Entrenching Conflicts of Interest

For usage of a substance to be deemed GRAS, the safety of that substance under its intended conditions of use must be common knowledge among qualified experts.[123] Under the Final GRAS Rule, industry can meet this "common knowledge" requirement in a number of ways. These include assembling scientific review articles, convening a panel of experts, or using reports from authoritative bodies.[124] However, various investigations, both internal and external to FDA, indicate that the independent GRAS determination process undertaken by industry is inherently laden with conflicts of interest, which make it unlikely that the appropriate safety threshold is being met.[125] The "experts" that companies hire to make GRAS determinations are often employees of the companies themselves or otherwise employees of consulting firms engaged by the companies.[126] Needless to say, incentives are skewed against fair safety evaluation when evaluators are paid by the substance manufacturers themselves.

Following its issuance of the Final GRAS Rule, FDA released a draft guidance detailing certain "best practices for convening a GRAS panel."[127] In it, FDA recommends that companies "take steps to reduce the risk that bias . . . will affect the credibility of the GRAS panel's report" and limit the scope of the GRAS panel's assessment to publicly available information.[128] While articulation of best practices is a step in the right direction, a guidance is not binding[129] and thus, like the GRAS notification process more generally, is an empty initiative. For one thing, many GRAS determinations are not made in house by the additive manufacturers themselves but rather by the trade organization of which they are a part.[130] The Flavor and Extract Manufacturers Association (FEMA) represents manufacturers of flavoring substances.[131] Using a "standing panel of eight academic experts," FEMA conducts GRAS determinations on behalf of its 119 members,[132] who themselves generally do not participate in FDA's GRAS notification program.[133] Still, FEMA claims to have

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[123] 21 C.F.R. § 170.30(a) (2020).

[124] *GAO Report*, *supra* note 39, at 15.

[125] *Id.*

[126] NRDC REPORT, *supra* note 16, at 11. *See also* Pew Charitable Tr., *supra* note 121, at 9 ("Of the 451 GRAS notifications voluntarily submitted to FDA for review from 1997 to 2012, Pew found that financial conflicts of interest in these decisions are ubiquitous.").

[127] Best Practices for Convening a Generally Recognized as Safe Panel: Draft Guidance for Industry, 82 Fed. Reg. 53,433 (Nov. 16, 2017), https://www.federalregister.gov/documents/2017/11/16/2017-24845/best-practices-for-convening-a-generally-recognized-as-safe-panel-draft-guidance-for-industry [https://perma.cc/6YSG-SR4Q].

[128] *Id.*

[129] *Id.* at 53,433 ("The draft guidance, when finalized, will represent the current thinking of FDA on this topic. It does not establish any rights for any person and is not binding on FDA or the public.").

[130] *GAO Report*, *supra* note 39, at 17.

[131] *Id.*

[132] FEMA ORGANIZATION PUBLIC DIRECTORY, https://members.femaflavor.org/organization_list [https://perma.cc/UC8L-EZQA] (last visited May 2018).

[133] *GAO Report*, *supra* note 39, at 18.

informed FDA of each of its GRAS determinations, "including the name of the substance, its properties, and the basis of the determination."[134] To minimize potential for conflicts of interest, FEMA anonymizes GRAS review and has its panelists disclose information pertaining to their financial interests.[135]

Notwithstanding the minimal transparency that FEMA's extra-agency protocol lends to the food supply,[136] FEMA ultimately is a trade organization whose mission it is to "further[ ] the business interests of its members."[137] And though "safety" and "sound science" are self-proclaimed linchpins of its operations,[138] FEMA is a private entity beholden to its dues-paying members, not a government body with a legal mandate to ensure the integrity of the American food supply.[139] So, while FEMA's self-imposed measures could very well help mitigate risk of undue industry influence, FEMA is itself industry and does not—nor should it—serve as an adequate substitute for government oversight.

3. Can There Be Consensus on Novel Substances?

Stakeholders also decry that the voluntary GRAS notification system has seen industry's application of GRAS status to novel substances.[140] By definition, "generally recognized as safe" should apply only to those substances that experts are aware of and on which there is consensus as to safety.[141] Ironically, there is evidence that in making GRAS self-determinations, companies extend GRAS status to entirely "unknown and unproven substances,"[142] the very practice Congress sought to avoid in passing the FAA.[143] Where authoritative international bodies relate grave concerns about a particular substance, industry cannot reasonably claim there exists general consensus as to the substance's safety.[144]

One class of problematic GRAS determinations comprises engineered nanomaterials. Engineered nanomaterials result from the application of nanotechnology whereby materials manipulated at a molecular scale take on enhanced physical properties.[145] Nanomaterials are perfect examples of "novel substances," which categorically should be ineligible for GRAS status because no scientific consensus exists as to their safety.[146] Indeed, there is wide concern that nanomaterials can accumulate in organs of the body and trigger inflammatory immune responses,

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134 *Id.*

135 *Id.* at 17–18.

