United States Government Accountability Office

Report to Congressional Requesters

November 2022

FOOD SAFETY

FDA Oversight of Substances Used in Manufacturing, Packaging, and Transporting Food Could Be Strengthened

GAO-23-104434

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GAO Highlights

Highlights of GAO-23-104434, a report to congressional requesters

Why GAO Did This Study

Thousands of food contact substances are available for use in manufacturing, packaging, and transporting food. These substances are used, for example, in food wrappers and in the lining of metal food cans. Academic, consumer, and other stakeholders have raised concerns that some of the substances may, by themselves or in combination with other substances, contribute to adverse health effects, such as thyroid disease and hormone disruption.

This report (1) identifies the primary means that companies use to bring food contact substances to the market and describes FDA's premarket safety review process and (2) examines FDA's postmarket safety review actions and the limitations of such reviews. To conduct this work, GAO interviewed FDA officials and stakeholders and reviewed, among other things, FDA documents and the agency's website for actions it took from January 2000 to May 2022 to stop the use of potentially unsafe substances.

What GAO Recommends

GAO is making two recommendations to FDA to (1) request from Congress specific legal authority to compel companies to provide the information needed to reassess the safety of substances and (2) track the dates of the last reviews for all food contact substances to allow FDA to readily identify substances that may warrant postmarket review. FDA neither agreed nor disagreed with the first recommendation and agreed with the second recommendation.

View GAO-23-104434. For more information, contact Steve D. Morris at (202) 512-3841 or morriss@gao.gov.

What GAO Found

The Department of Health and Human Services' Food and Drug Administration (FDA) has primary responsibility for reviewing the safety of food contact substances before and after they enter the market. These substances come into contact with food during processes such as manufacturing, packaging, and transporting food (see fig.). Such substances may migrate into food, where they could pose a risk to human health. FDA conducts premarket reviews of the safety of substances largely by reviewing companies' submissions of supporting evidence before substances enter the market. FDA bases its postmarket reviews on safety information, including new information published since the substance's initial approval for use.

Source: Ivan/stock.adobe.com. | GAO-23-104434

Some food contact substances are used to greaseproof hamburger and French fry containers.

Since 2000, FDA has helped to stop the use of three types of unsafe substances, such as some per- and polyfluoroalkyl substances (PFAS) that are used to greaseproof food packages. These substances may cause health effects, such as liver damage. However, FDA faces two limitations that impede a risk-informed, postmarket review process for food contact substances:

- FDA does not have specific legal authority to compel companies to provide information and data on substances' safety and extent of use. FDA needs such information to prioritize and conduct postmarket reviews. FDA officials said they have begun to develop options to systematically reassess the safety of food additives, which include food contact substances, in response to a House Appropriations Committee report. Also, FDA has a strategic plan to improve data-driven, postmarket surveillance of substances added to the food supply. In its report to the committee, FDA could support its strategic plan and have additional options for obtaining information on food contact substances if it requested specific authority to compel companies to provide information and data on food contact substances' safety and use.
- FDA staff can search the agency's information system for each food contact substance and find the date of the last premarket review. However, FDA's system cannot readily identify all substances that, according to their last review dates, may warrant additional review because new safety information may have emerged. Tracking review dates in a way that allows FDA to identify these substances may help address challenges FDA faces in making risk-informed decisions on which substances to prioritize for postmarket review.

Contents

Figures

Abbreviations

BPA	Bisphenol A
CEDI	cumulative estimated daily intake
CLARITY-BPA	Consortium Linking Academic and Regulatory Insights on BPA Toxicity
EFSA	European Food Safety Authority
FCN	food contact substance notifications
FDA	Food and Drug Administration
FFDCA	Federal Food, Drug, and Cosmetic Act
GRAS	generally recognized as safe
HHS	Department of Health and Human Services
PFAS	per- and polyfluoroalkyl substances
PFOA	perfluorooctanoic acid
PFOS	perfluorooctane sulfonate
TOR	threshold of regulation

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November 8, 2022

The Honorable Rosa DeLauro
Chair
Subcommittee on Labor, Health and Human Services, Education, and Related Agencies
Committee on Appropriations
House of Representatives

The Honorable Chellie Pingree
House of Representatives

Substances that come into contact with food during processes such as manufacturing, packaging, or transporting may migrate into food, where they could pose a risk to human health. These substances—known as "food contact substances"—may be used, for example, in the lining of metal food cans to prevent corrosion or for greaseproofing paper food packaging. The Department of Health and Human Services' (HHS) Food and Drug Administration (FDA) has primary responsibility for reviewing the safety of food contact substances before and after their authorization and use. Such reviews are known as "premarket" and "postmarket" reviews. FDA is also responsible for taking action when the agency identifies safety concerns.[1]

Thousands of such substances have entered the market, according to a study by the Pew Health Group, but there are no data available on how many are currently in use.[2] Academic, consumer, environmental, health, and other stakeholders have raised concerns that some of the substances on the market may, by themselves or in combination with

[1]In carrying out its responsibilities, FDA may also collaborate with other HHS agencies, as well as with the Environmental Protection Agency (EPA) and the U.S. Department of Agriculture's Food Safety and Inspection Service (FSIS), as appropriate. Other HHS agencies, such as the National Institutes of Health and Centers for Disease Control and Prevention, sponsor research to examine the toxic effects of these substances and monitor their levels in people. EPA has responsibility for regulating toxic chemicals in general, including those that may be present at limited levels in food or food packaging. FSIS conducts inspections to ensure that only approved food packaging is used for meat and poultry.

[2]Thomas G. Neltner et al., "Navigating the U.S. Food Additive Regulatory Program," *Comprehensive Reviews in Food Science and Food Safety,* vol. 10 (Pew Health Group: 2011): 342-368.

other substances, contribute to adverse health effects such thyroid disease, hormone disruption, and neurodevelopmental disruption in infants and children.[3] Some of these stakeholders have petitioned FDA to take action to remove certain substances from the market and to improve aspects of the agency's safety review process.[4]

You asked us to review FDA's oversight of food contact substances. This report (1) identifies the primary means that companies use to bring food contact substances to the market and describes FDA's premarket safety review process and (2) examines FDA's postmarket safety review actions and the limitations of such reviews.

To identify the primary means that companies use to bring food contact substances to the market, we analyzed FDA data on the reviews of substances that the agency conducted from January 2000 through mid-September 2021, the most recent data available at the time of our analysis.[5] We analyzed the results of a 2014 FDA study covering 10 years of data on FDA's review of food contact substance notifications (FCN).[6] We reviewed the reliability of FDA data on the agency's review of substances and its 2014 study, including by looking for omissions and anomalies, and determined that they were sufficiently reliable for the purposes of our reporting objectives. To describe FDA's premarket safety review process for food contact substances, we reviewed relevant

[3]As additional background information, GAO provides a summary of the views of 13 stakeholders we interviewed. In apps. I and II, we name the stakeholders and provide their views.

[4]FDA defines a petition as "a petition, application, or other document requesting the Commissioner [of FDA] to establish, amend, or revoke a regulation or order, or to take or not to take any other form of administrative action, under the laws administered by the Food and Drug Administration." 21 C.F.R. § 10.3. As additional background information, we provide a summary of six stakeholder petitions in app. II.

[5]Data for FDA's reviews of food contact substance notifications (FCN) cover the period March 1, 2000, through September 8, 2021; threshold of regulation (TOR) exemptions—January 1, 2000, through September 15, 2021; food additive petitions—January 1, 2000, through September 14, 2021; and generally recognized as safe (GRAS) notices—January 1, 2000, through September 15, 2021. We selected 2000 as the starting year for our analysis because that is the year that FCNs were introduced, and the other means of market entry have data going back to that year as well.

[6]A. Neal-Kluever et al., "Ten-year Retrospective Assessment of the Performance of the Food Contact Notification (FCN) Programme," *Food Additives & Contaminants: Part A Chemistry, Analysis, Control, Exposure, and Risk Assessment*, vol. 32, no. 3 (2015): 261–270. The FDA study was published online in 2014 and in print form in 2015.

statutory and regulatory requirements, and agency guidance. We also interviewed FDA officials.[7]

To examine postmarket safety review actions that FDA took from January 2000 through May 2022 and postmarket review limitations, we analyzed agency web pages and final rules and interviewed agency officials. We compared FDA's postmarket review process to relevant objectives and strategies that the agency set forth in its strategic plan for its foods program.[8] Specifically, the plan includes improving the data-driven, postmarket surveillance of substances added to the food supply as a strategy for enhancing the safety of food additives. The plan also includes an objective to achieve optimal risk-informed resource allocation throughout the program.

As part of our review, we individually interviewed stakeholders from 13 academic, consumer, environmental, health, industry, and other organizations and analyzed documents from these and other organizations to gather background and contextual information for this review. On the basis of this work, we describe stakeholder views on FDA's pre- and postmarket review processes in appendix II. We asked each stakeholder questions, in part, based on each stakeholder's area of expertise (e.g., scientific, legal) and on topics that they had written about. We also reviewed written responses and reviewed documents—such as petitions, studies, and journal articles—that these stakeholders or others had written, as identified by stakeholders and through internet searches. We identified stakeholders through recommendations from FDA officials and other stakeholders. We described views that were expressed by four or more stakeholders, according to our analysis of interviews and documents we reviewed.

We conducted this performance audit from August 2020 to November 2022 in accordance with generally accepted government auditing standards. Those standards require that we plan and perform the audit to obtain sufficient, appropriate evidence to provide a reasonable basis for our findings and conclusions based on our audit objectives. We believe

[7]We did not evaluate the effectiveness of FDA's premarket review process for food contact substances.

[8]See Food and Drug Administration, *Foods and Veterinary Medicine Program Strategic Plan*, *Fiscal Years 2016-2025*. The program, which is now called the foods program, includes food safety.

that the evidence obtained provides a reasonable basis for our findings and conclusions based on our audit objectives.

Background

FDA carries out its mission to protect public health, in part, by ensuring the safety of the nation's food supply. To this end, FDA oversees the safety of ingredients added directly to food, referred to as "direct food additives," as well as substances that come into contact with food, such as those found in packaging materials used to wrap food for the purpose of serving it, or containers that store food. Food contact substances can also be used to seal or form metal parts that overlap in food processing equipment for the purpose of durability, including gaskets and O-rings.[9] Additionally, these substances can be used as processing aids for manufacturing other food contact substances to reduce buildup on manufacturing equipment. Moreover, they can be used in food contact materials by shippers, loaders, and carriers by motor and rail vehicle to transport food, and they can be used in various types of cookware. All these substances may migrate into food.

