
Generally Recognized as Secret: Chemicals Added to Food in the United States

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EXECUTIVE SUMMARY

When President Eisenhower signed the Food Additives Amendment of 1958, he established a regulatory program intended to restore public confidence that chemicals^a added to foods are safe. In the intervening 56 years, the basic structure of the law has changed little. However, the regulatory programs the U.S. Food and Drug Administration (FDA) established to implement the law have fallen behind over time as the agency strived to keep up with the explosion in the number and variety of chemicals in food, and to manage its huge workload with limited resources.

The 1958 law exempted from the formal, extended FDA approval process common food ingredients like vinegar and vegetable oil that are “generally recognized as safe” (GRAS). It may have appeared reasonable at the time, but that exemption has been stretched into a loophole that has swallowed the law. The exemption allows manufacturers to make safety determinations that the uses of their newest chemicals in food are safe without notifying the FDA. The agency’s attempts to limit these undisclosed GRAS determinations by asking industry to voluntarily inform the FDA about their chemicals are insufficient to ensure the safety of our food in today’s global marketplace with a complex food supply. Furthermore, no other developed country in the world has a system like GRAS to provide oversight of food ingredients.

Because of the apparent frequency with which companies make GRAS safety determinations without telling the FDA, NRDC undertook a study to better understand companies’ rationale for not participating in the agency’s voluntary notification program. First, we built a list of companies and the chemicals they market. Then we reviewed public records, company websites, and trade journals to identify additives that appear to be marketed in the U.S. pursuant to an undisclosed GRAS determination, i.e. without notification to the FDA.

All told, we were able to identify 275 chemicals^a from 56 companies that appear to be marketed for use in food based

on undisclosed GRAS safety determinations. This is likely the tip of the iceberg—we previously published in an industry journal an estimate that there have been 1,000 such secret GRAS determinations.¹ For each chemical we identified in this study, we did not find evidence that FDA had cleared them.

In addition, using the Freedom of Information Act (FOIA), we obtained from the FDA copies of communications between the agency and companies who voluntarily sought agency review of their GRAS determinations. We found this glimpse into the review process shows that often the agency has had serious concerns about the safety of certain chemicals, and that companies sometimes make safety decisions with little understanding of the law or the science. As discussed later, companies found their chemicals safe for use in food despite potentially serious allergic reactions, interactions with common drugs, or proposed uses much greater than company-established safe doses.

On those occasions when the FDA is asked to review a GRAS determination, the agency rejects or triggers withdrawal of about one in five notices. Moreover, the public has even less information about the many substances with GRAS determinations that are never submitted to the agency in the first place—and which may pose a much greater danger. It is often virtually impossible for the public to find out about the safety—or in many cases even the existence—of these chemicals in our food.

“Generally Recognized as SECRET” rather than “Generally Recognized as SAFE” is a better name for the GRAS loophole that has allowed manufacturers to sanction the use of hundreds of chemicals in food that Americans eat every day.

^a We use the term “chemicals” to apply to the products sold by additive manufacturers. They may be individual substances or mixtures of substances. They are sometimes referred to as substances, additives, or ingredients, which, in reality, are all chemicals or mixtures of them. They may be extracted from natural products or synthesized from other chemicals.

"We cannot require anything, as this is a voluntary program and we don't want to frighten anyone away. Having said that, we would typical [sic] tell any notifier that their submission would have to address the total dietary exposure from new and current uses, [h]ow else could you conclude that the uses were safe, without a notion of what total exposure is[?]"²

FDA reviewer of GRAS determination submitted by manufacturer

NRDC believes that "Generally Recognized as SECRET" rather than "Generally Recognized as SAFE" is a better name for the GRAS loophole. A chemical additive cannot be "generally recognized as safe" if its identity, chemical composition, and safety determination are not publicly disclosed. If the FDA does not know the identity of these chemicals and does not have documentation showing that they are safe to use in food, it cannot do its job.

In an increasingly global marketplace where many additives and foods are imported into the United States, this loophole presents an unsettling situation that undermines public confidence in the safety of food and calls into question whether the FDA is performing its duty to protect public health.

The problem is rooted in a law adopted in 1958 when Dwight Eisenhower was president and Elvis was drafted. It is time for the FDA and Congress to fix the problems. In the meantime, consumers need to demand that their grocery stores and their favorite brands sell only those food products with ingredients that the FDA has found to be safe.

GRAS: HOW THE LOOPHOLE SWALLOWED THE LAW

Over the last five years, there have been many news stories about unsafe foods that have sickened people. There have been a few reports of acute health problems related to chemicals added to foods, such as energy drinks containing a mixture of caffeine and alcohol, or rice with excessive amounts of the vitamin niacin. But chemicals 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. The 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.