136 *See id.* at 17 (explaining the positive aspects of FEMA's participation in GRAS determinations).

137 FEMA MISSION, https://www.femaflavor.org/about [https://perma.cc/KD7L-THYZ] (last visited May 2018).

138 FEMA CORE VALUES, https://www.femaflavor.org/about [https://perma.cc/KD7L-THYZ] (last visited May 2018).

139 21 U.S.C. § 393(b) (2018) (setting forth the mission of FDA).

140 *CSPI Comment Letter*, *supra* note 44, at 18.

141 *Final GRAS Rule*, *supra* note 32, at 54,966–67.

142 *CSPI Comment Letter*, *supra* note 44, at 18.

143 H.R. REP. NO. 2356, 82d Cong., 2d Sess. 3–4 (1952).

144 *CSPI Comment Letter*, *supra* note 44, at 19.

145 *Id.* at 59.

146 *See generally* FDA NEW TECHNOLOGIES GUIDANCE, *supra* note 78.

among other things.[147] Nevertheless, reports suggest that nanomaterials have, by way of undisclosed GRAS self-determinations, entered the food supply as components of food products themselves and food packaging.[148] FDA has in recent years issued guidance containing non-binding recommendations on use of nanotechnology in food.[149] This guidance states that FDA is not aware of any uses of nanomaterials for which there are generally available safety data sufficient as foundation for GRAS status.[150] Unsurprisingly, FDA reports it has not received any GRAS notifications for the usage of nanomaterials.[151] Surely, manufacturers have no inclination to submit GRAS notifications when (1) doing so is not required; and (2) FDA has already made known that a GRAS notification would be met with an "insufficient basis" letter. Thus, the prophylactic measures FDA has taken are self-defeating as they only further motivate manufacturers to conceal their uses of these potentially harmful substances.

4. Definition: What is "Harm"?

Another shortcoming of the Final GRAS Rule is its failure to define "harm."[152] FDA regulation provides that "[s]afe or safety means that there is a reasonable certainty in the minds of competent scientists that the substance is not harmful under the conditions of its intended use."[153] Any substance usage accorded GRAS status must meet that standard.[154] The problem is that FDA has refrained from specifying an appropriate conception of harm to human health. Case studies by the Center for Science in the Public Interest show that some companies' independent GRAS determinations turn on a too-narrow conception of harm: "[I]n the absence of a regulatory definition of harm, industry has literally defined 'GRAS' as anything that will not kill you—a grossly insufficient standard to protect public health."[155] Such a constricted definition of "harm" flouts the spirit of the FAA, which was predicated upon concern that additives in small amounts could lead to chronic health problems over a person's lifetime.[156] Studies on the cocktail effects of food additives have verified that those concerns were well founded as the harm posed by food additives in many cases is not acute but rather chronic in nature.[157] And yet, despite calls for a definition, FDA stated in the Final GRAS Rule that such a development would fall

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147 Rebecca Kessler, *Engineered Nanoparticles in Consumer Products*, 119 (3) ENVTL. HEALTH PERSP. A120, A123 (2011), https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3060016/pdf/ehp-119-a120.pdf [https://perma.cc/9XMZ-2RS3].

148 *Id.*

149 FDA NEW TECHNOLOGIES GUIDANCE, *supra* note 78.

150 *Id.* at 15.

151 *Id.*

152 *Final GRAS Rule*, *supra* note 32, at 54,968.

153 21 C.F.R. § 170.3(i) (2020).

154 *See supra* Section I.D.2.

155 *CSPI Comment Letter*, *supra* note 44, at 53.

156 *See* H.R. REP. NO. 2356, 82d Cong., 2d Sess. 3–4 (1952) ("The potential danger of food additives, indeed, is more insidious [than untested drugs] because it is a danger from the daily intake of small amounts of chemical substances . . . .").

157 NRDC REPORT, *supra* note 16, at 3 ("[C]hemicals added to food are more likely to be associated with health problems that may appear after years of frequent food and beverage consumption. These problems are often chronic in nature. FDA is unlikely to detect an adverse health effect (short of immediate serious injury) unless companies notify it about the chemical and its use in food.").

"outside the scope of this rule" and so declined to expound on what that term actually means.[158]

The Final GRAS Rule, preserving the voluntary GRAS notification program, deprives science and consumers of important information about the American food supply; it enshrines the conflicts of interest that abound when industry is expected to self-police; it does not rectify the trend whereby GRAS status is applied to novel substances; and it fails to require that companies engage in cumulative risk assessment as part of standard safety testing to account for the cocktail effects of additives.[159] In light of these and other shortcomings, many public interest groups have contemplated how, if at all, this system can be reworked.