The Federal Food, Drug, and Cosmetic Act (FFDCA) governs FDA's oversight responsibilities, as well as requirements for companies regarding the use of direct food additives and food contact substances in the market.[10] FFDCA defines a food additive, in part, as 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 characteristic of any food.[11] The act also defines a food contact substance as any substance that is intended for use as a component of materials used, for example, in manufacturing, packaging, or transporting of food, if such use is not intended to have any technical effect in the food.[12]

FDA reviews companies' evidence regarding the safety of a food contact substance for its intended use before the substance enters the market, as well as public information and information that FDA may have collected

[9]An O-ring is a doughnut-shaped object that is often used for sealing.

[10]*See* 21 U.S.C. §§ 348, 393(b)(2)(A).

[11]21 U.S.C. § 321(s).

[12]21 U.S.C. § 348(h)(6). The term "technical effect" is not defined in the FFDCA, but the 2011 Pew Health Group study states that it generally means that the substance does not affect the characteristics of food so as to make the substance a direct food additive.

over time. Also, FDA is responsible for ensuring the continued safety of food contact substances after they are on the market.

A food contact substance may enter the market through one of the following:

- **Food additive petitions.** A company may file a petition to request that FDA issue a regulation establishing conditions under which a substance can be safely used, including the maximum quantity of the substance.[13] Food additive petitions are often used for direct food additives, such as artificial flavor or preservatives added directly to the food, according to FDA officials. These petitions can also be used for food contact substances and were often used for these substances prior to 2000. Food additive petitions for food contact substances must contain the name, chemical identity, and composition of the food additive; conditions of proposed use; and all relevant safety data.[14] This process for issuing a regulation provides an opportunity for public comment on the notice of the filing of the petition, followed by the issuance of an order granting or denying the petition to authorize the use of the substance. The regulations authorizing the use of these substances are listed in the *U.S. Code of Federal Regulations* and can be relied on by any company that wishes to market the substance, as long as the company meets the intended use conditions and limitations within the regulation.
- **Food contact substance notifications.** Since 2000, a company may submit a notice indicating the company's intent to market a food contact substance. Such a notice, called an FCN, must contain evidence supporting the company's claim that the substance is safe for its intended use. The Food and Drug Administration Modernization Act of 1997 authorized the FCN as an alternative for food additive petitions to streamline the food contact substance review process.[15]

  Through an FCN, companies submit evidence that includes a description of the substance's chemical profile; its intended use; and its estimated level of migration and consumer exposure, along with the results of safety testing. FDA has issued guidance documents

[13]Stakeholder groups have also filed food additive petitions to remove a substance. In addition, stakeholders may file citizen petitions to request that FDA take an action, such as removing a substance from the market.

[14]*See* 21 CFR § 171.1(c).

[15]Pub. L. No. 105-115, § 309, 111 Stat. 2296, 2354.

describing information that FDA recommends companies provide in their submissions.[16] These documents discuss what chemical and toxicological information and principles are needed for safety assessments, how to conduct migration testing and estimate exposure, and how to conduct safety testing and organize safety information.

With an FCN, FDA has 120 days to determine whether the evidence supports a company's assertion that the purported use of the food contact substance has been shown to be safe. If, after 120 days, FDA has not objected to the FCN on the grounds that the evidence does not support that the food contact use of the substance is safe, the FCN becomes effective, and the company may market the substance. FCNs avoid the lengthy administrative processes associated with food additive petitions, according to FDA officials. Each FCN applies only to the company that submitted it. Effective FCNs are listed on FDA's website, with information on the notifying company, the substance's intended use, and FDA's decision. However, the complete FCN, as filed, is not posted on FDA's website, and FCN documents are only available through a Freedom of Information Act request.

- **Threshold of regulation (TOR) exemption requests.** A company's request that FDA exempt a food contact substance from regulation as a food additive must provide the company estimates showing that the substance will migrate to food at a level that will result in dietary exposure equal to or below 0.5 parts per billion—the threshold of regulation. In addition, the request must provide the company's estimates showing that the substance is not carcinogenic and does not present other health or safety concerns based on its intended use. The TOR exemption may apply only if the substance has no technical effect in or on the food to which it migrates and the substance's use has no significant adverse impact on the environment. TOR exemption requests that FDA has granted are listed on the agency's website.

[16]Food and Drug Administration, Center for Food Safety and Applied Nutrition (CFSAN), *Guidance for Industry: Preparation of Premarket Submissions for Food Contact Substances (Chemistry Recommendations)*, Docket No. FDA-2020-D-1925 (December 2007); *Guidance for Industry: Preparation of Food Contact Notifications for Food Contact Substances (Toxicology Recommendations)*, Docket No. FDA-1999-D-0062 (October 2021); and *Redbook 2000: Guidance for Industry and Other Stakeholders, Toxicological Principles for the Safety Assessment of Food Ingredients* (updated July 2007).

- **Generally recognized as safe (GRAS) notices.** Companies may, either with or without consulting or alerting FDA, conclude that the intended use of a substance is generally recognized, among qualified experts, as having been adequately shown to be safe under the conditions of its intended use. General recognition of safety includes both general availability of the supporting information as well as evidence of general acceptance by experts qualified by training and experience.[17] Under the FFDCA, the use of a substance that is GRAS is not considered a food additive and, thus, is not required to obtain authorization as a food additive.

  Companies may notify FDA of their GRAS conclusions without seeking an FDA affirmation in regulation.[18] If FDA asks for evidence supporting the conclusion, a company notifying FDA must provide this evidence if the company chooses to continue the evaluation process. After reviewing the company's GRAS notice, FDA issues a letter that states that the agency (1) has no questions about the company's GRAS conclusion or (2) believes that the company did not provide a sufficient basis for its GRAS conclusion.[19] If FDA has no questions, that means the agency does not disagree with the company's GRAS conclusion. Unlike FCN submissions, GRAS notice submissions are available in their entirety on FDA's website, but substances for which a notification to FDA is lacking are not listed.

- **Prior sanctions.** The use of a food contact substance may be the subject of a letter or other approval issued by FDA or the U.S. Department of Agriculture prior to September 6, 1958. These approvals indicate that there was no objection to the substance's use based on the substance having a substantial history of use in food without known detrimental effects or safety hazards. Some prior-

[17]Prior to 2016, a company making such a conclusion could apply to FDA for an affirmation of the substance's GRAS status. If the substance was affirmed, the affirmation would appear in the *U.S. Code of Federal Regulations*. For more information on GRAS, see GAO, *Food Safety: FDA Should Strengthen Its Oversight of Food Ingredients Determined to be Generally Recognized as Safe*, GAO-10-246 (Washington, D.C.: Feb. 3, 2010).

[18]A 1997 proposed rulemaking and an accompanying FDA policy provided the option for companies to submit GRAS notices—the first of which FDA received in 1998—in lieu of petition affirmations. The rule was not finalized until 2016. Thus, petition affirmations were still an option until 2016. However, as of 1997, FDA no longer committed resources to processing them and, instead, operated the interim program to allow GRAS notice submissions.

[19]In addition, at any time throughout the process that the company requests it, an FDA letter stating that FDA has ceased to evaluate the GRAS notice will be issued.

sanctioned substances are listed in the *U.S. Code of Federal Regulations*. If a company finds that its substance is already on this list, it may use the substance. No new substances have been added to the list of prior-sanctioned substances since 1958. Under the FFDCA, a prior-sanctioned use of a substance is not considered the use of a food additive and is, therefore, exempt from the requirement for authorization as a food additive.

FDA Conducts Most Premarket Safety Reviews through Food Contact Substance Notifications Using a Two-Phase Process

Since 2000, companies most often used FCNs for food contact substances. FDA's safety review process has two phases. In the first phase, FDA determines whether the company's submission is complete and if the company has provided all of the required documentation. In the second phase, FDA determines whether the evidence of safety supports the company's assertion that the purported use of the food contact substance has been shown to be safe. FDA found deficiencies in the completeness of the documentation FDA requires as part of a company's FCN submission or adequacy of the safety evidence in about half of its reviews.

Most of the Premarket Reviews FDA Conducted for Its Process Involved FCNs

Since 2000, companies most often used the FCNs as a means of market entry. FCN reviews represented about 93 percent of FDA's total reviews resulting in food contact substances being allowed to enter the market, according to our analysis of FDA website data (see table 1). FCNs have advantages over other means of market entry—they are company specific and have a 4-month review process, compared with at least 24 months for review of a food additive petition, according to FDA officials.

TOR exemption requests that have been granted, and food additive petitions with a final rule, represent 7 percent of the total number of FDA reviews resulting in food contact substances being allowed to enter the market. For the period of our review, we found no instances of companies using a GRAS notice for market entry or independently designating food contact substances as GRAS without notifying FDA.[20] In addition, as described above, no new substances have been added to the list of prior-sanctioned substances since 1958.

[20]FDA officials and three stakeholders, including industry groups, told us that they did not think independent GRAS conclusions were being used for food contact substances or were not aware of any examples of companies using independent GRAS conclusions for food contact substances. Also, we reviewed one industry consulting firm's online database of independent GRAS determinations that it tracked and found no food contact substances. All of the substances were direct food ingredients.

Table 1: Number and Percentage of FDA Reviews of Food Contact Substances Allowed, by Means of Market Entry, Since 2000

	FDA reviews resulting in food contact substances being allowed for market entry	
Means of market entry	**Number**	**Percentage**
Effective food contact substance notifications (FCN)[a]	1,463	93%
Granted threshold of regulation (TOR) exemption requests[b]	61	4%
Food additive petitions with a final rule to add the use of one or more food contact substances[c]	44	3%
Total	**1,568**	**100%**

Source: GAO analysis of Food and Drug Administration (FDA) data. | GAO-23-104434

Note: The table excludes generally recognized as safe (GRAS) substances because we found no examples of GRAS notices being published on FDA's website for food contact substances from January 1, 2000, through September 15, 2021. It also excludes prior sanctions because no new substances have been added to the list of prior-sanctioned substances since 1958.

[a]FCN data cover the period March 1, 2000, through September 8, 2021. FCN is a means of market entry in which, rather than issue a regulation for the use of a substance, FDA reviews a company's submission within 120 days to determine whether the evidence supports a company's assertion that the purported use of the food contact substance has been shown to be safe. If, after 120 days, FDA has not objected to the FCN on the grounds that the evidence does not support that the food contact use of the substance is safe, the FCN becomes effective, and the company may market the substance.

