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An Overview of Food Safety Regulatory Violations Found in Foodborne Outbreak-Linked Warning Letters Issued by the United States Food and Drug Administration

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ABSTRACT

The United States Food and Drug Administration (FDA), in collaboration with federal, state, and local partners, identifies, responds to, and prevents outbreaks linked to FDA-regulated products. If FDA determines a firm is not in compliance with applicable FDA requirements, the firm may be informed through a Warning Letter (WL). This study provides an overview of the WLs issued to firms that were involved in FDA-led multistate foodborne outbreak investigations. WLs, issued from January 2018 through August 2023, were obtained from the FDA.gov website. Twenty-two of these WLs were issued to domestic firms after the conclusion of foodborne outbreak investigations. Forty-six regulatory citations were identified across the WLs, with 1-8 violations per WL. Microbial pathogens accounted for the food safety hazards cited in all but one letter, with *Salmonella* representing the majority of hazards. Two citations were issued most frequently: deficiencies in Foreign Supplier Verification Plans, and failure to identify and evaluate hazards requiring a preventive control. FDA is committed to protecting the nation's food supply, and WLs help achieve prompt voluntary compliance. Understanding the regulatory violations identified during outbreak investigations may help the food industry and regulators alike focus prevention efforts and reduce the burden of foodborne illness.

INTRODUCTION

In the United States, an estimated 15,000 outbreak-associated illnesses occur annually linked to approximately 800 outbreaks of foodborne illness *(5)*. However, as foodborne illnesses are predominantly sporadic in nature, outbreak-associated illnesses constitute a fraction of the total estimated 48 million foodborne illnesses that occur each year *(21)*. The large burden of foodborne illness in the United States highlights one of the imperative missions of the United States Food and Drug Administration (FDA) to detect, mitigate, and prevent outbreaks linked to FDA-regulated food products. As a result of the Food Safety Modernization Act (FSMA) of 2011 and its promotion of an integrated food safety system, FDA established the Coordinated Outbreak Response & Evaluation (CORE) Network to manage outbreak surveillance, response, and analysis activities related to incidents involving outbreaks linked to FDA-regulated human foods *(23)*. CORE has served as the coordination focal point for all FDA resources during foodborne illness investigations and has provided a platform for all involved partners to exchange and analyze information aimed at timely decision-making.

The outbreak investigation process

During outbreak investigations, federal, state, and local partners collect three types of information to determine if a common food was consumed by ill people: epidemiologic, traceback, and laboratory *(12)*. During multistate outbreak investigations, the Centers for Disease Control and Prevention (CDC), FDA, or the United States Department of Agriculture (USDA) Food Safety Inspection Service (FSIS), depending on the regulated food, collaborate with state and local partners involved to protect public health *(6)*. CDC, state, and local partners identify outbreaks and potentially associated foods through public health surveillance and epidemiologic analyses. FDA, state, and local partners conduct traceback investigations to determine the source of the food(s) that potentially caused the outbreak *(8)*. Lastly, FDA, state, and local partners can collect and analyze product and environmental samples to confirm the suspect food as the outbreak source *(59)*. The combination of epidemiologic, laboratory, and traceback evidence may result in the identification of a food as the source of an outbreak. Subsequently, investigative partners and the FDA share guidance and information with the public to protect them from illness, and the FDA also uses its regulatory tools to remove contaminated product from the market or to deny entry into the country *(23)*.

FDA actions after foodborne outbreaks

Outbreak investigations, adverse events, or other potential signals may serve as an impetus to conduct an inspection at an FDA-regulated firm. Inspections of firms that manufacture, process, pack, or hold FDA-regulated product are a vital component of the food safety system. The FDA and its state, local, territorial, tribal, and international partners may conduct inspections under their own respective authorities. These inspections can be used to verify compliance with laws administered by the FDA and to inform the agency's response and regulatory actions.

FDA Warning Letters

If the FDA finds that a company has violated FDA statutes or regulations, the FDA often informs the responsible firm

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through a Warning Letter (WL). As outlined in the FDA Regulatory Procedures Manual (RPM):

"When it is consistent with the public protection responsibilities of the agency and depending on the nature of the violation, it is FDA's practice to give individuals and firms an opportunity to take voluntary and prompt corrective action before it initiates an enforcement action. WLs are issued to achieve voluntary compliance and to establish prior notice. The use of WLs and prior notice are based on the expectation that most individuals and firms will voluntarily comply with the law" *(46)*.