That is why Congress required that a chemical's intentional use in food be determined to be safe prior to its entering the marketplace.³ In 1958 President Eisenhower signed the Food Additives Amendment to the Federal Food Drug and

Cosmetic Act to address these concerns.⁴ The law presumed that a chemical intentionally added to food was potentially unsafe and required that no chemical be used without a "reasonable certainty in the minds of competent scientists that the substance is not harmful under the intended conditions of use."⁵ Congress required food companies to file a "food additive petition" as the primary means by which to get an FDA approval of a chemical's use in food. If the agency did propose to approve the chemical, it would inform the public and request comments before adopting a regulation allowing the use.⁶ The system was designed at a time when an estimated 800 chemical additives were in use, far fewer than the more than 10,000 allowed today.^{7,8}

"The next day, [notifier] called and asked whether [notifier] would have an option to withdraw the notice rather than receive a letter that the notice did not provide a basis for a GRAS determination. I replied that this was an option. On September 4, [notifier] asked whether [notifier] could still sell its [name] product if it withdrew its GRAS notice. Consistent with my response to her earlier question about marketing [name], I said yes."⁹

FDA officer summarizing telephone conversations with manufacturer regarding its GRAS notice review

Determining that a chemical's use in food is and remains safe typically involves significant professional judgment. Rarely are these decisions clear cut; there is no bright line. So who decides is critical. Congress concluded that the FDA would make all safety decisions, except in the most obvious situations in which a chemical's use in food was "generally recognized as safe." This is known as the GRAS exemption. Examples include such common food ingredients as oil and vinegar. When a chemical's use was determined to be GRAS, the FDA did not need to adopt a regulation specifically allowing its use, and the formal public notice and comment rulemaking process was not required.¹⁰ In other words, the

chemical didn't need premarket approval by the agency, and manufacturers could use it without delay. To qualify as GRAS, a chemical's safety had to be generally recognized by knowledgeable scientists, as borne out by published safety studies unless commonly and safely used before 1958.¹¹

However, the FDA and the food industry interpreted the law as allowing manufacturers to determine that a chemical's use in food was safe without notifying the agency.¹² As a result, the identity of the chemical and the foods in which it was being used could be unknown to the public and the agency. Since 1958, an estimated 1,000 chemicals have been determined as GRAS by manufacturers and have been used in food without any approval or review by the FDA.¹³ The exemption has become a loophole that has swallowed the law.

THE FDA'S ATTEMPTS TO LIMIT UNDISCLOSED INDUSTRY SAFETY DECISIONS

Recognizing the problem of undisclosed safety decisions, the FDA adopted regulations in 1972 inviting manufacturers to voluntarily submit "GRAS affirmation petitions" in a rulemaking process that was similar to the one for food additive petitions, but without statutory deadlines for action.¹⁴ Companies sought FDA's approval, it appears, because their product would be more widely accepted by food manufacturers.

By the early 1990s, confronted with limited resources and an increasingly complicated and time-consuming formal rulemaking process, the FDA faced an overwhelming backlog of unresolved reviews.¹⁵ In response, the agency proposed a rule in 1997 to replace the 1972 GRAS petition process with a less formal review process that did not involve adopting regulations for specific chemicals.¹⁶ The next year, the FDA began accepting voluntary notifications from the companies that summarized the safety evidence and issuing decision letters.¹⁷ In some cases, these decision letters are often cited by the companies as evidence of FDA clearance, although the agency maintains that the letters are informal and do not constitute approval. This process, however, largely cuts the public and outside experts out of meaningful participation in decision making. The proposed rule has never been finalized despite its wide use by industry and the FDA.¹⁸ Since 2000, almost all new chemicals have passed through the loophole rather than being subjected to the food additive petition process established by Congress in 1958.

In 2010, the Government Accountability Office (GAO), the nonpartisan investigative arm of Congress, scrutinized the agency's GRAS program and found serious shortcomings. It concluded that "FDA's oversight process does not help ensure the safety of all new GRAS determinations" and that "FDA is not systematically ensuring the continued safety of current GRAS substances."¹⁹

Given these concerns, NRDC sought to identify examples of chemicals marketed pursuant to undisclosed GRAS safety determinations, procure such safety determinations from companies, and examine why companies choose to forgo even the voluntary FDA notification process.

CLAIMING GENERAL RECOGNITION WHILE AVOIDING DISCLOSURE

As mentioned above, some 1,000 chemicals have been determined by manufacturers to be safe for use in food without FDA review or approval. Some of them, like artificial *trans* fat, were self-certified by industry as safe ingredients decades ago and are well known.

NRDC's investigation focused on newer, less known chemicals marketed as GRAS for use in food in the United States since 1997. We looked at situations in which:

- the manufacturer opted to rely on an undisclosed GRAS determination, without using the FDA's voluntary notification process;
- the manufacturer notified the FDA, and the agency subsequently rejected the company's GRAS notice;
- the manufacturer notified the FDA but subsequently withdrew its notice from FDA review. (We will discuss the problems with withdrawal of notices later.)

Our investigation began with a list of companies and chemicals from three sources:

- the little-known (outside of the food additives industry) web-based "GRAS Self-Determination Inventory Database," compiled by a consulting firm that makes GRAS safety determinations for industry;²⁰
- consultants who provided company names based on their experience at food industry trade shows;
- withdrawn or rejected notices in FDA's GRAS Notice Inventory.²¹

Overall, we identified 398 chemicals marketed by 163 companies that appear to be marketed in the U.S. based on GRAS determinations not reviewed by FDA.^b

For each chemical, we sought a copy of the written documentation of the GRAS safety determination required by FDA's regulations (21 CFR §170.30), which companies must have completed before marketing a product as GRAS. This documentation must provide the chemical composition of the substance, describe how it is made, estimate how much people are likely to consume (exposure), and describe what is known about the chemical's potential hazards. Unless a chemical was commonly and safely used before 1958, the key studies evaluating the hazards ordinarily must be published, preferably in a peer review journal but the FDA does not exclude publication on a company's website. While identifying a key study is helpful, it is not a substitute for providing the full safety determination.