III. FATE OF THE FINAL GRAS RULE

A. Center for Food Safety Versus Price

In May 2017, the Center for Food Safety (CFS) and other pro-consumer organizations[160] filed a lawsuit against FDA and its leadership on the basis of the recently promulgated Final GRAS Rule, making arguments based in tenets of administrative law.[161] This Section examines whether CFS is likely to prevail on its arguments. CFS alleges that the Final GRAS Rule violates the APA.[162] Specifically, CFS argues that FDA exceeds the statutory authority granted it under the FDCA by effectively placing the additive review process in the hands of private companies by virtue of the voluntary GRAS notification program.[163] Furthermore, CFS contends that FDA's construction of the FDCA—that the FDCA does not grant FDA statutory authority to mandate GRAS notifications—is arbitrary and capricious and thus violates the APA.[164] Discussion in this Article is limited to the latter of these claims.

B. Chevron: Judicial Deference to Agency Interpretation

When reviewing challenges to an agency's statutory interpretation, courts may[165] apply the two-step doctrine of *Chevron* deference.[166] The standard of deference applied determines the degree to which a court will yield to an agency's statutory

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158 *Final GRAS Rule*, *supra* note 32, at 54,968.

159 *See generally id.*

160 In September 2018, Plaintiffs Breast Cancer Fund, Center for Science in the Public Interest, and Environmental Working Group were dismissed from the case for lack of standing. Opinion and Order re: Motion to Dismiss for Lack of Jurisdiction at 17, Ctr. for Food Safety v. Price, No. 1:17-cv-03833 (S.D.N.Y. Sept. 12, 2018).

161 *Groups Sue FDA to Protect Food Safety*, CTR. FOR FOOD SAFETY (May 22, 2017), https://www.centerforfoodsafety.org/press-releases/4956/groups-sue-fda-to-protect-food-safety [https://perma.cc/YND2-QQFG].

162 Complaint for Declaratory & Injunctive Relief at 35, Ctr. for Food Safety v. Price, No. 1:17-cv-03833 (S.D.N.Y. May 22, 2017).

163 *Id.*

164 *Id.* at 36.

165 *See generally* William N. Eskridge, Jr. & Lauren E. Baer, *The Continuum of Deference: Supreme Court Treatment of Agency Statutory Interpretations from Chevron to Hamdan*, 96 GEO. L.J. 1083, 1121 (2008) (explaining, pursuant to an empirical study, when the Supreme Court tends to apply *Chevron* deference and when it applies a different deference regime).

166 Chevron U.S.A. Inc. v. Natural Res. Def. Council, Inc., 467 U.S. 837 (1984).

interpretation as opposed to supplying its own.[167] The *Chevron* standard will likely be applied here because at issue is FDA's interpretation of a statutory provision that it administers, the FAA to the FDCA.[168] Furthermore, the FDCA delegates to FDA the authority to make rules carrying the force of law, and the rule at issue is one promulgated pursuant to that authority.[169] Finally, FDA's statutory interpretation[170] formalized in the Final GRAS Rule is one FDA has held consistently for decades.[171] Step one of the *Chevron* analysis requires that the court determine whether Congress has made its intent known on the specific question at issue.[172] If Congress' intent is clear, then court and agency alike must give effect to it.[173] On the other hand, the court might find that Congress has not addressed the specific question at issue or that its intent on the matter is ambiguous.[174] In that case, the agency's construction of the statute must be given controlling weight unless such construction is "arbitrary, capricious, or manifestly contrary to the statute."[175] In applying the "arbitrary or capricious" standard, "the court may not substitute its own construction of a statutory provision for a reasonable interpretation made by the . . . agency."[176]

If it is found that congressional intent is not clear, the court's next step is to assess the reasonableness of the agency's statutory interpretation.[177] Here, the court is to review FDA's interpretation of the FDCA with regard to GRAS determinations: Does the FDCA give FDA authority to require that industry notify FDA of all independent GRAS determinations it makes? As noted above, FDA has long asserted that the FDCA does not grant it such authority, a position FDA made absolute by promulgating the Final GRAS Rule.[178]

1. Clear Congressional Intent

If Congress has made its intent known with respect to a particular issue, then *Chevron* requires that both court and agency give effect to that intent.[179] To determine

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[167] *See generally* Graham G. Martin & David A. Super, *Judicial Deference to Administrative Agencies and Its Limits*, CLEARINGHOUSE REV. J. POVERTY L. & POL'Y 596 (Mar.–Apr. 2007) (describing the various standards of deference).

[168] Catskill Mountains Chapter of Trout Unlimited v. EPA, 846 F.3d 492, 507 (2d Cir. 2017).