A WL is a critical means of achieving prompt voluntary compliance with the Federal Food, Drug, and Cosmetic Act (the Act). The stated position of FDA is that WLs are issued only for significant violations of federal requirements *(60)*. Significant violations are those violations that may lead to enforcement action if not promptly and adequately corrected *(63)*.

WLs are informal and advisory. FDA is generally not under legal obligation to warn firms that their products are in violation of the law before taking enforcement action. A WL communicates the agency's position on a matter, but it does not commit FDA to taking enforcement action. For these reasons, the agency does not consider WLs to be final agency action *(46)*. In some circumstances, the agency may find it necessary to take other actions as an alternative to or simultaneously with the issuance of a WL.

Warning Letter reviews in the literature

WLs are a frequent subject of research in the peer-reviewed literature, as well as in commentary, from those in the regulated industry. In an informal review of articles indexed via the PubMed database *(15)*, reports in the literature have examined patterns in WLs issued in virtually every product area of FDA authority: human drug manufacturers *(11, 14, 17, 19, 66)*, compounding pharmacies *(9, 69)*, clinical researchers *(3, 10, 18, 20, 24)*, medical device firms *(1, 25)*, and tobacco and cannabis operations *(22, 65)*. Human food has been relatively less examined, with a single article reviewing food and dietary supplement WLs for labeling violations *(4)*.

Here, we provide an overview of the concepts and processes used to issue WLs to firms that have been involved in FDA-led multistate foodborne outbreak investigations and the findings of those inquiries that may indicate areas where additional prevention efforts may be needed.

METHODS

Data collection and inclusion criteria

The complete dataset of publicly available WLs was downloaded from the FDA WLs website for the period of January 1, 2018, through August 1, 2023, which contained a total of 3,196 WLs *(64)*. WLs were sorted by issuing entity; those issued by units of the FDA Office of Regulatory Affairs (ORA) or FDA Centers that regulate drugs, biological products, medical devices, tobacco, or radiological products were excluded to remove those unrelated to human foods. Letters issued to firms outside the United States were excluded. The remaining letters were reviewed, and content related to dietary supplements, cosmetics, food intended for animals, and cannabinoid products were excluded. A total of 385 WLs met criteria for potential inclusion in the overview.

Data collection/scoring methodology

WLs meeting the inclusion criteria were searched for the terms "outbreak," "illness," or "complaint." Letters returned in the search were manually reviewed to confirm they were issued after a focused investigation or for-cause inspection. WLs were included if the text of the letter included implication in a foodborne outbreak investigation, or the underlying investigation was due to follow-up to a consumer complaint of foodborne illness linked to the subject firm. A total of 22 WLs were identified as being issued after a foodborne illness investigation.

Data were collected by manual review of each WL to catalog the statutory and regulation citations noted in the WL. Each letter was scored independently by at least two reviewers and discrepancies in scoring were resolved by re-review and authorship team concurrence.

RESULTS

Twenty-two outbreak-linked WLs issued to domestic firms were identified and reviewed *(26, 28-30, 34-39, 41-43, 47-50, 53-57)*. Collectively, 46 regulatory citations were identified across all the letters, with a mean of 2.1 (standard deviation 1.8; range 1-8) violations per letter. One letter issued to corporate headquarters of an entity that operates retail food establishments in multiple locations contained only a statutory citation due to the firm having legal obligations under the Federal Food, Drug, and Cosmetic Act (FFDCA). The collected data by WL and regulation is fully detailed in *Table 1*.

Microbial pathogens accounted for the food safety hazard cited in all but one letter (21/22; 95%), with the remaining due to undeclared allergens *(Table 2)*. *Salmonella* represented the majority of the implicated hazards (13/22; 59%), with additional outbreaks linked to *Listeria monocytogenes* (3/22; 14%), *Escherichia coli* (3/22; 14%), *Cyclospora cayetanensis* (1/22; 5%), and *Clostridium botulinum* (1/22; 5%). The distribution of hazards noted in WLs approximates the distribution of hazards identified in all FDA multistate foodborne outbreak investigations, irrespective of whether a WL was issued. FDA's Coordinated Outbreak Response & Evaluation (CORE) Network investigated a total of 145 outbreaks in the period 2018-2023, in which microbial pathogens were implicated in 139 (96% of incidents) (unpublished data). Allergen, chemical, and other non-pathogen hazards were implicated in 6 outbreaks (4%). *Salmonella* spp. was implicated in 58 outbreaks (40%),