Where a company appeared to be marketing a chemical for use in the United States as GRAS without final FDA review, NRDC contacted the company to request a copy of the

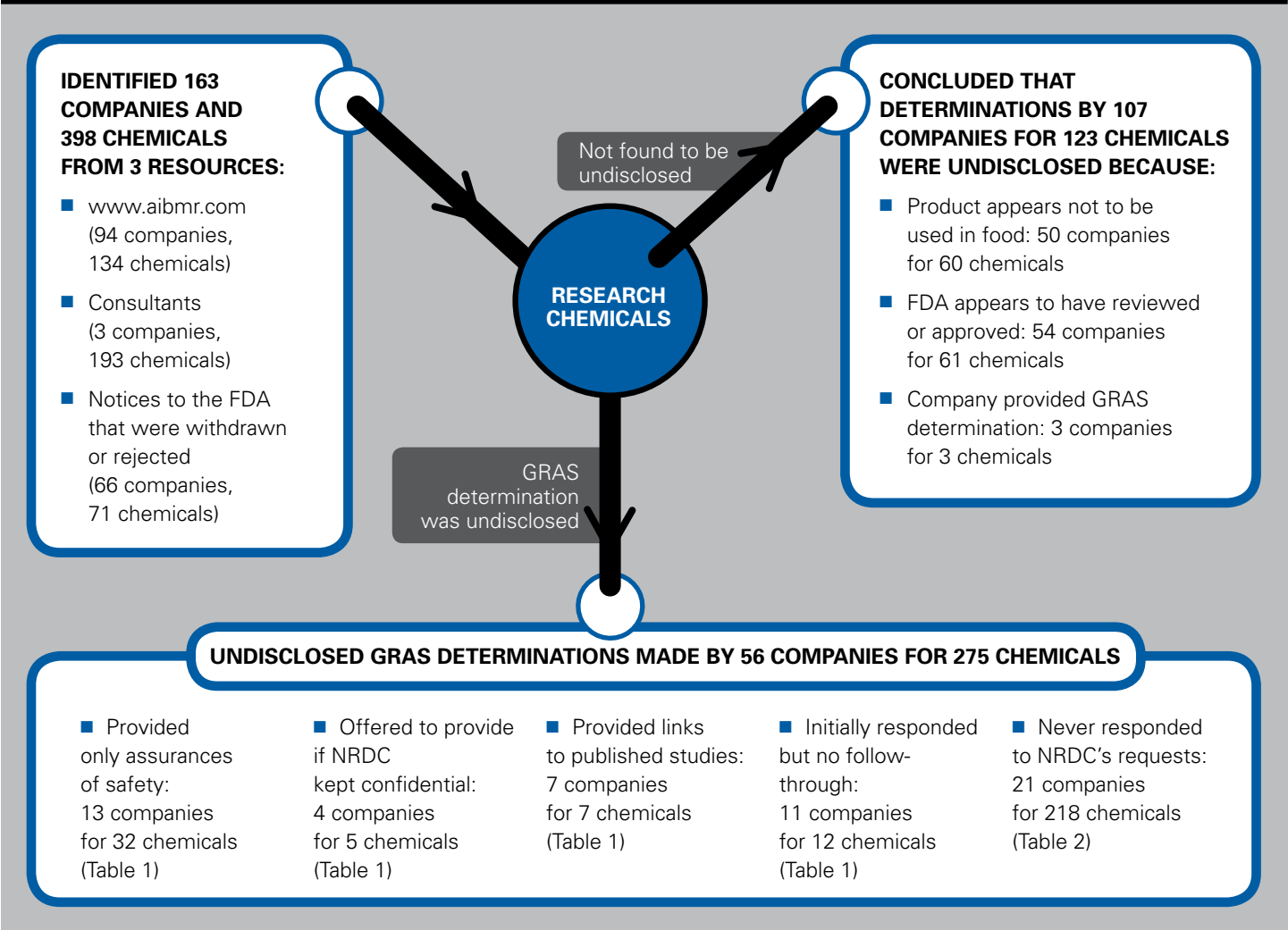
undisclosed safety determination. If the company declined or did not respond to our request, we classified the GRAS determination as "undisclosed". Also, if the company did not provide us with a revised GRAS determination that addressed the FDA's concerns after the agency rejected the company's notice, or if the company withdrew its notice before the agency made a final decision, we considered the GRAS determination to be undisclosed.

"GENERALLY RECOGNIZED AS SECRET"

All told, 56 companies appear to rely on undisclosed GRAS safety determinations for 275 chemicals (Figure 1):

- 35 companies selling 57 chemicals responded to our inquiries, but did not provide their GRAS safety determination (Table 1).
- 21 companies selling 218 chemicals did not respond to our repeated inquiries (Table 2).

Figure 1: Process to Identify and Evaluate Companies and Chemicals



^b Where chemicals had similar names but different manufacturers, we treated them as separate chemicals.