[b]TOR exemption data cover the period January 1, 2000, through September 15, 2021. TOR is a means of market entry in which a company requests that FDA exempt a food contact substance from regulation as a food additive based on an estimate that the substance will migrate to food at a level that will result in dietary exposure equal to or below 0.5 parts per billion, among other requirements.

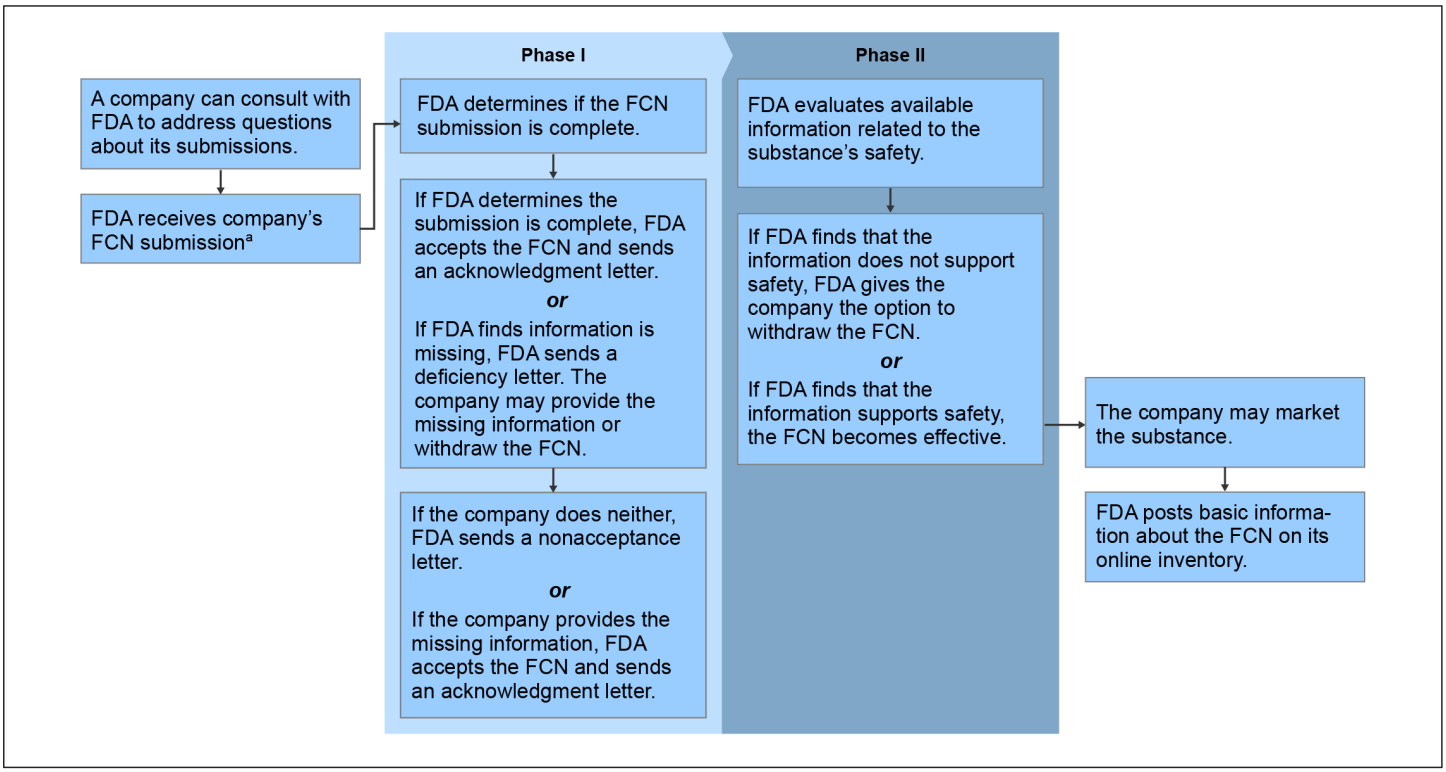
[c]Food additive petition data for petitions with final rules cover the period January 1, 2000, through September 14, 2021. A food additive petition is a means of market entry in which a company may file a petition to request that FDA issue a regulation establishing the conditions under which a substance can be safely used.

FDA's Premarket Review Process for FCNs Has Two Phases

FDA has a two-phase process for reviewing the evidence that companies provide in their FCN submissions (see fig. 1). Of the 120 days FDA has to complete its review, FDA generally spends most of those days in phase II. As previously discussed, if FDA takes no action prior to that deadline, the FCN automatically becomes effective.

However, prior to initiating the two-phase review process, FDA offers companies the option to consult with the agency to (1) help decide which means of market entry to pursue, (2) answer questions that companies or others may have about their submissions and their interpretations of the data and conclusions about safety from the data, and (3) know what actions to take to help ensure that their submission addresses all FDA requirements.

Figure 1: Key Steps in the FDA Food Contact Substance Notification (FCN) Review Process



Source: GAO analysis of Food and Drug Administration (FDA) documents and interviews. | GAO-23-104434

Note: An FCN is a means of market entry in which FDA reviews a company's submission within 120 days to determine whether the evidence supports a company's assertion that the purported use of the food contact substance has been shown to be safe.

[a]The FCN submission must include a description of the substance's chemical profile; its intended use; and the estimated level of migration and consumer exposure, along with the results of safety testing.

- **Phase I of the review.** During phase I of the review, FDA determines whether the company's FCN submission is complete and if the company has provided all of the required documentation. If not, FDA issues a deficiency letter to the company, and the submission is returned to the company to provide the missing information. According to an FDA study, the company is typically given 10 business days to address the deficiencies by amending its submission.[21] If the company cannot address the deficiencies in a timely manner, the company has the option of withdrawing the FCN to have more time to address the deficiencies.

[21]A. Neal-Kluever et al., "Ten-year Retrospective Assessment."

If a company receives a deficiency letter and does not amend its submission to address any deficiencies or withdraw it by the end of the phase I review, FDA issues a nonacceptance letter. If FDA determines that the submission is complete, either upon initial receipt or after the company addresses any deficiencies and provides additional documentation, FDA accepts the FCN and sends an acknowledgement letter, and the FCN proceeds to phase II of the review.

- **Phase II of the review.** During phase II of the review, FDA conducts a full safety evaluation of the available information related to the company's assertion that the purported use of the substance is safe, according to FDA. If FDA determines the information does not support safety, FDA may give the company the option of withdrawing the FCN to address the deficiencies and resubmit the FCN at a later date. Resubmitted FCNs are treated as new FCNs and undergo new FDA reviews.

  If the company does not withdraw the notification, FDA sends an objection letter. According to FDA guidance, the letter explains why the information provided does not support the claim that the substance would be safe for its intended use.[22] The FCN does not become effective, and the company cannot market the substance.

  If FDA does not object to the FCN within 120 days of receipt of a completed FCN, the FCN automatically becomes effective, and the company can market the substance. FDA sends a final letter to the notifying company confirming the effective date of the FCN, according to an FDA report, and adds it to FDA's inventory of effective FCNs posted on the agency's website.[23]

Information in an FCN is protected from disclosure during review if the FCN is withdrawn or if a nonacceptance letter is issued. However, this particular protection lapses once an FCN becomes effective or if FDA objects to the FCN.

[22]Food and Drug Administration, *Guidance for Industry: Preparation of Food Contact Notifications* (Administrative), Docket No. FDA-2013-S-0610 (May 2002).

[23]A. P. Shanklin and E. R. Sánchez, *Regulatory Report: FDA's Food Contact Substance* (reprinted from *Food Safety Magazine*) (Silver Spring, MD: Food and Drug Administration: July 28, 2015).

FDA Requested Additional Information from Companies to Address Deficiencies in Nearly Half of All FCNs Submitted

According to our analysis of an FDA study, FDA requested that companies address deficiencies in the completeness of the documentation FDA requires as part of a company's FCN submission or in the adequacy of the safety evidence for nearly half of the FCNs that the agency has reviewed. Specifically, a study commissioned by FDA in 2014 analyzed the results of FDA reviews of 924 FCNs that the agency had received from January 3, 2001, through December 31, 2010.[24] Overall, 489 FCNs (53 percent) of the 924 FCNs examined had no deficiencies and became effective, and 435 FCNs (47 percent) had deficiencies that FDA requested companies to address (see fig. 2). In addition, our analysis of the study showed that

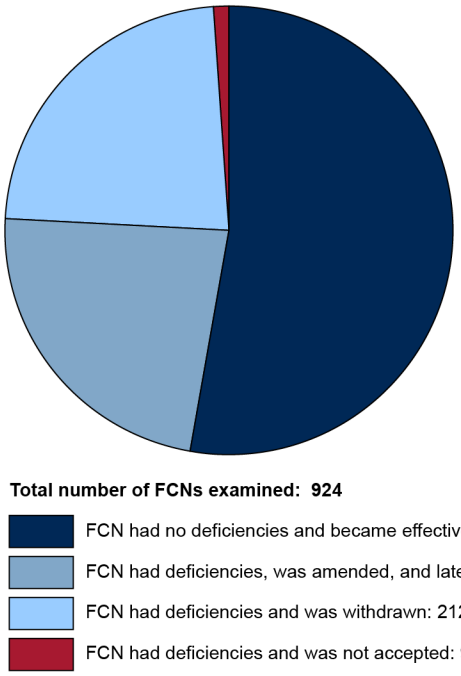
- 214 FCNs (23 percent) had deficiencies in the completeness of the documentation FDA requires as part of a company's FCN submission; these FCNs were amended and later became effective;[25] and
- 212 FCNs (23 percent) had deficiencies in either the completeness of the documentation FDA requires as part of a company's FCN submission or in the adequacy of the safety evidence and were withdrawn; these include 23 FCNs that had been resubmitted but were withdrawn a second time. Nine FCNs (1 percent) were not accepted. Specifically, four were not accepted for administrative reasons because they were for cigarette paper (not food contact substances), two were not accepted based on toxicological concerns, one was not accepted because of environmental concerns, and two were not accepted because they had multiple deficiencies.[26]

[24]Neal-Kluever et al., "Ten-year Retrospective Assessment."

[25]In the FDA study, FDA considers amendments to apply only to phase I review.[26]In addition, a company had amended one of these nine FCNs, but FDA ultimately did not accept it for phase II review.

[26]In addition, a company had amended one of these nine FCNs, but FDA ultimately did not accept it for phase II review.