[169] United States v. Mead Corp., 533 U.S. 218, 226–27 (2001) (explaining that *Chevron* is applicable "when it appears that Congress delegated authority to the agency generally to make rules carrying the force of law, and that the agency interpretation claiming deference was promulgated in the exercise of that authority. Delegation of such authority may be shown in a variety of ways, as by an agency's power to engage in adjudication or notice-and-comment rulemaking, or by some other indication of a comparable congressional intent.").

[170] *See Final GRAS Rule*, *supra* note 32, at 54,971 ("This rule replaces one longstanding voluntary administrative procedure with a different voluntary administrative procedure.").

[171] Catskill, 846 F.3d at 521 (explaining that *State Farm* review, as opposed to the *Chevron* standard, may be applicable in a case involving a "rule setting forth a changed interpretation of a statute").

[172] Eskridge & Baer, *supra* note 165, at 1086 (describing the two-step *Chevron* deference inquiry).

[173] *Chevron*, 467 U.S. at 842.

[174] *Id.* at 843.

[175] *Id.* at 844.

[176] *Id.*

[177] Eskridge & Baer, *supra* note 165, at 1086.

[178] *See supra* Section II.B.

[179] *Chevron*, 467 U.S. at 842.

whether Congress has made its intent known, courts are to employ the standard tools of statutory construction, namely the statutory text and structure and the statutory purpose as informed by the statute's legislative history.[180]

Proponents of the Final GRAS Rule will argue that congressional intent as to GRAS substances is made perfectly clear in the FAA. Congress did, after all, include the GRAS exemption in the FAA, providing that GRAS status is to accord with the scientific training and experience of qualified experts."[181] The Final GRAS Rule's voluntary notification process fully gives effect to that intent because industry GRAS determinations are presumably being made by qualified experts, whether by way of in-house specialists or FEMA panels.[182] Nowhere in the FAA did Congress indicate that such independent GRAS determinations are required to be subject of FDA review or even that the companies rendering them are obliged to inform FDA of their decisions.[183] Thus, the GRAS exemption is being administered in accordance with the plain meaning of the statute.[184]

Proponents of the Final GRAS Rule will further argue that the structure of the FAA supports its interpretation with respect to voluntary-versus-mandatory GRAS notifications. In the FAA, Congress sets forth in considerable detail the food additive petition process governing those substances not exempt from the definition of "food additive."[185] The FAA provides expressly that FDA is responsible for administering the food additive petition process.[186] Congress did not do the same in respect of GRAS determinations, indicating that Congress did not intend for FDA to play a part in GRAS determinations.

Finally, proponents, citing the legislative history of the GRAS exemption, will point to the FAA's dual purposes of safety and innovation.[187] Independent GRAS determinations allow FDA to devote more of its resources to food additive petitions wherein the true innovations in food technology—and risks to human health—are presented.[188] Congress could not have intended that FDA divert substantial resources away from food additive petitions and direct them instead toward assessment of GRAS substances. By allowing manufacturers to render their own GRAS determinations, the voluntary notification process of the Final GRAS Rule streamlines development and application of food technology and ensures that substances posing greater potential dangers are made FDA's priority.[189]

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[180] *Chevron*, 467 U.S. at 843 n.9.

[181] 21 U.S.C. § 321(s) (2018).

[182] *See generally Final GRAS Rule*, *supra* note 32.

[183] 21 U.S.C. § 321(s) (2018).

[184] 21 U.S.C. § 321(s) or § 321(s).

[185] *See* INST. OF MED., *supra* note 8, at 30 (describing the food additive petition process as being "governed by fairly precise statutory procedures formulated by Congress").

[186] 21 U.S.C. § 348(b) (2018).

[187] *See supra* Section I.C. (discussing Congress' dual motivations for enacting the FAA).

[188] INST. OF MED., *supra* note 8, at 27.

[189] Carvajal & Shah, *supra* note 31, at 1.

2. Ambiguous Congressional Intent

Opponents of the Final GRAS Rule will argue that the FAA's text is ambiguous, failing to make clear Congress' intent as regards FDA's role in the GRAS determination process. The FAA's silence with respect to FDA's role in GRAS determinations is not a wholesale negation of FDA's role but rather a gap in the statute's language that FDA is expected to fill. Accordingly, pursuant to step two of the *Chevron* analysis, the court must determine whether FDA's interpretation of the FAA is reasonable.[190] A reasonable interpretation is one "supported by a reasoned explanation that sets forth a reasonable interpretation of the [statute]."[191]

Courts often refer to a statute's legislative history and contemplate the statute as a whole to help assess the reasonableness of an agency's statutory construction.[192] Opponents of the Final GRAS Rule will argue that the legislative history of the FAA indicates that it was enacted primarily to combat entry of unknown substances into an increasingly processed American food supply.[193] Indeed, Congress passed the FAA for the very purpose of replacing post-market review of food additives with pre-market review based on adequate science.[194]