Table 1: Companies with undisclosed GRAS determinations that responded to NRDC

Company	Country	No. of Chemicals	Declined Requests	Only if Confidential	Only Gave Studies	No Follow-up
Albion	USA	2	Yes	Yes		
Aloecorp	Korea	1				Yes
BASF	Germany	2				Yes
BioCell Technology	USA	1	Yes			
Bioriginal	Canada	1	Yes	Yes	Yes	
ChromaDex	USA	1				Yes
Cyvex Nutrition	USA	3	Yes			
DSM	Netherlands	8	Yes			
Embria Health Sciences	USA	1	Yes			
ESM Technologies	USA	1	Yes		Yes	
Frutarom Health	Israel	1				Yes
Genosa	Spain	1	Yes			
GTC Nutrition	USA	1				Yes
HG&H Pharmaceuticals (Pty) Ltd.	South Africa	1	Yes			
House Wellness Foods	Japan	1	Yes			
InterHealth Nutraceuticals	USA	4	Yes			
Ixoreal Biomed	India	1				Yes
Jungbunzlauer	Switzerland	1	Yes			
Kaneka	Japan	1	Yes		Yes	
Kemin	USA	1	Yes			
Lonza	Switzerland	1				Yes
Merck Eprova AG	Germany	1	Yes		Yes	
NattoPharma	Norway	1				Yes
NuLiv Science	USA	1	Yes		Yes	
NutraGenesis	USA	4	Yes			
P.L. Thomas	USA	1				Yes
PhenoFarm	Italy	1				Yes
RIBUS	USA	1	Yes			
Sabinsa Corporation	USA	5	Yes			
SoluBlend Technologies	USA	1	Yes	Yes		
Stepan	Netherlands	1	Yes			
Trace Minerals Research	USA	1	Yes		Yes	
TSI Health Sciences	USA	1	Yes	Yes		
Unibar	USA	1				Yes
Verdure Sciences Trim	USA	1	Yes		Yes	
Totals	35 companies	57	24	4	7	11

The 35 companies that responded but did not provide us with their GRAS determinations fit into the following four categories:

- 13 companies provided us only with assurances that their chemicals were safe and complied with the law.
- 4 companies were willing to share the documentation only if NRDC signed a confidentiality agreement, which we declined to do.
- 7 companies declined to provide the GRAS determination but identified a published toxicology study that supported their analysis without providing the additional information such as exposure calculations and product composition needed to evaluate the safety.
- 11 companies acknowledged the inquiry but did not follow through.

The remaining 107 companies selling 123 chemicals fell into three general categories:

- 50 companies did not appear to market their chemicals for use in food in the United States.^c
- 54 companies that withdrew notices to the FDA later submitted revised notices and received a final review by the agency confirming product safety.
- 3 companies provided NRDC with a copy of their GRAS determination without requiring confidentiality.

Figure 2 summarizes our findings. Of the 163 companies we reviewed, 56, or 34 percent, appear to rely on undisclosed GRAS determinations.

UNDISCLOSED SAFETY DETERMINATIONS: NOT JUST U.S. COMPANIES

As stated earlier, no other developed country in the world has a system like GRAS for food ingredients.²² On the basis of each company's website and communications, NRDC identified the home country of the 56 companies with undisclosed GRAS determinations. See Tables 1 and 2. Figure 3 provides the results by region.

Fifty-six percent of the companies are from the United States, and 44 percent are based outside the country. This distribution is similar to what one might see at a typical food expo.

WHY DID COMPANIES FORGO FDA REVIEW?

About 20 companies provided explanations for why they decided not to submit a voluntary notification to the FDA. These can be distilled into the following categories:

- **Concerns about too much FDA transparency.** The most common concern was the FDA's routine posting of GRAS safety determinations to its website. These companies said they were worried that easy access to information about product composition and the manufacturing process would enable competitors to develop identical or similar chemicals and would simplify the competition's own GRAS determinations.
- **Concerns about FDA delays.** Several companies claimed they did not want to wait for the FDA to make a decision, even though the agency explicitly allows the use and marketing of a chemical while a review is under way.

*"In other words, if a panel of experts reviews data that are not publicly available and subsequently renders an opinion regarding safety, even if the experts are well-recognized, the opinion does not meet the general recognition of safety for GRAS ingredients because the data were not publicly available."*²³

FDA reviewer of GRAS notice

^c Either these chemicals appear to be used only in dietary supplements and not food, or we could not find an active website for the company or the chemical, or the chemicals appear to be marketed only overseas.

- **Desire to keep investment low.** Submitting a GRAS determination to FDA typically means additional work whether by company employees or a consultant doing the analysis. The agency asks many questions that must be answered. Often there are meetings with the agency. We found that almost all of the chemicals NRDC reviewed were also ingredients in dietary supplements and served no essential purpose in food other than to attract consumers' attention. Several companies indicated that a GRAS determination sometimes is done in connection with a test of the food market for a chemical previously used only as a dietary supplement ingredient, thus minimizing the investment in an unproven market by opting out of the FDA review process.
- **Wish to avoid new dietary ingredient review:** The Dietary Supplement Health and Education Act of 1994 (DSHEA) requires manufacturers to notify FDA about dietary ingredients that either were not on the market before 1994 or whose use in food is not GRAS. Several dietary supplement manufacturers appear to be making a GRAS determination to avoid having to notify the FDA under both DSHEA and the Food Additives Amendment of 1958.
- **Misunderstanding of the law:** Some companies apparently did not understand the requirements for a GRAS determination. It appears that they did not realize that the determination must be written, that safety information must be drawn from published scientific studies, or that "generally recognized as safe" means more than obtaining the opinion an employee or consultant. Others apparently believed that an independent panel of experts was required even though the FDA states that no panel is needed.²⁴ Finally, some companies appeared not to understand the difference between an efficacy study, which determines whether a chemical is effective in addressing a health problem, and a toxicology study, which evaluates whether a chemical may cause harm. The scope of most efficacy studies falls far short of an adequate toxicology study.