Figure 2: Number and Percentage of Food Contact Substance Notifications (FCN) for Which FDA Did or Did Not Find Deficiencies, January 3, 2001, through December 31, 2010



Source: GAO analysis of Food and Drug Administration (FDA) data. | GAO-23-104434

Note: If a company withdraws an FCN for a food contact substance and later resubmits it for review, the resubmitted FCN is treated as a new FCN. Therefore, such resubmissions could count twice in the overall totals and percentages presented in the figure above—once as a withdrawn FCN and again as either an effective FCN or another withdrawn FCN.

In addition, the study found that companies later resubmitted 132 of the 212 withdrawn FCNs to FDA for another review after attempting to address the deficiencies that FDA had identified. Of these resubmitted FCNs, FDA allowed 109 (83 percent) to become effective, and companies withdrew 23 (17 percent) again to address deficiencies.[27] The study did

[27]As described above, if a company withdraws an FCN for a food contact substance and later resubmits it for review, the resubmitted FCN is treated as a new FCN. Therefore, such resubmissions could count twice in the overall totals and percentages presented in the figure above—once as a withdrawn FCN and again as either an effective FCN or another withdrawn FCN. As a result, the analysis of FCNs may tend to understate the percentage of food contact substances that entered the market with effective FCNs and overstate the percentage of substances that failed to enter the market because companies ultimately withdrew them.

not discuss the ultimate outcome of FCNs that were withdrawn but not resubmitted during the study's review period.

We asked FDA officials about the level of effort that would be required to update the analysis conducted in the 2014 study covering January 2000 through September 2021. According to these officials, such an update would entail a large amount of work that would compete with other agency priorities and resources, and they did not believe that the percentages for the more recent period would be substantially different than those reported for the period January 2001 to December 2010.

FDA Has Stopped the Use of Three Types of Food Contact Substances, but Its Postmarket Review Process Has Limitations

FDA-initiated postmarket reviews helped stop the use of three types of substances after identifying safety concerns. However, data limitations impede the implementation of a risk-informed postmarket review process.

FDA-Initiated Reviews Helped Stop the Use of Three Types of Food Contact Substances

In addition to premarket review, FDA occasionally conducts postmarket reviews of the safety of food contact substances on its own initiative. Such reviews do not have a deadline and could include substances that entered the market through various means—for example, through a food additive petition or an FCN premarket review from prior years. FDA conducts such reviews at its staff's discretion as resources are available. FDA officials said that while they do not track these FDA-initiated reviews, they could identify a few substances for which they have conducted postmarket safety reviews since 2000.

FDA staff select substances for these FDA-initiated reviews based on information from literature searches, the agency's research and databases, discussions with external experts, and petitions from stakeholders. Through these agency-initiated reviews, since 2000, FDA has identified safety concerns and taken action to stop the use of three types of substances:

- **Long-chain per- and polyfluoroalkyl substances (PFAS).** PFAS are commonly used in coatings to greaseproof and waterproof paper

food packaging.[28] The most common PFAS used in consumer products and studied are perfluorooctanoic acid (PFOA) and perfluorooctane sulfonate (PFOS). Long-chain PFAS entered the market as food contact substances before 2000. Studies indicate that certain long-chain PFAS persist in the human body and have toxic effects in humans. For example, according to EPA, exposure to PFOA and PFOS over certain levels may have effects on fetal development, the immune system, and the thyroid gland, as well as cause liver damage and cancer.[29]

As of November 2016, FDA had worked with companies to voluntarily phase out certain long-chain PFAS substances used in food packaging. FDA had revoked the regulations authorizing the use of others.[30] Long-chain PFAS are no longer used in food contact applications in the United States, according to FDA's website.

- **Short-chain PFAS.** Short-chain PFAS emerged to replace long-chain PFAS for use in food packaging.[31] In the spring of 2020, two journal articles authored by FDA scientists were published with findings from a postmarket scientific review of certain short-chain PFAS.[32] These findings raised questions about the potential human health risks associated with short-chain PFAS toxicity and persistence in the human body. FDA officials worked with manufacturers in July 2020 to voluntarily phase out sales of certain short-chain PFAS for food

[28]PFAS are chemicals that have a carbon bond that is one of the strongest bonds in existence. There are thousands of PFAS, and they have been used in a wide range of products, including nonstick cookware, waterproof clothing, and fire-fighting foam. According to the Centers for Disease Control and Prevention, people are most likely to be exposed to PFAS by consuming water or food that contains PFAS.

[29]See GAO, *Man-Made Chemicals and Potential Health Risks: EPA Has Completed Some Regulatory-Related Actions for PFAS*, GAO-21-37 (Washington, D.C.: Jan. 27, 2021).

[30]See *Indirect Food Additives: Paper and Paperboard Components,* 81 Fed. Reg. 5 (Jan. 4, 2016); and *Indirect Food Additives: Paper and Paperboard Components,* 81 Fed. Reg. 83672, (Nov. 22, 2016).

[31]Short-chain PFAS are perfluoroalkyl carboxylic acids with fewer than eight carbon molecules or perfluoroalkyl sulfonic acids with fewer than six carbon molecules.

[32]P. Rice et al., "Comparative analysis of the toxicological databases for 6:2 fluorotelomer alcohol (6:2 FTOH) and perfluorohexanoic acid (PFHxA)," *Food and Chemical Toxicology*, vol.138 (April 2020): 111210; and S.V. Kabadi et al., "Characterizing biopersistence potential of the metabolite 5:3 fluorotelomer carboxylic acid after repeated oral exposure to the 6:2 fluorotelomer alcohol," *Pharmacology,* vol. 388 (February 2020): 114878.

contact applications over 3 years, beginning in January 2021.[33] These actions affected 15 FCNs covering 11 substances.

- **Diphenyl ketone.** This substance was used to increase the flexibility of rubber articles that are used in food packaging or processing. A 2016 food additive petition from consumer, environmental, and health stakeholders pointed to information demonstrating that diphenyl ketone had been shown to cause cancer. On the basis of this information, FDA officials began a postmarket review and found that the carcinogenicity rendered diphenyl ketone ‘‘unsafe’’ as a matter of law as a food additive. FDA was compelled to revoke the regulation authorizing its use in contact with food.[34] FDA completed this action in October 2018.[35]

According to FDA officials, they consider some 120-day FCN premarket reviews to also be postmarket in nature because many are for substances that FDA has reviewed for previous FCNs. These reviews are conducted when companies submit new FCNs (with the required safety evidence) for previously reviewed substances.[36] FDA officials told us that they give priority to these reviews over self-initiated postmarket reviews because of the 120-day deadline, not because of concerns about safety. Such postmarket reviews have not led to FDA actions to stop the use of any substances.

[33]In particular, three manufacturers, over 3 years beginning in 2021, agreed to phase out from food packaging, in the United States, the use of compounds that contain 6:2 fluorotelomer alcohol (FTOH), which is used to greaseproof food packaging. After 3 years, it could take up to 18 months to exhaust existing stocks of products containing these substances from the market. A fourth manufacturer informed FDA in 2019 that it had already stopped sales of its food contact substances that may contain 6:2 FTOH.

[34]The Delaney clause of the FFDCA prohibits FDA from authorizing the use of any food additive found to induce cancer in animals or humans. Pub. L. No. 85-929, § 4, 72 Stat. 1784, 1786 (codified at 21 U.S.C. § 348(c)(3)(A)).

[35]83 Fed. Reg. 50,490 (Oct. 9, 2018).

[36]Multiple companies often seek an FCN review for the same substance that was previously reviewed for use by another company, or a company may seek an FCN review for expanded use of a substance for which the company already has an effective FCN. FDA follows a similar process for these postmarket reviews as for substances being reviewed for the first time, including reviewing the scientific literature for safety information about the substance.

Data Limitations Impede FDA Efforts to Implement a Risk-Informed Process for FDA-Initiated Postmarket Reviews

FDA faces two data limitations that impede its ability to implement a risk-informed, postmarket review process for FDA-initiated reviews. First, FDA has limited access to unpublished information and data from companies on the safety of food contact substances and how extensively they are used. Second, FDA does not track the date of the last review for all food contact substances in a way that allows FDA to readily create a summary list of substances that may warrant additional review.

FDA Has Limited Access to Information Needed to Implement a Risk-Informed, Postmarket Review Process

When conducting postmarket safety reviews on its own initiative and prioritizing food contact substances for such reviews, FDA has limited access to companies' information and data on the safety of these substances and on how extensively they are used. Such information could inform this review process.[37] Also, as previously noted, research shows that thousands of food contact substances have entered the market.[38] FDA does not have the resources to conduct postmarket reviews for every substance, according to FDA officials. FDA's 2023 budget justification document discussed the need to increase postmarket safety review efforts, noting the increasing number and complexity of premarket FCN reviews. Such reviews limit agency resources available for additional oversight activities, such as FDA-initiated postmarket reviews. In its written responses to our questions, FDA noted that the postmarket review process is resource intensive because of the level of effort involved in requesting and obtaining updated information and data on safety and on the extent of use of the substances.[39]

FDA needs information on a food contact substance's safety and extent of use to help the agency select substances for risk-based, FDA-initiated postmarket reviews, according to FDA officials. For example, if a substance is no longer being used as a food contact substance, it would not be selected for postmarket review. However, if the substance is extensively used, human exposure would be greater, and the risk to human health may be higher—particularly if updated safety information indicates potential concerns. Likewise, data on safety and the extent of a

[37]Companies must provide safety information for premarket reviews.

[38]See Neltner et al., "Navigating the U.S. Food Additive Regulatory Program," 342-368. There are no data available on how many such substances are currently in use, and FDA officials said they could not provide an estimate.

[39]FDA's fiscal year 2023 budget justification states that additional resources are needed for FDA to acquire new tools to prioritize postmarket reviews in a science-based, systematic way to focus on the substances with the greatest potential for public health impact. The justification also states that experts, such as toxicologists, are needed to conduct postmarket review work related to PFAS substances.

substance's use are important to FDA in conducting the postmarket review. For example, FDA uses the outcome of toxicity studies (a type of safety study) to help the agency consider the substance's potential safety concerns. FDA also uses data on a substance's extent of use to help consider the probable consumption of the substance in the human diet. The extent of use is considered because consumption levels impact a substance's safety.

According to FDA officials, access to this information is limited for FDA-initiated postmarket reviews because much of the information and data are unpublished and reside solely with the companies that produce the substances. FDA rarely knows about unpublished studies outside of those included as part of an FCN submission. Also, FDA does not have specific legal authority to compel companies to provide information they have about a food contact substance to help FDA implement a risk-informed postmarket review process. Further, companies may choose not to respond to FDA's requests for information. We asked FDA whether it gets the data it needs from industry for postmarket review, but FDA officials said that they did not keep records of its data requests or industry's responses to those requests. FDA said that specific authority to compel industry to provide data would be helpful. They added that when the agency lacks sufficient information to show that a substance may be harmful, it cannot take action to stop its use.