TABLE 1. Regulatory violations according to implicated hazards for outbreak-associated warning letters related to human foods issued by the U.S. Food and Drug Administration between January 1, 2018, and August 1, 2023

Implicated Hazard	FSVP (1.502)	FSVP (1.504)	FSVP (1.505)	FSVP (1.506)	Produce standards (112.1 et seq.)	Personnel (117.10)	Plants and grounds (117.20)	Sanitary operations (117.35)	Sanitary facilities and controls (117.37)	Processes and controls (117.80)	Food safety plan (117.126)	Hazard analysis (117.130)	Preventive controls (117.135)	Monitoring (117.145)	Corrective actions (117.150)	Verification of implementation and effectiveness (117.165)	Reanalysis (117.170)	Supply chain program (117.405)	Shell eggs (118.1 et seq.)	Hazard analysis (123.6)	Corrective actions (123.7)	Sanitation controls (123.11)
Allergens						X			X			X	X	X		X	X	X				
Clostridium botulinum							X					X		X								
Salmonella								X		X										X	X	X
Salmonella	X																					
Listeria											X											
Salmonella	X																					
E. coli					X																	
Cyclospora													X									
Salmonella																			X			
Salmonella												X			X							
E. coli																						
Salmonella										X												
Salmonella	X																					
Salmonella										X										X		X
Salmonella								X														X
Listeria							X	X				X	X									
Salmonella					X																	
Salmonella																			X			
E. coli					X																	
Salmonella		X										X	X			X						
Listeria	X	X		X																		
Salmonella	X		X																			
Total	5	1	1	1	3	1	2	3	1	3	1	5	4	2	1	2	1	1	2	2	1	3

TABLE 2. Summary of implicated hazards reported in outbreak-associated Warning Letters related to human foods issued by the U.S. Food and Drug Administration between January 1, 2018, and August 1, 2023

Food hazard	Number of occurrences implicated	Percentage of total
Salmonella spp.	13	59%
Listeria monocytogenes	3	14%
Pathogenic *Escherichia coli*	3	14%
Cyclospora cayetanensis	1	5%
Clostridium botulinum	1	5%
Allergen cross-contamination	1	5%

*Total may not add to 100 due to rounding

Listeria monocytogenes in 22 (15%), Shiga toxin-producing *Escherichia coli* in 33 (23%), and all other pathogens in 7 (5%).

The regulations implicated include Current Good Manufacturing Practice, Hazard Analysis, and Risk-Based Preventive Controls for Human Food (CGMP & PC Rule), Title 21, Code of Federal Regulations, Part 117 (21 CFR § 117); Foreign Supplier Verification Programs for Food Importers (21 CFR §1.502 et seq.; FSVP Rule); Fish and Fishery Products (21 CFR §123; Seafood HACCP Rule); Standards for the Growing, Harvesting, Packing, and Holding of Produce for Human Consumption (21 CFR § 112; Produce Rule); and the Production, Storage, and Transportation of Shell Eggs (21 CFR § 118; Egg Rule). No violations of the Low Acid Canned Food Regulations (21 CFR §113), Acidified Foods Regulations (21 CFR §114), or FDA Juice HACCP Rule (21 CFR §120) were noted. The number and proportion by rule set is detailed more fully in *Table 3*. Two regulatory citations were equally cited most frequently - failure to develop, maintain, and follow a Foreign Supplier Verification Plan (21 CFR §1.502(a)) for importers of food products (5/46; 11%) and failure to identify and evaluate hazards requiring a preventive control (21 CFR §117.130) for firms subject to the PC rule (5/46; 11%).

DISCUSSION

FDA's approach to compliance

FDA is committed to protecting the nation's food supply from hazards that could endanger public health. A WL is a critical means of achieving prompt voluntary compliance with the Federal Food, Drug, and Cosmetic Act. Most firms voluntarily comply with the law when informed of what is required, what violations seem to exist, and, in the case of violations of regulatory significance, that failure to comply may result in the initiation of enforcement action. This is a fundamental tenet of the FDA's enforcement policy. As WLs are publicly posted on the internet, industry may review the WLs and apply the recommendations more broadly. FDA WLs serve as a valuable tool in ensuring the safety of our food supply, although they are not the sole method employed.