Figure 2: Undisclosed vs. Resolved GRAS Determinations

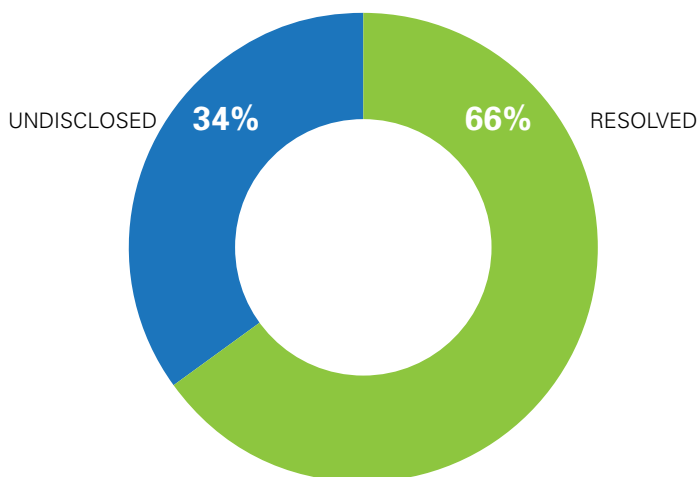
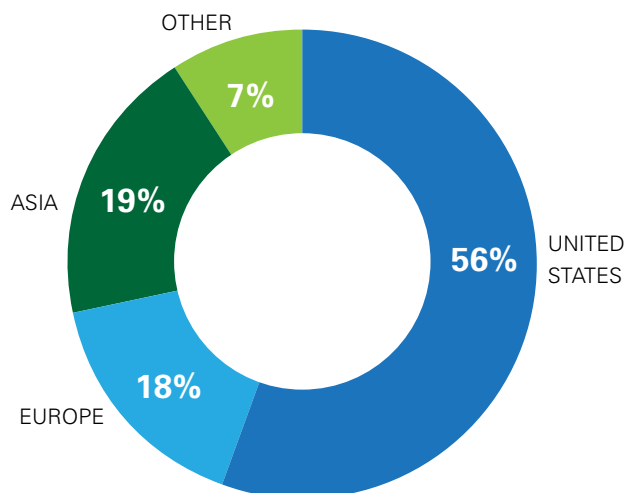


Figure 3: Undisclosed GRAS Determinations by Company's Region



FDA REVIEWS OF NOTICES REVEALED TROUBLING RISKS

As described earlier, companies may voluntarily submit GRAS notices (which contain the GRAS safety determination) to FDA seeking the agency's agreement with their safety determination, and when they do, the agency posts these notices on its website. We reviewed the quality of the industry's notices and identified three, still under review by the FDA as of September 2013 (listed as "pending" on the FDA site), that appeared to be poorly done. They were GRN No. 466 for polyglycerol polyricinoleic acid by McCormick and Co., GRN No. 471 for annatto seed extract by DeltaGold, and GRN No. 474 for Bioperine by Sabinsa Corp.^{25,26,27} All three had the same weaknesses: limited toxicology data, poor or inadequate exposure assessment, and lack of consideration of children's exposures. For each we submitted to the FDA detailed comments on the shortcomings of the safety determinations.²⁸ See www.nrdc.org/food/safety-loop-hole-for-chemicals-in-food.asp.

If the FDA rejects a GRAS notice, it explains its safety concerns in a letter to the company and publishes the letter on the agency's website. But when 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.

Between 1998 and the end of February 2014, the FDA rejected 17 out of 466 notices submitted to the agency; another 32 are still pending. During that time, 80 notices were withdrawn by the companies. For notices no longer pending, one out of five were either withdrawn or rejected.²⁹

After analyzing the poor quality of notices and the number of withdrawn notices, NRDC filed a FOIA request for communications between the FDA and manufacturers for 20 GRAS notifications. We chose notices for chemicals whose use in food we were able to document through a commercial database³⁰ that provides product information for more than 200,000 food products; and the notices were submitted throughout the length of the program, starting in 1998. Sixteen of these notices were withdrawn, several of them multiple times. Although interested primarily in understanding what concerns raised by FDA prompted manufacturers to ask the agency to stop reviewing the notices, we also included two notices that the agency rejected and two that FDA accepted as sufficient, issuing what is known as a "no questions" letter. To see the FDA's FOIA response, go to www.nrdc.org/food/safety-loop-hole-for-chemicals-in-food.asp.