We asked two industry stakeholders what the pros and cons were of providing such authority to FDA and how such authority might affect industry, but neither stakeholder answered this question. One company representative said that they did not think such authority was needed, in part, because FDA's letters accompanying effective FCNs state that if the company becomes aware of data that raise safety questions about a substance's use, the company should notify FDA immediately and be prepared to supply such data. However, FDA officials said that if companies chose not to provide such information, FDA's lack of specific authority could hamper FDA's ability to take action to stop the use of a substance, if warranted.

Three health and environmental stakeholder groups have published their concerns about FDA's lack of specific authority to compel companies to provide information and data on food contact substances' safety and use, according to our analysis of documents provided by stakeholder groups. One of the groups noted that the law does not give FDA the specific authority it needs to efficiently obtain the information necessary to identify chemicals of concern that are already on the market, set priorities to

reassess these chemicals, and then complete a review of their safety. Moreover, the stakeholders noted that a lack of specific authority to require companies to provide data on the safety of and exposure to food contact substances that have entered the market hinders FDA's ability to make safety decisions for these substances.[40]

FDA officials told us that they have begun to develop options to systematically reassess the safety of food additives, which include food contact substances. They are doing so in response to a provision in a House Appropriations Committee report that also directs the agency to report to Congress by March 15, 2023, on such options, including on how to obtain information on companies' uses of food contact substances.[41] However, FDA officials did not provide any information on the types of options they may develop for the report.

FDA has developed a strategic plan for its foods program that includes improving the data-driven, postmarket surveillance of substances added to the food supply as a strategy for enhancing the safety of food additives.[42] The plan also includes an objective to achieve optimal risk-informed resource allocation throughout the program. FDA's plan states that it is imperative that the agency "continue driving toward a more proactive, preventive, risk-informed approach to food and feed safety, nutrition, and animal health that makes excellent use of scarce resources."

In its report to the House Appropriations Committee, FDA could support its strategic plan and have additional options for obtaining information on food contact substances, if it requested specific legal authority to compel companies to provide information and data on food contact substances' safety and use. Such authority could ultimately strengthen FDA's ability to implement a risk-informed, postmarket review process to better ensure that food contact substances do not harm human health.

[40]Exposure is related to the extent of a substance's use.

[41]H. Rpt. 117-82 (2021), p. 95. This report accompanied the fiscal year Agriculture, Rural Development, Food and Drug Administration, and Related Agencies, 2022, appropriations bill.

[42]See Food and Drug Administration, *FDA Foods and Veterinary Medicine Program Strategic Plan, Fiscal Years 2016-2025.* The program, which is now called the foods program, includes food safety.

FDA Does Not Track the Last Review Dates for Food Contact Substances in a Way That Helps FDA Implement a Risk-Informed, Postmarket Review Process

FDA staff can search the agency's information system for an individual food contact substance and find the date of the last premarket review. However, FDA's system cannot readily identify substances that may warrant additional review because new safety information may have emerged.[43] Not tracking these review dates in a way that allows FDA to identify substances that may warrant postmarket review may compound the challenges that FDA faces in making risk-informed decisions on which substances to prioritize for postmarket review.

After substances are allowed to enter the market, new and credible information about the substances' potential human exposure or harm to human health could indicate that the substances pose more or less risk than initially indicated at the time of FDA's premarket review. FDA has the authority to reassess its safety determinations for the substances based on this information. For example, as described earlier in the report, FDA helped stop the use of several types of PFAS based on new safety information.

FDA officials said that if a substance with an effective FCN was still in use, it had likely been reviewed for another company in subsequent years because other companies usually would want to produce the substance as well. They added that it would be helpful to track the date of the last pre- or postmarket review for all food contact substances in a way that allows FDA to create a summary list of substances that may warrant postmarket review.

As noted above, in its strategic plan for its foods program, FDA has developed a strategy of improving data-driven, postmarket surveillance of substances added to the food supply.[44] The strategic plan also includes an objective to achieve optimal, risk-informed resource allocation throughout the program. Tracking the date of the last review for all food contact substances in a way that allows FDA to readily identify substances that may warrant a postmarket review could support FDA's strategic plan. Tracking dates could also help the agency make risk-informed decisions on where to focus its resources for conducting future reviews.

[43]These substances include those that entered the market through an FCN, food additive petition, prior sanction, GRAS notice, or TOR exemption.

[44]See Food and Drug Administration, *FDA Foods and Veterinary Medicine Program Strategic Plan, Fiscal Years 2016-2025*.

Conclusions

FDA's premarket and postmarket reviews are an important part of ensuring the safety of substances that come in contact with food. Since 2000, FDA has identified safety concerns with three types of substances through FDA-initiated postmarket reviews. For these substances, FDA either worked with companies to phase out the substances' use or took regulatory action to stop their use.

However, FDA's postmarket review process has limitations that may impede its ability to implement a more risk-informed approach. In particular, FDA does not have specific legal authority to compel companies to provide information on food contact substances' safety or use for substances that are already on the market. FDA could strengthen its review process by requesting, in its required 2023 report to the House Appropriations Committee, specific authority to compel companies to provide such information and data, when directed. In addition, FDA does not track the date of the last pre- or postmarket review for all food contact substances in a way that allows FDA to readily identify substances that may warrant a postmarket review because new safety information may have emerged.

Recommendations for Executive Action

We are making the following two recommendations to FDA:

The Commissioner of FDA should request specific legal authority to compel companies to provide specific information that they have about food contact substances already on the market. FDA could do so when it submits its report to the House Appropriations Committee on options to systematically reassess the safety of food additives and obtain information on their use. (Recommendation 1)

The Commissioner of FDA should direct the agency to track the dates of the last pre- and postmarket reviews for all food contact substances in a way that allows FDA to readily identify substances that may warrant postmarket review. (Recommendation 2)

Agency Comments and Our Evaluation

We provided a draft of this report to HHS for review and comment. In its written comments, reproduced in appendix III, HHS neither agreed nor disagreed with the first recommendation on requesting specific legal authority and agreed with the second recommendation on tracking review dates.

Specifically, HHS neither agreed nor disagreed with our first recommendation to request from Congress specific legal authority to compel companies to provide specific information they have about food

contact substances that are already on the market. However, HHS said FDA will consider implementing this recommendation in its report to the House Appropriations Committee scheduled for March 2023. HHS noted that the Administration has not yet taken a position on requesting Congress to grant FDA the authority to compel companies to provide new information post-authorization to inform such reassessments. As noted in our report, Congress has directed the Commissioner of FDA to provide a report on options to systematically reassess the safety of food contact substances, including how to obtain information.

HHS agreed with our second recommendation on tracking review dates, stating that additional capabilities to systematically identify substances based on information, such as the last review date, would be valuable for prioritizing substances for reevaluation. HHS indicated that FDA has begun and will continue to work on implementing this recommendation. HHS also provided technical comments on the draft, which we incorporated as appropriate.

We are sending copies of this report to the appropriate congressional committees, the Secretary of HHS, and the Commissioner of FDA. In addition, the report is available at no charge on the GAO website at http://www.gao.gov.

If you or your staff have any questions about this report, please contact me at (202) 512-3841 or morriss@gao.gov. Contact points for our Offices of Congressional Relations and Public Affairs may be found on the last page of this report. Key contributors to this report are listed in appendix IV.

Steve D. Morris
Director, Natural Resources and Environment

Appendix I: List of Stakeholders That GAO Interviewed

Table 2: Stakeholders That GAO Interviewed

Type of stakeholder	Name of group or individual
Academic	Dr. Linda Birnbaum, Scientist Emeritus and Former Director, National Institute of Environmental Health Sciences and National Toxicology Program and Scholar in Residence, Duke University
	Dr. Leonardo Trasande, Division of Environmental Pediatrics, New York University Langone Health
	Dr. Laura Vandenberg, Associate Professor of Environmental Health Sciences, University of Massachusetts Amherst
Consumer	Center for Science in the Public Interest
Environmental	Earthjustice
	Environmental Defense Fund
	Environmental Working Group
Health	Endocrine Society (Dr. Heather Patisaul)
Industry	AIBMR Life Sciences, Inc.
	American Chemistry Council
	Intertek Group PLC
	Keller and Heckman LLP
Other	Food Packaging Forum

Source: GAO analysis of stakeholder interviews. | GAO-23-104434

Appendix II: Stakeholders' Views and FDA's Comments on FDA's Oversight of Food Contact Substances

To gather background and contextual information for our review, we individually interviewed stakeholders from 13 academic, consumer, environmental, health, industry, and other organizations. We asked each stakeholder questions based on each stakeholder's area of expertise (e.g., scientific, legal) and on topics that they had written about. We also reviewed written responses and documents—such as petitions, studies, and journal articles—that these stakeholders or other stakeholders had written. These documents were identified by the stakeholders we interviewed or through internet searches. We identified stakeholders through recommendations from Food and Drug Administration (FDA) officials and other stakeholders. Table 3 summarizes views that were expressed by four or more stakeholders, according to our analysis of interviews and documents we reviewed.[1] Table 4 summarizes petitions submitted by stakeholders on the safety of specific food contact substances. We also include comments that FDA officials made on the topics listed in tables 3 and 4.

[1]We also interviewed four industry stakeholders, but they generally did not express views about FDA's review process.