Taking the FAA as a whole, opponents will point to the fact that Congress accorded "food additive" an expansive definition[195] and devoted the bulk of the Amendment to describing in detail the process by which FDA is to issue in each instance a regulation approving a particular use of a food additive.[196] Therefore, it may be deduced that Congress intended for the food additive petition process, not the GRAS exemption, to be the predominant regulatory channel through which new substances enter the market.[197] That is why GRAS status is termed a mere exemption to the food additive petition process, not the controlling process itself.[198]

The Final GRAS Rule's voluntary GRAS notification scheme completely contravenes the purpose of the FAA and Congress' intended mechanism for pre-market additive review. A study funded by The Pew Charitable Trusts reveals that approximately 1,000 manufacturer safety decisions have never been reported to FDA or otherwise.[199] An additional 2,000 decisions have been rendered by expert panels convened by FEMA, whose decisions are reported in trade publications but not

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[190] Catskill Mountains Chapter of Trout Unlimited v. EPA, 846 F.3d 492, 520 (2d Cir. 2017) (describing "*Chevron* Step Two").

[191] *Id.* at 507.

[192] Eskridge & Baer, *supra* note 165, at 1136.

[193] *See* Pub. L. No. 85-929, 72 Stat. 1784 (1958) (setting forth the long title of the FAA: "An Act to protect the public health by amending the Federal Food, Drug, and Cosmetic Act to prohibit the use in food of additives which have not been adequately tested to establish their safety").

[194] *NRDC Report*, *supra* note 16, at 3.

[195] *See Navigating*, *supra* note 97, at 343.

[196] 21 U.S.C. § 348 (2018).

[197] *See* NRDC REPORT, *supra* note 16, at 3 (arguing that the GRAS exemption has "swallowed" the food additive petition process).

[198] *But see Final GRAS Rule*, *supra* note 32, at 54,984 (responding to objections that the term GRAS "exemption" is not appropriate based on the language of the FAA).

[199] *Navigating*, *supra* note 97, at 367.

reviewed by FDA.[200] An NRDC report indicates that "[s]ince [year] 2000, almost all new chemicals have passed through the [GRAS] loophole rather than being subjected to the food additive petition process established by Congress in 1958."[201] These findings demonstrate that, by virtue of the current voluntary GRAS notification regime, the GRAS exemption renders the pre-market review mechanism defunct. The GRAS exemption does not function as such.[202] What Congress intended to be an exemption to the rule now operates as the rule itself, resulting in the troubling fact that food additives largely are not subject to pre-market review.[203] Thus, the Final GRAS Rule is contrary to the FAA and is thus unreasonable.[204] As a result, FDA's interpretation of the FAA should not be accorded deference on judicial review.

Supporters of the Final GRAS Rule, however, will surely argue that the purpose of the FAA is two-fold: protection of consumer health and "sound progress in food technology."[205] The voluntary GRAS notification process gives effect to the latter of these two policy goals. Rather than wait months for FDA review, companies can engage qualified experts to assess safety and proceed to market without the headache and expense of regulatory red tape and inefficient government oversight.[206] A happy result is that FDA can devote more of its time, money, and manpower to evaluation of food additive petitions, which pose true potential for health risks.[207] The Final GRAS Rule does not contravene congressional intent. Rather it fulfills congressional intent, if only in part.

a. Second Circuit Precedent on Reasonableness

In the 2017 Second Circuit case *Catskill Mountains Chapter of Trout Unlimited, Inc. v. EPA*, the court examined the reasonableness of the Water Transfers Rule, a regulation promulgated by the Environmental Protection Agency (EPA) under the Clean Water Act (CWA).[208] Pursuant to its Water Transfers Rule, EPA formalized its long-time stance that water transfers are not subject to the requirements of the National Pollutant Discharge Elimination System (NPDES) permitting program.[209] Opponents of the Water Transfers Rule argued that water transfers should be subject to NPDES permitting requirements because "water transfers can move harmful pollutants from one body of water to another, potentially putting local ecosystems, economies, and public health at risk."[210] Such a result, they contended, would be in direct

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[200] Pew Charitable Tr., *supra* note 121, at 5.

[201] NRDC REPORT, *supra* note 16, at 4.

[202] *Id.*

[203] *Id.*

[204] Catskill, 846 F.3d at 507 ("We will not disturb an agency rule at *Chevron* Step Two unless it is "arbitrary or capricious in substance, or manifestly contrary to the statute.").

[205] *See supra* Section I.C. (discussing Congress' dual motivations for enacting the FAA).

[206] Ilene Ringel Heller, *Functional Foods: Regulatory and Marketing Developments*, 56 FOOD & DRUG L.J. 197, 198 (2001) (discussing industry complaints about the costs of the food additive petition process).