The FOIA documents reveal that the FDA does carefully review the notifications and asks tough questions. The agency's reviews often raise serious safety concerns or reveal that the company's scientific analysis is flawed or inconsistent with the law. Often the FDA tells the company that it will reject a notice if it is not voluntarily withdrawn. If rejected, food manufacturers would be more reluctant to buy the product since FDA posts its rejection letter and its reasoning on its website.

The following are examples of four withdrawn GRAS notices and our summary of the back-and-forth communications between the FDA and manufacturers. Despite the safety concerns, these chemicals have been listed as an ingredient in some food products:

Epigallocatechin-3-gallate (EGCG):

A Japanese company declared this chemical to be GRAS for use in beverages including teas, sport drinks, and juices, despite evidence it may cause leukemia in fetuses based on studies using newborn and adult human cells grown on a dish.³¹ Moreover, the company did not address a short-term study on rats showing it affected the thyroid, testis, spleen, pituitary, liver, and gastrointestinal tract. The notice did not explain potentially dangerous interactions with sodium nitrite, a common preservative, or with acetaminophen (the active ingredient in Tylenol® and many other over the counter pain-killers).³² The company withdrew the notice, resubmitted it, but withdrew that one as well.³³ In response to our inquiries, the company assured us it was not marketing the product in the United States. However, two other companies, DSM and Kemin, appear to market chemicals high in EGCG in the United States pursuant to undisclosed GRAS determinations (Table 1). We identified more than 25 food products with EGCG as a named ingredient.

Gamma-amino butyric acid (GABA):

A Japanese company declared this neurotransmitter to be GRAS for use in beverages, chewing gum, coffee, tea, and candy.³⁴ It did so despite having estimated exposure well in excess of what the company considered safe, relying on unpublished safety studies, providing the specifications in Japanese, and failing to consider existing exposures.³⁵ The company told NRDC that it withdrew the notice "from a business perspective" and was selling the product in the United States only as an ingredient in a dietary supplement. It also indicated that it would not use the chemical in food without an FDA final review. We identified five food products with GABA as a named ingredient. These products included bottled tea and nutrition bars.

Sweet lupin protein, fiber, and flour:

An Australian firm declared these chemicals to be GRAS for use in baked goods, dairy products, gelatin, meats, and candy, despite concerns that the chemicals would cause allergic reactions in those with peanut allergies.³⁶ The FDA noted that a warning label for sweet lupin would be insufficient to alert consumers who suffered from peanut allergies.³⁷ The company did not respond to our inquiries and we could not find evidence that the company was marketing the product in the U.S. However, sweet lupin was a listed ingredient in more than 20 food products, none of which appear to bear any warning to those allergic to peanuts.

Theobromine:

A U.S. firm declared it to be GRAS for use in bread, cereal, beverages, chewing gum, tea, soy milk, gelatin, candy, and yogurt and fruit smoothies, despite having an estimated consumption rate more than five times the safe consumption level reported by the company's consultant.³⁸ In addition, the manufacturer did not provide convincing explanations for the testicular degeneration in rats and rabbits and delayed bone formation in rats that were seen in animal studies of theobromine.³⁹ The FDA was especially concerned that the product would be used in baby food.⁴⁰ The company did not respond to our inquiries. Although we don't know the provider, theobromine was a named ingredient in more than 20 food products, including isotonic waters, nutrition bars, and diet foods. Fortunately, from what we could tell, none appeared in baby food.

The evidence from these FOIA responses makes it clear: the FDA's review adds value, and many companies' GRAS safety determinations are seriously flawed. The agency should make its concerns publicly available when companies withdraw their notices. Chemicals that, at least in some instances, prompted the FDA to raise safety concerns are used as ingredients in our food supply, and consumers are unprotected from their health effects.

Table 2: Companies with undisclosed GRAS determinations that did not respond to NRDC*

Company	Country	No. of Chemicals
ADM	USA	1
AHD International	USA	1
Ametis JSC	Russia	1
Applied Food Sciences	USA	2
CBC Group	USA	1
Davos Life Sciences	Singapore	1
FutureCeuticals	USA	1
Gencor Pacific	USA	1
Hamari Chemicals	Japan	1
Hanzhong TRG Biotech	China	32
Horizon Science	USA	1
Kyowa Hakko	USA	2
Laurus Labs	India	1
Naturex	Canada	4
Nexira	France	1
NutraMax	China	154
Oxis International	USA	1
Skyherb	China	7
Terry Laboratories	USA	1
Triarco Industries	USA	2
Ventria Bioscience	USA	2
Totals	21 companies	218 chemicals

*In each case, we confirmed that we had either a: 1) confirmation from the company's website that the webform was accepted; or 2) valid email address from website because we did not get a notice from the company's email server that the email had bounced or was not deliverable.

MANY GRAS CHEMICALS BEGAN AS DIETARY SUPPLEMENT INGREDIENTS

Most of the GRAS chemicals NRDC examined were primarily marketed as “active” ingredients in dietary supplements. The availability of the GRAS loophole allows for the expansion of the market for such into conventional foods with claims that they made food “better for you.” The chemicals were often extracts of plants or highly purified or synthetic versions of the biologically active chemicals in those extracts, such as antioxidants, which were purported to have possible health benefits.