Table 3: Views of Stakeholders and FDA Comments on the Agency's Premarket and Postmarket Reviews of Food Contact Substances

Topic and stakeholders (type and number)	Stakeholders' views	FDA officials' comments on these topics
Cumulative effects		
September 2020 citizen petition:[a] 12 stakeholders *Additional stakeholder:* **Consumer**: 1	**Stakeholders said** that FDA has not taken into account the chemicals consumed in our diets that are similar in structure or affect similar functions of organs when making safety determinations, despite their legal requirement to do so. In particular, the Federal Food, Drug and Cosmetic Act (FFDCA) requires FDA to consider the cumulative effects of food additives in the diet, taking into account any "chemically and pharmacologically related" substances.[b] FDA should update its rules and issue clear guidance for companies (for example, by defining the terms used in this law) and revise its notification and petition forms to meet FDA's legal requirements.	**FDA officials said** that they are reviewing this petition and did not have a time frame for completion. They said that when relevant information is available, FDA has incorporated data pertaining to chemically and pharmacologically related substances that are present in the diet into its safety assessments. These officials said that FDA's premarket review approach uses conservative safety factors and provides more than adequate assurance of safety for food contact substances. For example, when FDA calculates the cumulative estimated daily intake (CEDI), the agency assumes that all companies are using the substance for the same food contact use all of the time across the entire market at the maximum authorized use level and does not consider in its estimates that some manufacturers may use another substance for the same use.[c] In addition, FDA identifies a safety level no greater than 1/100th the level, at a minimum, at which no adverse effects are observed in animals.
Exposure of vulnerable populations		
Current and former FDA employees and external stakeholders who took part in a 2014 FDA study.[d] *Additional stakeholders:* **Academic:** 1 **Consumer:** 1 **Environmental:** 2 **Health:** 2 **Other:** 2	**Stakeholders said** that FDA does not sufficiently consider health effects from exposure to food contact substances on vulnerable populations, such as infants and pregnant women, the endocrine system, reproductive organs and hormones, the brain, prenatal development, the immune system, allergies, cardiovascular outcomes, and obesity, as well as behavioral outcomes such as those related to autism and attention deficit/hyperactivity disorder.	**FDA officials said** that FDA's approach to safety assessment is the same approach that other international bodies conducting risk assessment use and involves a testing approach that is validated in public literature as a reasonable way to ensure safety. In 2019, FDA also issued guidance for food contact substances intended to be used with infants.[e] FDA officials said their experts are qualified to consider and recommend additional studies that might be relevant to certain health endpoints of concern to stakeholders.
Sensitive toxicological tests		
Academic: 1 **Consumer:** 1 **Health:** 1 **Other:** 1	**Stakeholders said** that FDA does not consider sensitive toxicological tests and, instead, uses tests that focus on organ weight and the presence of lesions to inform safety assessments.	**FDA officials said** that they incorporate all sensitive, reliable, and reproducible studies available into their safety assessments. Tests that claim to target specific biological or sensitive endpoints face the challenges of reproducibility, reliability, and relevance. Also, some of these tests may not be adequate or suitable for risk assessments related to food contact substances or other food additives because they may answer questions that are not as relevant for a safety assessment.

Topic and stakeholders (type and number)	Stakeholders' views	FDA officials' comments on these topics
Mixtures		
March 2016 food additive petition:[f] 10 stakeholders *Additional stakeholder documents and interviews:* **Consumer**: 1 **Environmental:** 2 **Health:** 2 **Other:** 1	**Stakeholders said** that FDA does not consider the interactive health effects of exposure to mixtures of food contact substances that may have a greater impact on human health than when CEDIs are added together individually.	**FDA officials said** that when available data permit, FDA has at times assessed combined exposures for multiple food contact substances.[g] However, FDA's conservative approach to safety reviews exaggerates exposure estimates by assuming that all companies are using the substance for the same food contact use all of the time across the market at the maximum authorized use level, even though some manufacturers may be using other substances for the same use. Because FDA makes the same assumption for those other similar substances, officials said that this creates "significant redundancy" in exposure estimates. Thus, FDA is reviewing the safety of all chemicals separately, assuming very high exposures instead of evaluating much smaller actual exposures of a mix of chemicals.
Exposure to low doses of substances		
Academic: 1 **Consumer:** 1 **Environmental:** 1 **Health:** 1 **Other:** 1	**Stakeholders said** that FDA does not recognize that some substances have a greater adverse effect at low doses than at medium doses, which is one example of what is referred to as a nonmonotonic dose-response relationship. (A nonmonotonic dose-response relationship does not hold to expected patterns, in which the effect increases as the dose of the substance increases.)	**FDA officials said** that they have reviewed the scientific literature but found that the available studies do not support concerns about health effects associated with nonmonotonic dose-response relationships.
Updating guidance		
Current and former FDA employees and external stakeholders who took part in a 2014 FDA study.[d] *Additional stakeholders:* Consumer: 1 Environmental: 2 Other: 1	**Stakeholders said** that FDA's guidance on conducting safety assessments and toxicology testing, such as the Redbook 2000, is outdated.[h]	**FDA officials said** that its guidance continues to be supported by current science and can be relied upon to support the safety of food contact substance notifications (FCN). Although FDA has not been able to update as much guidance as the agency would like to because of resource constraints, it did, in 2019, issue guidance on food contact substances in contact with infant formula and human milk.[e] Also, in 2014, FDA held a public meeting to solicit suggestions for revising the Redbook but did not revise the guidance document after that review.

Topic and stakeholders (type and number)	Stakeholders' views	FDA officials' comments on these topics
Coordination with others		
Current and former FDA employees and external stakeholders who took part in a 2014 FDA study.[d] *Additional stakeholders:* Academic: 1 Consumer: 1 Environmental: 2 Health: 1 Other: 1	**Stakeholders said** that FDA does not sufficiently collaborate, consult, or share information and data with external experts, stakeholders, or other federal agencies, regarding differing perspectives on chemical testing and safety assessments. FDA lacks some communication channels, mechanisms, and forums to facilitate this.	**FDA officials said** they do not often coordinate with the U.S. Department of Agriculture or the Environmental Protection Agency, as FDA does its own safety assessments based on its own requirements for evaluating FCNs. However, they have collaborated with other agencies regarding postmarket review of specific substances of concern, such as bisphenol A (BPA) and per- and polyfluroualkyl substances (PFAS), by participating in working groups and webinars and conducting collaborative studies.[i] FDA coordinates with nonfederal stakeholders informally through ad hoc meetings and conversations, responding to specific questions and requests, and sharing information and updates, as well as formally through coalition meetings, public meetings, webinars, and listening sessions. FDA holds meetings with the Health and Chemicals Coalition one to three times per year, in which stakeholders set the agenda. Also, the agency held a 2014 public meeting to obtain comments on the Redbook. One limitation is that FDA must keep FCN information confidential during the 120-day review period.
Systematic process for postmarket review		
Academic: 1 Consumer: 1 Environmental: 2 Health: 2 Other: 2	**Stakeholders said** that FDA does not have a systematic process for postmarket review (that is, for reassessing the safety of food contact substances) and should periodically and systematically reassess substances when new evidence comes to light about health concerns.	**FDA officials said** they said that having a more systematic way to prioritize substances would be helpful, and they plan to address a request in a House Appropriations Committee report for FDA to provide Congress with a report on how to set priorities for postmarket review and how to more effectively utilize modern scientific tools to evaluate the toxicity of and exposure to substances added to foods, among other things. The officials also said that, given the large number of submissions and notifications, resources are a challenge. If FDA develops a systematic process, that process needs to be risk-based. In addition, they would need reliable updated information from companies, including unpublished toxicology information and exposure data and data on current use. FDA is developing a tool that may help with postmarket prioritization efforts: the Expanded Decision Tree, which is an enhanced, science-based screening tool that may be used to quickly

Topic and stakeholders (type and number)	Stakeholders' views	FDA officials' comments on these topics
		characterize the relative potential toxicity and risk of chemicals, thus potentially helping FDA to prioritize resources and to focus on substances that have the greatest potential for human health impact.
Limitations on postmarket review		
March 2016 food additive petition:[f] 10 stakeholders *Additional stakeholder documents and interviews:* Academic: 1 Environmental: 1 Other: 1	Stakeholders said that limitations that hinder FDA's reassessment process include FDA's limited resources; lack of authority to require companies to provide safety, exposure, and use data postmarket; lack of authority to require companies to conduct additional testing on substances; and the inability to track uses of substances.	FDA officials said that such limitations can adversely affect their ability to do systematic postmarket reviews. Reassessments require reliable updated information from companies, and FDA experiences challenges with accessing unpublished toxicology information and data regarding the safety and industry use of marketed food contact substances. To fully realize the impact of a systematic postmarket review process, additional authorities to compel industry to provide FDA with this updated safety and market use data would be needed, officials said.
Epidemiological studies		
Academic: 1 **Consumer:** 1 **Environmental**: 1 **Health**: 1 **Other:** 1	Stakeholders said that FDA has only minimally used epidemiological data and studies to inform postmarket review safety assessments. FDA primarily relies on dated guideline studies conducted in accordance with Good Laboratory Practices, thus excluding some studies that would be useful for determining toxicity.	FDA officials said that epidemiological studies are usually unavailable at the premarket stage. In addition, the health effects of food contact substances, as opposed to direct food additives, are difficult to identify in epidemiological studies. FDA reviewed many epidemiological studies that were part of a program evaluating the potential health effects of exposure to BPA—called CLARITY-BPA.[j] However, these studies did not show causation or meet other FDA criteria, such as being relevant to risk assessment. FDA looked at the data and interpreted them but did not agree with the conclusions of many studies and, thus, did not consider the conclusions of those studies.

Source: GAO analysis of stakeholder and Food and Drug Administration (FDA) documents and interviews. | GAO-23-104434

[a]This citizen petition requested that FDA define key terms essential to considering the cumulative effect of a food contact substance, as well as other substances and additives. The petition was filed by the American Academy of Pediatrics, the American Public Health Association, Breast Cancer Prevention Partners, the Center for Food Safety, the Clean Label Project, the Consumer Federation of America, Consumer Reports, the Endocrine Society, the Environmental Health Strategy Center, the Environmental Defense Fund, the Environmental Working Group, and Healthy Babies Bright Futures.

[b]FDA has not defined the terms "chemically and pharmacologically related." However, this petition suggests defining "chemically related substances" as a group of substances the members of which are similar in molecular structure or in physical, chemical, or biological properties. It also suggests defining "pharmacologically related substances" as substances that share scientifically documented properties of a similar or related pharmacological effect. It suggests defining "pharmacological effect" as an effect of a substance based on one of three attributes: (1) a mechanism of action based on the pharmacologic action at the receptor, membrane, or tissue level; (2) a physiological effect at the cellular, organ, system, or whole-body level; or (3) chemical structure.

[c]"Cumulative estimated daily intake" is the concentration of a food contact substance in the daily diet based on exposure to that substance from all authorized uses, including food additive petitions, FCNs, and threshold of regulation exemptions. FDA uses it to evaluate the substance's safety.

[d]The current and former FDA employees and external stakeholders were anonymously interviewed to support the following FDA review of how the agency evaluates the harmful effects of chemicals in foods, among other products; FDA Takes Steps to Strengthen Program to Assess the Safety of Chemicals in Foods, Other Products: Constituent Update (Aug. 28, 2014).

[e]FDA officials referred to the document Food and Drug Administration, *Guidance for Industry: Preparation of Food Contact Notifications for Food Contact Substances in Contact with Infant Formula and/or Human Milk* (May 2019).