[207] *See* INST. OF MED., *supra* note 8, at 49 (describing the backlog in FDA's review of food additive petitions).

[208] *Catskill*, 846 F.3d at 506.

[209] *Id.* at 504.

[210] *Id.* at 500.

contravention of the CWA's "overall goal of restoring and protecting the quality of the nation's waters," making the Water Transfers Rule unreasonable.[211]

Still, the Second Circuit held that, though the Water Transfers Rule may not represent an interpretation of the CWA "best designed to achieve the [statute's] overall goal . . . it is nonetheless an interpretation supported by valid considerations."[212] In other words, the court found EPA's interpretation to be reasonable because it is "supported by several valid arguments—interpretive, theoretical, and practical."[213] Among its reasons for interpreting that the CWA does not require water transfers to be subject to NPDES permitting, EPA had invoked the "broader statutory scheme" of the CWA, pointing out that the statute provides for other ways that water transfer pollution could be mitigated.[214] EPA had also pointed to the CWA's statutory purpose and explained that a practical effect of an alternative interpretation would be to limit states' ability to effectively allocate water and water rights, in part because permittees would face burdensome costs.[215] By virtue of EPA having articulated an interpretation supported by valid considerations, the court found the agency's interpretation to be reasonable.[216]

b. Is the Final GRAS Rule Reasonable?

A deference-worthy agency interpretation is one "supported by a reasoned explanation that sets forth a reasonable interpretation of the [statute]."[217] Just as EPA did to support its interpretation of the CWA, FDA invokes valid considerations to support its interpretation of the FAA, including glaring practical concerns. FDA has limited resources.[218] FDA points out in the Executive Summary to the Final GRAS Rule that "streamlining our [FDA's] evaluation of conclusions of GRAS status will enable us to evaluate more, and higher priority, substances."[219] FDA also points to the fact that, in practice, firms do participate meaningfully in the voluntary notification process. FDA holds that "[t]he ongoing submission of GRAS notices during the Interim Pilot program demonstrates that the food industry is actively submitting GRAS notices."[220]

In opposition to calls for extending permit requirements to water transfers, EPA cited that the CWA provides for means other than permitting by which to mitigate water pollution.[221] In its Final GRAS Rule, FDA mentions means alternative to mandatory GRAS notification that promote transparency in and regulation of the American food supply. Companies can seek FDA review by partaking of the formal

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[211] *Id.* at 501.

[212] *Id.*

[213] *Id.* at 520.

[214] *Id.* at 524.

[215] *Id.*

[216] *Id.* at 525.

[217] *Id.* at 507.

[218] *See Final GRAS Rule, supra* note 32, at 55,023 (acknowledging FDA's goal of using resources efficiently and effectively).

[219] *Id.* at 54,961.

[220] *Id.* at 54,982.

[221] *Catskill*, 846 F.3d at 524 (2d Cir. 2017).

food additive petition process. Private individuals can utilize citizen petitions to challenge the GRAS status conferred on a substance.[222] Pursuant to the Freedom of Information Act (FOIA), third parties can compel FDA to release information on voluntary GRAS notifications submitted by companies.[223] FDA itself can employ regulatory agency action such as declaratory orders[224] and warning letters[225] to order unsafe or questionable substances off the market.[226] FDA could also conduct audits to "monitor compliance with the essence of the statutory requirements for GRAS status (i.e., that there is common knowledge among qualified experts that there is reasonable certainty that the substance is not harmful under the conditions of its intended use)."[227]

Opponents of the Final GRAS Rule will point out, however, that the FDA-supplied list of alternatives to mandatory GRAS notification is deficient. Noted repeatedly in this Article, companies make little use of the formal food additive petition process because they are not obliged to do so; instead, they simply opt out of classification, in legal terms, as a "food additive" by exploiting the GRAS loophole.[228] FDA's pointing to demonstrated industry participation in voluntary GRAS notification is not satisfactory; concern here is with respect to the many more GRAS determinations that are not subject of notification.[229] Furthermore, individuals and organizations can only utilize citizen petitions with respect to FDA, not as a tool of engagement with private companies who make in-house GRAS determinations unbeknownst to FDA, let alone to the general public.[230] As long as a company independently determines GRAS status, choosing not to participate in FDA's voluntary GRAS notification program, a citizen petition is futile because the company alone knows that such a GRAS determination has been made.[231] Similarly, FOIA reaches only government actors.[232] To the extent companies can elect to divorce their GRAS determinations from FDA oversight—made possible by the GRAS loophole—FOIA does not compel release of information by private companies.[233] While these alternative means enhance oversight of the American food supply to some extent, none tackle the problem posed by self-made GRAS determinations that are not disclosed to FDA or the public. That is, none of

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[222] In the Final GRAS Rule, FDA does not explicitly address citizen petitions as an alternative to mandatory GRAS notification. However, FDA does in the context of requests for expedited GRAS review refer to citizen petitions as a mechanism by which parties can prompt FDA action. *See Final GRAS Rule*, *supra* note 32, at 55,030.