Since the Dietary Supplement Health and Education Act of 1994⁴¹, when Congress created separate, less rigorous safety standards for dietary supplements under DSHEA, there has been an explosion of these products. Ingredients allowed in dietary supplements are not necessarily safe when used in conventional food.

A product may be a natural extract or a highly purified version of one, but that does not necessarily mean it is safe. In 2014, the FDA recognized the safety threat when it issued guidance regarding substances added to foods, including beverages and dietary supplements.⁴² The agency stated:

“We have seen a growth in the marketplace of beverages and other conventional foods that contain novel substances, such as added botanical ingredients or their extracts. Some of these substances have not previously been used in conventional foods and may be unapproved food additives. Other substances that have been present in the food supply for many years are now being added to beverages and other conventional foods at levels in excess of their traditional use levels, or in new beverages or other conventional foods. This trend raises questions regarding whether these new uses are unapproved food additive uses.”⁴³

It is likely that had the FDA reviewed the undisclosed GRAS determinations, it would have found some to be unapproved food additives.

THE SYSTEM IS BROKEN AND PLAGUED WITH CONFLICTS OF INTEREST

When the FDA reviewed GRAS determinations made by manufacturers, the agency found flaws with one in five, based on the number of notices rejected or withdrawn prior to a final decision.⁴⁴ These notices presumably were those in which the manufacturer’s had the most confidence, since the manufacturers voluntarily submitted them for agency scrutiny.

Food manufacturers are ultimately responsible for the safety of the food they make. However, in today’s highly competitive global marketplace, there are strong economic incentives to minimize expenditures, which may lead to insufficiently-justified decisions. Our understanding of the health effects of many of the more than 10,000 chemicals allowed in food is far from complete, and as the number grows over time, concerns grow as well. For example, some manufacturers still consider *trans* fats to be GRAS despite the FDA’s concluding that it causes eight deaths a day in the United States and that if it were banned from food, our country would realize more than \$117 billion in health benefits including reduced healthcare costs over 20 years.⁴⁵

Here is another issue of serious concern. For years, companies have used their own employees or hired consultants to evaluate their chemicals’ safety and then relied on such undisclosed safety determinations to market their products for use in food. This raises serious conflict-of-interest concerns because a company’s financial benefit from selling a particular product can bias its employees’ or contractors’ judgment.⁴⁶ The lack of independent review in GRAS determinations compromises the integrity of the process and calls into question whether it can effectively ensure the safety of the food supply.⁴⁷

The FDA has acknowledged that a company’s potential legal liability and its interest in protecting its brand are insufficient to ensure that food is safe.⁴⁸ In 2013 the agency said, “Because the demand for many manufactured or processed foods may not be sufficiently affected by safety considerations, incentives to invest in safety measures from farm to fork is diminished. Consequently, the market may not provide the incentives necessary for optimal food safety.”⁴⁹

“Even in cases where consumers are aware that their illness was contracted from a specific food,” the FDA explained, “it is often difficult to determine who is ultimately responsible for their illness, since the particular source of contamination is not known in many circumstances.”⁵⁰ It concluded that “it is unlikely that the existence of brands in the food sector creates the optimal level of safety for society.”⁵¹

As the Institute of Medicine explained in the context of medical safety, conflicts of interest can result in bad decisions.⁵² Similarly, undisclosed safety determinations affecting the food that Americans eat may be undermining public health. Without FDA and public scrutiny—as Congress intended that there be—we cannot be confident in the safety of chemicals added to food.

CONCLUSIONS

A chemical additive cannot be “generally recognized as safe” if its identity, chemical composition, and safety determination are not publicly disclosed. Congress never intended that almost all new food chemicals would pass through the GRAS loophole without formal agency review and approval. The law places responsibility on FDA to ensure that food additive petitions are submitted for additives without general recognition of safety and to ensure that manufacturers’ GRAS determinations are properly made. If the FDA does not know the identity of these chemicals and does not have documentation showing that their uses in food are safe, it cannot not do its job.

In an increasingly global marketplace where many additives and foods are imported into the United States, this loophole presents an unsettling situation that undermines public confidence in the safety of food and calls into question whether the FDA is performing its duty to protect public health. Until conflicts of interest are minimized and safety decisions are subject to mandatory FDA review, the safety of chemicals in food will depend largely on the integrity and competence of food manufacturers. That is not in the public’s best interest, because manufacturers have a financial incentive that may bias their judgment about an additive’s safety.

When consumers buy dietary supplements, they make a choice to consume chemicals that the FDA has not reviewed for safety. Indeed, under the law, consumers must be told that FDA has not reviewed the health claims made for ingredients in dietary supplements. As a result, dietary supplements carry labels disclosing that they have not been reviewed for safety by the FDA. However, when buying food, consumers can’t make informed choices because they don’t know which ones contain reviewed chemicals or which contain substances not reviewed by the FDA for safety. There are no warning labels. There is no disclosure. As a consequence, they may unknowingly be putting their health at risk. The current processes allowing this to occur should be addressed and changed to better protect the health of the American public.

NRDC’S RECOMMENDATIONS

The problems identified in this report are rooted in a law adopted more than a half century ago. Ultimately, Congress needs to fix these problems. Until it does, the FDA should implement the recommendations made by the GAO in 2010 including strictly limiting conflicts of interests and requiring that the FDA be informed of GRAS determinations so it can confirm that the chemical’s use in food is generally recognized as safe. The agency should also make its concerns with all notices it reviews, even those that are withdrawn, publicly available.