[f]Stakeholders filing this petition were the Natural Resources Defense Council, the Center for Science in the Public Interest, the Center for Environmental Health, the Center for Food Safety, Clean Water Action, the Consumer Federation of America, Earthjustice, the Environmental Defense Fund, Improving Kids' Environment, and the Learning Disabilities Association of America.

[g]FDA officials did not identify any substances for which they did such an assessment.

[h]The Redbook 2000 refers to the document Food and Drug Administration, Redbook 2000, *Guidance for Industry and Other Stakeholders: Toxicological Principles for the Safety of Food Ingredients* (July 2007).

[i]BPA is a chemical produced in large quantities for use primarily in the production of polycarbonate plastics, such as beverage bottles and water supply pipes, and it is also sometimes used in epoxy resins that coat metal cans. PFAS are chemical substances commonly used as components in coatings to greaseproof and waterproof paper food packaging.

[j]CLARITY-BPA, the Consortium Linking Academic and Regulatory Insights on BPA Toxicity, is a program that studied the potential health effects from exposure to BPA through both a core FDA study and grantee studies conducted by university researchers.

Table 4: Summary of Six Petitions and FDA Comments Related to FDA's Postmarket Review of, and Actions Related to, Specific Food Contact Substances

Date of petition and number of stakeholders filing the petition	Petitions' recommendations	FDA officials' comments on these topics
Per- and polyfluoroalkyl substances (PFAS)[a]		
June 2021 citizen petition:[b] 11 stakeholders	Stakeholders said that FDA should protect consumers from harm to human health by banning all long- and short-chain PFAS as food contact substances. FDA should systematically reassess its past actions on PFAS based on a presumption that all per- and poly-fluorinated compounds biopersist in the human body unless there is affirmative evidence to the contrary.	FDA officials said that they are reviewing this petition and did not have a time frame for completion. They said that for PFAS, FDA utilizes a case-by-case approach to its postmarket review. In particular, FDA does not treat all PFAS the same way because not all substances considered to be PFAS have been shown to be harmful to human health. Regarding biopersistence, it is very rare among food contact substances, so some PFAS are a unique case. In addition, the presence of biopersistence does not inherently mean there is toxicity. FDA also has assigned four or five staff part-time to addressing PFAS, including this petition.

Date of petition and number of stakeholders filing the petition	Petitions' recommendations	FDA officials' comments on these topics
Ortho-phthalates[c]		
March 2016 food additive petition:[d] 10 stakeholders **April 2016 citizen petition:**[e] 11 stakeholders	**Stakeholders filed** two petitions in March and April 2016. The March 2016 food additive petition asserts that because studies show that 11 ortho-phthalates have harmful reproductive, developmental, and endocrine health effects, FDA should strike from its existing regulations its allowances of 30 ortho-phthalates as food contact substances. For ortho-phthalates that have not yet been studied, because they are members of a similar class of substances, FDA should assume they have the same health effects as other substances in that class, in line with FDA's rationale for revoking the use of three PFAS in its final rule, according to the March 2016 petition.[f] In addition, stakeholders questioned the validity of the cumulative estimated daily intake supporting the previous allowance of several ortho-phthalates.[g] The April 2016 petition was filed as a related follow-on citizen petition and requested that FDA remove its prior sanction of five ortho-phthalates and ban eight ortho-phthalates.	**In May 2022, FDA published** a Federal Register Notice denying the petition with respect to 28 ortho-phthalates out of the 30 original substances. (The petitioners later removed two substances from the petition because they stated that the substances were not actually ortho-phthalates.) FDA concluded that not all of these ortho-phthalates are chemically related with respect to sharing a "structural framework" and that it is not appropriate to group the substances as a class because of their structural variations. FDA also stated that the data cited in the petition do not support the ortho-phthalates as having similar pharmacological effects on the endocrine system.[h] FDA also questioned the petition's use of certain datasets to estimate acceptable amounts of substances. As a result of these and other findings, FDA could not conclude that the dietary exposure levels from ortho-phthalates that are in use are unsafe. FDA simultaneously granted an industry petition to revise regulations because the use of 23 ortho-phthalates and two other substances used as plasticizers have been abandoned. FDA also denied the April 2016 citizen petition in May 2022. However, FDA published a notice in the Federal Register requesting scientific data and information on uses, use levels, dietary exposure, and safety data for ortho-phthalates that remain in use. FDA said that it may use this information to update the dietary exposure estimates and safety assessments for the permitted food contact uses of these ortho-phthalates.
Lead[i]		
December 2020 citizen petition:[j] 11 stakeholders	Stakeholders said that despite FDA's 2017 finding that there is no safe level of lead in the human bloodstream, FDA still allows lead to be added to metal cans. Stakeholders requested FDA to ban lead as an additive to products that come into contact with food and establish a presumption that lead levels over 100 parts per million result from intentional use as an additive rather than contamination.	FDA officials said that they are reviewing this petition and did not have a time frame for completion. They added that there are no approved uses of lead. FDA has a "Closer to Zero" action plan for heavy metals such as lead. This action plan identifies actions that FDA will take to reduce exposure to toxic elements from foods eaten by babies and young children to an as-low-as-possible level. Through the food contact substance notification (FCN) program, FDA tracks exposure to residual heavy metals found in food contact substances as a result of the manufacturing process or migration from food packaging or containers. FDA officials consider this exposure, which could occur through a substance with an effective FCN, to ensure that the exposure would be at a safe level.

Date of petition and number of stakeholders filing the petition	Petitions' recommendations	FDA officials' comments on these topics
Perchlorate[k]		
July 2014 food additive petition:[l] 6 stakeholders	In 2014, stakeholders said that the uses of perchlorate allowed by FDA were not safe because there was no longer a reasonable certainty that perchlorate is not harmful under the intended conditions of use when considering (1) the probable consumption of perchlorate; (2) the cumulative effect of perchlorate after taking into account pharmacologically related substances; and (3) additional safety factors necessary to protect the developing brains of fetuses and infants from irreversible harm. Therefore, stakeholders asked FDA to prohibit the use of perchlorate in antistatic agents in contact with dry food and in sealing gaskets for food containers.	In 2017, FDA denied this petition to ban perchlorate but revoked its food additive regulation authorizing certain food contact uses of potassium perchlorate because industry petitioned FDA to do so as a result of industry's abandonment of the substance's use. In FDA's denial of the petition, FDA declined to revoke the threshold of regulation (TOR) exemption for the use of perchlorate in articles intended for use in contact with dry food.[m] Regarding the safety of the use of perchlorate covered under the TOR exemption, FDA officials said that when FDA conducted premarket review of the substance, they conservatively assumed a 100 percent migration of it into food. When officials later received questions about the TOR exemption for perchlorate, FDA obtained new analytical chemistry studies on perchlorate migration that demonstrated that the majority of perchlorate does not migrate into food. As a result, human exposures to perchlorate were very low, according to FDA's postmarket review. FDA acknowledges that human exposure to high dosages of perchlorate can interfere with iodide uptake into the thyroid gland, creating the possibility of disruption to the endocrine system and hormones, which is especially of concern with pregnant women and infants.
Bisphenol A (BPA)[n]		
January 2022 food additive petition:[o] 9 stakeholders	Stakeholders said that FDA should remove or restrict its approvals of BPA that are currently authorized in regulation based on a substantial body of studies of the health effects of dietary BPA exposure published since 2013. According to the petition, these studies were reevaluated in a draft comprehensive safety assessment of BPA released by the European Food Safety Authority (EFSA) in 2021. In the draft safety assessment, an EFSA expert panel recalculated the tolerable daily intake based on an updated analysis and compared this with dietary exposure estimates.[p] The panel concluded that there is a health concern from dietary BPA exposure for all age groups.[q]	FDA has acknowledged receipt of this petition. Over many years of research, FDA has consistently concluded that the current uses of BPA in food containers and packaging are safe. For example, FDA came to this conclusion after a 2014 FDA review of more than 300 studies and after completion of studies by the Consortium Linking Academic and Regulatory Insights on BPA Toxicity (CLARITY-BPA) from 2015 to 2020. The CLARITY-BPA studies were designed to examine the full range of potential health effects from exposure to BPA and featured (1) a core study conducted by several U.S. Department of Health and Human Service agencies, including FDA, regarding the full range of potential health effects from BPA exposure to rats; and (2) multiple grantees' studies conducted by university researchers covering various endpoints

Date of petition and number of stakeholders filing the petition	Petitions' recommendations	FDA officials' comments on these topics
	Stakeholders, in the petition, said the average American is exposed to more than 5,000 times the safe level of BPA exposure set by the EFSA panel, thus warranting FDA's expedited review of this petition to ensure the safety of the food supply.	FDA's core study included a review of factors such as body and organ weight that were observed in rats exposed to BPA.[r] The study concluded that there were a few observed variances in health effects when comparing rat treatment groups with the control group. For most of the groups of rats that were given varying doses of BPA, the differences in the doses of BPA administered to the rats were not the reason for the variances in health effects, according to the National Toxicology Program research report showing the study's results.[s] However, the study's authors observed that some effects on reproductive and endocrine organs of rats that were exposed to BPA at a high dose may have been related to treating them with that higher amount of BPA. While FDA has never taken any actions to restrict the use of BPA based on safety concerns, FDA did issue a regulation to remove the use of certain BPA-based materials in baby bottles, sippy cups, and infant formula packaging in response to two industry petitions stating that these uses have been abandoned.

Source: GAO analysis of stakeholder and Food and Drug Administration (FDA) documents and interviews. | GAO-23-104434

Note: We also interviewed four industry stakeholders, but they did not provide concerns with FDA's review process.

[a]PFAS are chemical substances commonly used as components in coatings to greaseproof and waterproof paper food packaging.

[b]Stakeholders filing this petition were the Environmental Defense Fund, Breast Cancer Prevention Partners, the Center for Environmental Health, the Center for Food Safety, the Consumer Federation of America, Consumer Reports, Defend Our Health, the Environmental Working Group, the Green Science Policy Institute, Healthy Babies Bright Futures, and the League of Conservation Voters.

[c]Ortho-phthalates, also known simply as "phthalates," are a group of chemicals used to make plastics more durable or to help dissolve other materials. For example, they can make materials soft and less brittle. Phthalates are used in hundreds of products, including in personal-care products and plastic food packaging.

[d]Stakeholders filing this petition were the Natural Resources Defense Council, the Center for Science in the Public Interest, the Center for Environmental Health, the Center for Food Safety, Clean Water Action, the Consumer Federation of America, Earthjustice, the Environmental Defense Fund, Improving Kids' Environment, and the Learning Disabilities Association of America.