[223] *Id.* at 54,980.

[224] *See, e.g.*, *id.* at 54,965.

[225] *See, e.g.*, *id.* (discussing the warning letters issued by FDA regarding GRAS use of caffeine in cola-type drinks).

[226] *Id.* at 54,983.

[227] *Id.* at 55,030.

[228] Maricel V. Maffini et al., *Looking Back to Look Forward: A Review of FDA's Food Additives Safety Assessment and Recommendations for Modernizing its Program*, 12 COMPREHENSIVE REV. FOOD SCI. & FOOD SAFETY 439, 449 (2013) ("Today, virtually all new chemicals added directly to food rely on the GRAS program rather than the food additives petition process established by Congress.").

[229] *See supra* Section II.B.1. (discussing statistics reported by NRDC as to the prevalence of undisclosed GRAS determinations).

[230] *See CSPI Comment Letter*, *supra* note 44, at 76.

[231] *See id.* at 76–77.

[232] 5 U.S.C. § 552 (2018).

[233] *See CSPI Comment Letter*, *supra* note 44, at 77.

foregoing tools amount to pre-market review. Instead, they operate as post-market review such that the burden is shifted away from industry and on to FDA and the public to demonstrate that a substance is not safe.

Finally, regulatory powers as exercised by FDA, for example declaratory orders and warning letters, are meaningful insofar as FDA knows to exercise them. For example, FDA issued warning letters in 2010 against four companies that marketed the addition of caffeine to their alcoholic beverages.[234] Likewise, in 2015, FDA issued a declaratory order denying GRAS status for use of partially hydrogenated oils (PHOs) in human food.[235] In the former case, warning letters could be effectively wielded because the companies stated in their labelling that the products were alcoholic beverages containing added caffeine—that is, the companies openly declared the additive as a facet of their marketing scheme.[236] In the latter case, some PHOs had been deemed GRAS by virtue of their having been commonly used prior to 1958 and others by regulation or scientific procedure.[237] Use of PHOs was on FDA's radar because the substances' GRAS status had not been rendered behind the shroud of industry self-policing and FDA's labelling regime happened to capture the substances' use in food. As further discussed below, this is often not the case when manufacturers make undisclosed GRAS determinations.

Unlike the two foregoing examples, many substances added to food escape detection by FDA because companies make independent GRAS determinations that skirt FDA oversight of food additives. Additionally, many substances are exempted from FDA ingredient labelling requirements, and companies are not otherwise required to disclose the substances' presence in food. For example, "[i]f an ingredient is present at an incidental level and has no functional or technical effect in the finished product, then it need not be declared on the label."[238] Also, a substance qualifying as, or as a component of, a spice or flavor can be listed under blanket terms like "spices," "flavor" or "natural flavor," or "artificial flavor," terms which shed little light on the underlying components or their properties.[239] These loose labeling requirements allow undisclosed GRAS determinations to funnel into the food supply undetected.

In spite of the foregoing arguments against the reasonability of a voluntary GRAS notification process, the court may be hard-pressed to find that the Final GRAS Rule is anything other than reasonable given binding Second Circuit precedent. As in EPA's Water Transfers Rule, FDA's Final GRAS Rule sets forth the agency's reasoning for settling on an entirely voluntary GRAS notification procedure. And though they may leave some feeling far from satisfied that FDA's interpretation effectively champions

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234 *Final GRAS Rule*, *supra* note 32, at 54,978.

235 *Id.*

236 *See Caffeinated Alcoholic Beverages*, FOOD & DRUG ADMIN. (Nov. 17, 2010), http://wayback.archive-it.org/7993/20170406022220/ https://www.fda.gov/Food/IngredientsPackaging Labeling/FoodAdditivesIngredients/ucm190366.htm [https://perma.cc/3GDM-GUHJ] (describing with accompanying images the products of the four manufacturers of caffeinated alcoholic beverages who were issued warning letters).

237 *See generally* Final Determination Regarding Partially Hydrogenated Oils, 80 Fed. Reg. 34,650 (June 17, 2015).

238 *FDA Guidance for Industry: A Food Labelling Guide*, FOOD & DRUG ADMIN. (Jan. 2013) https://www.fda.gov/downloads/Food/GuidanceRegulation/GuidanceDocumentsRegulatoryInformation/ UCM265446.pdf [https://perma.cc/H8CB-PKU8].