In the meantime, consumers should demand that their grocery stores and their favorite brands sell only food products with ingredients that the FDA has found safe, and call on the FDA and Congress to make the necessary changes to better ensure that food consumed in the U.S. is safe.

ENDNOTES

- 1 Thomas G. Neltner et al., "Navigating the U.S. Food Additive Regulatory Program," *Comprehensive Reviews in Food Science and Food Safety* 10 (2011), p. 342.
- 2 NRDC, Main FDA Response to FOIA, 2014, p. 210, www.nrdc.org/food/files/chemicals-in-food-FOIA-Main.pdf regarding GRN No. 257.
- 3 21 U.S.C. § 321(s) and § 348.
- 4 Pub. L. No. 85-929, 72 Stat. 1784 (1958).
- 5 21 C.F.R. § 170.3(i).
- 6 21 U.S.C. § 348. Fred H. Degnan, *FDA's Creative Application of the Law*, Food Drug Law Institute, 2000, p. 25.
- 7 Degnan, p. 22.
- 8 Neltner, "Navigating," p. 342.
- 9 NRDC, GRN No. 59 FDA Response to FOIA, 2014, p. 271, www.nrdc.org/food/files/chemicals-in-food-FOIA-59.pdf.
- 10 21 U.S.C. §§ 321(s), 348(a).
- 11 21 C.F.R. § 170.30. Neltner, "Navigating," p. 347.
- 12 Ibid.
- 13 Ibid. Unlike individual food manufacturers, since 1963 the flavor industry has publicly identified its chemicals and their allowed uses for those it found to be GRAS. It also submitted its safety documentation to the agency. See Flavor and Extract Manufacturers Association, *About the FEMA GRAS Program*, www.femaflavor.org/gras (accessed March 4, 2014).
- 14 21 C.F.R. § 170.35.
- 15 Neltner, "Navigating," p. 347; Linda S. Kahl to Docket No. FDA-1997-N-0020, *Substances That Are Generally Recognized as Safe (GRAS); Experience with GRAS Notices* (Nov. 4, 2010), p. 26. Degnan, p. 32.
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- 19 Government Accountability Office, *Food Safety: FDA Should Strengthen Its Oversight of Food Ingredients Determined to Be Generally Recognized as Safe (GRAS)*, 2010, p. 8, 20, www.gao.gov/products/GAO-10-246.
- 20 American Institute for Biosocial and Medical Research, GRAS Self-determination Inventory Database, www.aibmr.com/resources/GRAS-database.php (accessed November 15, 2013).
- 21 FDA, GRAS Notice Inventory, www.accessdata.fda.gov/scripts/fdcc/?set=GRASNotices (accessed November 15, 2013).
- 22 Magnuson B et al., "Review of the regulation and safety assessment of food substances in various countries and jurisdictions," *Food Additives & Contaminants: Part A*. 2013. DOI: 10.1080/19440049.2013.795293
- 23 NRDC, Main FDA Response to FOIA, 2014, p. 207, www.nrdc.org/food/files/chemicals-in-food-FOIA-Main.pdf regarding GRN No. 257.
- 24 Kahl, p. 5.
- 25 FDA, GRAS Notice Inventory, GRN No. 466. www.accessdata.fda.gov/scripts/fdcc/?set=GRASNotices. The FDA issued a "no questions" letter before the NRDC submitted its comments.
- 26 Ibid, GRN No. 471. It was pending as of February 28, 2014.
- 27 Ibid, GRN No. 474. It was withdrawn before the NRDC submitted its comments.
- 28 NRDC, Comments on GRN No. 466, 2013, www.nrdc.org/food/files/chemicals-in-food-GRN-466.pdf and NRDC, Comments on GRN No. 471, 2013, www.nrdc.org/food/files/chemicals-in-food-GRN-471.pdf and NRDC, Comments on GRN No. 474, 2013, www.nrdc.org/food/files/chemicals-in-food-GRN-474.pdf.
- 29 As of February 28, 2014, the FDA's website listed 498 notices with 32 pending, 80 withdrawn, and 17 rejected because they had an insufficient basis to determine the chemical was GRAS. $20.8\% = (80+17)/(498-32)*100\%$.
- 30 See www.gladson.com. March 15, 2013 version
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- 32 Ibid.
- 33 FDA, GRAS Notice Inventory, GRN No. 259.
- 34 FDA, GRAS Notice Inventory, GRN No. 257.
- 35 NRDC, Main FDA Response to FOIA, 2014, p. 206, www.nrdc.org/food/files/chemicals-in-food-FOIA-Main.pdf.
- 36 FDA, GRAS Notice Inventory, GRN Nos. 262, 263, and 264 and NRDC, Main FDA Response to FOIA, 2014, p. 218, www.nrdc.org/food/files/chemicals-in-food-FOIA-Main.pdf.
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- 39 Ibid, p. 223.
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- 49 Ibid., p. 2.
- 50 Ibid., p. 3.
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- 52 Bernard Lo and Marilyn J. Field, eds., *Conflict of Interest in Medical Research, Education, and Practice* (Washington, D.C.: National Academies Press, 2009).

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