[e]Stakeholders signing this petition are the same as for the March 2016 petition, with one addition for the Breast Cancer Fund (later renamed as Breast Cancer Prevention Partners).

[f]In this decision, FDA issued a final rule "to no longer provide for the use of three specific perfluoroalkyl ethyl containing food contact substances … as oil and water repellants for paper and paperboard for use in contact with aqueous and fatty foods because new data are available as to the toxicity of substances structurally similar to these compounds that demonstrate there is no longer a reasonable certainty of no harm from the food contact use of these [substances]." Stakeholders suggested that FDA's approach in this decision to categorize these PFAS substances as a class in which FDA considered structurally similar substances to assess these substances' safety should also be applied to determining the safety of a class of 30 ortho-phthalates.

[g]"Cumulative estimated daily intake" is the concentration of a food contact substance in the daily diet based on exposure to that substance from all authorized uses, including uses occurring as a result of food additive petitions, FCNs, and threshold of regulation exemptions. FDA uses it to evaluate the substance's safety.

[h]FDA has not defined the term "pharmacological effect." However, a September 2020 citizen petition on the subject of cumulative effects suggests defining "pharmacological effect" as an effect of a substance based on either (1) a mechanism of action based on the pharmacologic action at the receptor, membrane, or tissue level; (2) a physiological effect at the cellular, organ, system, or whole-body level; or (3) chemical structure. Further, a pharmacologically related substance shares scientifically documented properties of a similar or related pharmacological effect, according to the petition.

[i]Lead is a heavy metal that is naturally occurring in the environment, but it can also be found in the food supply as a result of the manufacturing process or because it is a component of food contact surfaces for containers in which food is prepared, served, or stored.

[j]Stakeholders filing this petition were the Environmental Defense Fund, Breast Cancer Prevention Partners, the Center for Environmental Health, the Center for Food Safety, the Childhood Lead Action Project, the Clean Label Project, Consumer Reports, Defend Our Health, the Environmental Working Group, Healthy Babies Bright Futures, and Utah Physicians for a Healthy Environment.

[k]Perchlorate occurs naturally in the atmosphere and in nitrate fertilizer deposits. When it is manufactured, it may serve as an industrial chemical added to rocket propellant. It may also be used as a component in certain containers and in food processing equipment for dry foods.

[l]Stakeholders filing this petition were the Natural Resources Defense Council, the Center for Food Safety, the Breast Cancer Fund, the Center for Environmental Health, the Environmental Working Group, and Improving Kids' Environment.

[m]However, stakeholders requested a public hearing regarding their objections to FDA's denial of the original petition. FDA denied this request in 2019 in a *Federal Register* Notice. Petitioners then filed a lawsuit "to overturn FDA's decision to continue allowing perchlorate in plastic packaging and processing equipment," according to the environmental group that filed the suit. In 2022, a federal judge upheld FDA's decision to deny the original petition.

[n]BPA is a chemical produced in large quantities for use primarily in the production of polycarbonate plastics, such as beverage bottles and water supply pipes, and it is also sometimes used in epoxy resins that coat metal food cans.

[o]Stakeholders filing this petition were the Environmental Defense Fund, Breast Cancer Prevention Partners, Clean Water Action, Consumer Reports, the Endocrine Society, the Environmental Working Group, Healthy Babies Bright Futures, Maricel Maffini, and Linda Birnbaum.

[p]FDA typically refers to "tolerable daily intake" as "acceptable daily intake." It is based on a dose level of a food additive in animal studies that does not result in any adverse effects. Ingesting the substance at this level must have "a reasonable certainty of no harm."

[q]As previously stated, this document is a draft, but it was endorsed for public consultation in November 2021 and is publicly available. The petitioners state that even though it is not yet finalized, the document "is sufficient to support the petition." European Food Safety Authority (EFSA) Panel on Food Contact Materials, Enzymes and Processing Aids (CEP), "Re-evaluation of the Risks to Public Health Related to the Presence of Bisphenol A (BPA) in Foodstuffs," EFSA Journal (Draft scientific opinion, not yet published) (November 24, 2021, endorsed for public consultation).

[r]U.S. Department of Health and Human Services, National Toxicology Program (NTP), NTP Research Report on the CLARITY-BPA Core Study: A Perinatal and Chronic Extended-Dose Range Study of Bisphenol A in Rats, Research Report 9 (Research Triangle Park, NC: September 2018).

[s]The study also examined effects from administering two doses of a certain estrogen hormone (called estrogen ethinyl estradiol) as a way to determine whether several treatment groups of rats would be sensitive to low doses of the hormone. It found that, in contrast to BPA, the estrogen had clear hormonal effects in female rats.

Appendix III: Comments from the Department of Health and Human Services

DEPARTMENT OF HEALTH & HUMAN SERVICES

OFFICE OF THE SECRETARY

Assistant Secretary for Legislation
Washington, DC 20201

October 17, 2022

Steve D. Morris
Director, Natural Resources and Environment
U.S. Government Accountability Office
441 G Street NW
Washington, DC 20548

Dear Mr. Morris:

Attached are comments on the U.S. Government Accountability Office's (GAO) report entitled, **"FOOD SAFETY: FDA Oversight of Substances Used in Manufacturing, Packaging, and Transporting Food Could Be Strengthened"** (GAO-23-104434).

The Department appreciates the opportunity to review this report prior to publication.

Sincerely,

Melanie Anne Egorin

Melanie Anne Egorin, PhD
Assistant Secretary for Legislation

Attachment

GENERAL COMMENTS FROM THE DEPARTMENT OF HEALTH & HUMAN SERVICES ON THE GOVERNMENT ACCOUNTABILITY OFFICE'S DRAFT REPORT ENTITLED — FOOD SAFETY FDA Oversight of Substances Used in Manufacturing, Packaging, and Transporting Food Could Be Strengthened (GAO-23-104434)

The U.S. Department of Health & Human Services (HHS) appreciates the opportunity from the Government Accountability Office (GAO) to review and comment on this draft report.

General Comments

The U.S. Department of Health & Human Services (HHS) appreciates the opportunity from the Government Accountability Office (GAO) to review and comment on this draft report. The Food and Drug Administration (FDA) oversees the safety of food additives, including substances that are expected to migrate into food when used in contact with food. As specified under the Federal Food, Drug, and Cosmetics Act, the Agency administers a robust pre-market authorization program which requires that the safety of these substances be demonstrated prior to them being placed on the market. As noted in the GAO report, FDA's pre-market evaluation uses multiple overestimates in assumptions used in its safety assessment to ensure the safety of the substance for its intended use, even as the science of safety assessment continues to evolve. Because food contact notification(s) (FCN) are specific to the notifier and specific to the specified intended use of the substance, FDA's FCN program also serves a post-authorization re-evaluation function in that current data on substances are submitted to the Agency for review every time a new manufacturer/supplier submits an FCN because they intend to sell the substance for an authorized use, or they seek expansion of authorized uses. In addition, FDA re-evaluates authorized substances on a case-by-case basis should new information be identified that may impact FDA's safety conclusion. FDA would like to emphasize that irrespective of the regulatory path (i.e., food additive petition, FCN) a food contact substance takes to become authorized for use in contact with food, the safety standard for each is the same: available information must demonstrate that there is a "reasonable certainty" of no harm as defined in 21 CFR 170.3(i).

We value GAO's recommendations that FDA's post-authorization oversight of the safety of food contact substances could be further supported through the granting of additional authorities to compel submission of new relevant data and information on authorized substances, and the development of a systematic approach to tracking review dates for all food contact substances. We also note that timely progress in addressing GAO's recommendations hinges upon a significant increase in funding devoted to these issues. Accordingly, the President's FY 23 Budget Request for FDA includes a $6M increase in funding for CFSAN to enhance and update the FDA's approach to chemicals, both directly added as food ingredients and those that come into the food supply through food contact. These resources will be instrumental in supporting the additional work envisioned by GAO.

Recommendation 1
The Commissioner of FDA should include a request for specific legal authority to compel companies to provide specific information they have about food contact substances that are already on the market. FDA could do so when it submits its report to the House Appropriations Committee on

options to systematically reassess the safety of food additives and obtain information on their use.

HHS Response
FDA will consider including the need for new authority to compel these data in its report to the House Appropriations Committee scheduled for March 2023. We note that FDA does have the authority to reassess the safe use of substances added to food and take action based on that reassessment. As noted in the draft GAO report, when conducting post-authorization reviews FDA has limited access to unpublished safety and use data on food contact substances, unless the review is part of a new FCN submission. Advancements in technology can lead to changes in use levels of additives and food contact substances, their manufacturing process, and levels of impurities and constituents. In addition, advancements in toxicological science may raise new questions not addressed in FDA's pre-market review. Also noted in the GAO report, Congress has directed FDA to provide a report on options to systematically reassess the safety of food additives and generally recognized as safe substances, including how to obtain updated information. The Administration has not taken a position on requesting Congress grant FDA the authority to compel industry to provide new information post-authorization to inform such reassessments.

Recommendation 2
The Commissioner of FDA should direct the agency to track the dates of the last pre- and post-market reviews for all food contact substances in a way that allows FDA to readily identify substances that may warrant post-market review.

HHS Response
HHS concurs with GAO's recommendation. As noted in the draft report, FDA's information tracking systems have been developed to ensure we can identify all previous determinations and data considered for a specific substance on an individual basis. However, we recognize added capabilities to systematically identify substances based on additional information such as last review date would be valuable data to consider for prioritization of re-evaluation. We have already begun to implement such functionality into our information systems to determine the percentage of food contact substances authorized through the FCN program have been re-evaluated through subsequent notifications for a new manufacturer/supplier or expansion of authorized use. We will continue to develop and incorporate systematic tracking functions related to dates of last pre- and post- market reviews into our information systems and include information on such development in our report to Congress on options to systematically reassess the safety of food additives.

Appendix IV: GAO Contacts and Staff Acknowledgments

GAO Contact

Steve D. Morris, (202) 512-3841 or morriss@gao.gov

Staff Acknowledgments

In addition to the contact named above, Anne K. Johnson (Assistant Director), Stephen Cleary (retired) (Analyst in Charge), Beverly Peterson (Analyst in Charge), Adrian Apodaca, Kevin Bray, Charlotte E. Hinkle, Scott Hiromoto, Nacole King, Serena Lo, Donna Morgan, Cynthia Norris, Caitlin Scoville, Wesley Sholtes, Nathaniel Walker, and Shelby Zangari made key contributions to this report.

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