239 *Id.*

the "principal focus" of the FAA, the reasons offered by FDA to justify its interpretation are reasons still.[240]

In summary, it is probable that the reviewing court would grant *Chevron* deference to FDA's Final GRAS Rule. Accordingly, the court would rule against CFS in its claim that the voluntary nature of the Final GRAS Rule contravenes the FAA and so violates the APA. FDA would point to the dual purpose of the Food Additives Amendment and contend that the Final GRAS Rule helps fulfill both: voluntary and less resource intensive, the Final GRAS Rule advances the policy of progress in food technology by doing away with a regulatory hurdle for manufacturers and allowing FDA to focus its resources on other riskier areas of the food supply. FDA articulates its reasoning for holding that it does not have the statutory authority to compel GRAS notification—even if that reasoning fails the FAA's overall goal of creating a safer food supply based on pre-market review of food additives. Consequently, FDA's interpretation of the FAA and its voluntary GRAS notification program would be upheld.

IV. PROPOSALS FOR REFORM OF GRAS NOTIFICATION

Even if the court upholds the Final GRAS Rule, the public may still look to Congress for statutory reform of the FAA. If indeed it were to reexamine the FAA, Congress would be well advised to better delineate the scope and mechanics of the GRAS exemption. First and foremost, GRAS notification should be made mandatory in all cases. As research on the cocktail effect demonstrates, sound science demands that FDA and other stakeholders be apprised of the entirety of the food supply, and that demand cannot be met if manufacturer-made GRAS determinations are allowed to be withheld from FDA and the general public. To compensate for the strain that a mandatory GRAS notification program would foist upon FDA, all participants in the program (i.e., all manufacturers making GRAS determinations) should be required to pay a user fee. Fee-based programs administered by federal regulatory bodies, including FDA itself, are numerous.[241] Structuring GRAS notification as a fee-based program would simply be a continuation of an existing practice and would allow FDA to handle the resulting influx in GRAS notifications that it would receive. In addition, Congress should expressly provide that GRAS status may not attach to novel substances. FDA, in turn, should be expressly delegated the task of developing a definition for "novel substance."[242]

In furtherance of adding transparency to the food supply as a whole, Congress should explicitly define "harm" to encompass both the acute and the chronic. Comprehensive testing requirements, namely cumulative risk assessment, would be a natural corollary to this reformulated definition of "harm." GRAS determinations should be made to include data not just on the substance at issue but also on the effects of that substance as just one component of an expansive matrix of substances. Congress should expressly delegate to FDA the task of developing standardized

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[240] *See generally Final GRAS Rule*, *supra* note 32.

[241] *See generally* JAMES MACDONALD ET AL., U.S. DEP'T OF AGRICULTURE, USER-FEE FINANCING OF USDA MEAT AND POULTRY INSPECTION, AGRIC. ECONOMIC REPORT NO. 775 (Mar. 1999) https://www.ers.usda.gov/webdocs/publications/40973/51055_aer775.pdf?v=42073 [https://perma.cc/K6QX-6AHY]; *Id.* at 6 (listing federal agencies reliant on user fees).

[242] *Final GRAS Rule*, *supra* note 32, at 54,976 ("We [FDA] do not have a regulatory definition for a 'novel' substance.").

methodologies by which to conduct such cumulative risk assessment.[243] Admittedly, both the development of standards for and the application of cumulative risk assessment are demanding undertakings. As a result, manufacturers and FDA alike should be allowed and even encouraged to work with their counterparts in the international community who have already begun such initiatives, including the European Food Safety Authority and Food Standards Australia New Zealand.[244]

CONCLUSION

To achieve Congress' intent in enacting the Food Additives Amendment, regulation of substances added to foods must account for the cumulative, chronic effects on human health. The Final GRAS Rule as it currently stands does not fulfill this mandate. Investigations have demonstrated that the GRAS exemption administered as a voluntary notification program continues to be abused, allowing substances that have been inadequately tested or even affirmatively shown by third parties to cause long-term harm to enter into the American food supply. Advances in cumulative risk assessment both in the United States and elsewhere indicate that, given the high incidence of additives in the Western diet, pre-market safety testing must include examination of any given additive in combination with others with which it is likely to be ingested. Though, based on precedential application of administrative law, the Final GRAS Rule is likely to withstand judicial review, the public can and should demand that their congressional representatives rework the Food Additives Amendment such that it provides for a mandatory fee-based GRAS notification program, a legal definition of "harm" that includes chronic impact on human health, and cumulative risk assessment as a predicate to GRAS status. Only then can we as consumers have some measure of confidence that we are fully aware of what we put in our shopping carts.

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[243] *See* Kortenkamp, *Mixture Effects*, *supra* note 51, at 236 (describing the need for cumulative risk assessment and the application of biomarkers to capture cumulative internal exposures).

[244] *See generally* Bernadene Magnuson et al., *Review of the Regulation and Safety Assessment of Food Substances in Various Countries and Jurisdictions*, 30 FOOD ADDITIVES & CONTAMINANTS: PART A 1147 (2013).