Criteria for issuing Warning Letters

For a WL to be issued due to an outbreak of foodborne illness, several conditions must be met: the outbreak must be detected by public health surveillance; the outbreak investigation must find adequate evidence (laboratory, epidemiologic, and/or traceback) to identify the food causing illness or injury; and subsequent regulatory investigations or inspections must find sufficient violations of food safety regulations to warrant a WL, as discussed above. Since not all investigations meet each of these criteria, not every outbreak investigation leads to the issuance of a WL, and the findings in this overview may not hold true for all foodborne illness outbreaks. Nevertheless, examining the linkages between foodborne illness and the regulatory violations observed provides an opportunity for the food industry to reduce and mitigate risk.

Hazard analysis and preventive controls implementation

In examining broad themes across the citation data, failures to properly identify hazards and develop a hazard analysis were frequently noted. Identifying the food safety hazards likely to occur for a given food product and process, and the steps that must be taken to prevent or mitigate the hazards, are foundational to food safety and quality assurance. Five WLs cited the hazard analysis provisions in the PC Rule at 21 CFR §117.130, while another two cited the hazard analysis requirements of the Seafood HACCP rule at 21 CFR §123.6 (7/22; 32%). Four letters (4/22; 18%) cited deficiencies in the design and implementation of preventive controls (21 CFR §117.135) to mitigate the hazards that were identified.

Correctly identifying food safety hazards and designing appropriate controls to eliminate or reduce those hazards are at the core of a proactive, prevention-focused food safety program. FDA provides assistance to firms needing support

TABLE 3. Summary of regulations cited in outbreak-associated warning letters related to human foods issued by the U.S. Food and Drug Administration between January 1, 2018, and August 1, 2023

Regulation	Citation	Number of occurrences implicated	Percentage of total*
Current Good Manufacturing Practice, Hazard Analysis, and Risk-Based Preventive Controls for Human Food (PC Rule)	21 CFR §117	27	59%
Foreign Supplier Verification Programs for Food Importers (FSVP Rule)	21 CFR §1.502 et seq.	8	17%
Fish and Fishery Products (Seafood HACCP)	21 CFR §123	6	13%
Standards for the Growing, Harvesting, Packing, and Holding of Produce for Human Consumption (Produce Rule)	21 CFR §112	3	7%
Production, Storage, and Transportation of Shell Eggs (Egg Rule)	21 CFR §118	2	4%

*Total may not add to 100 due to rounding

in implementing preventive controls through draft guidance documents that provide the agency's non-binding current thinking *(61)* and direct technical assistance for those with specific questions or concerns *(44)*.

Supply chain controls

In addition to the food safety measures directly within the control of a firm discussed above, citations related to inadequate management of the supply chain were another common observance. If a food safety hazard requires a preventive control and that control will be applied earlier in the supply chain, firms must verify those controls. Seven WLs (7/22; 32%) included failures to adequately ensure the safety of food products being received from upstream suppliers. Six were cited for the absence or deficiencies in FSVPs (21 CFR §1.502 et seq.) for imported products, while one firm was cited under the domestic supply chain assurance requirements at 21 CFR §117.405(a)(1). Similarly, FDA offers guidance representing the agency's current thinking to help firms subject to the FSVP rule develop and implement appropriate controls *(52)*.

An overview of selected outbreak investigations noted in Warning Letters

Of the 22 outbreaks noted in the WLs analyzed here, the following select examples illustrate how outbreak investigation and regulatory action lead to the mitigation of foodborne illness outbreaks.

2020 enoki mushroom listeriosis outbreak

Between 2017 and 2020, the FDA, CDC, state, local, and international partners investigated a multinational outbreak of *L. monocytogenes* infections linked to imported enoki mushrooms from one manufacturer in the Republic of Korea. A total of 48 illnesses in the United States (36/48; 75%) and Canada (12/48; 25%) were associated with this outbreak, and isolation dates ranged from August 4, 2016, to December 13, 2019 *(16)*. Historical Canadian isolates of *L. monocytogenes* uploaded to the genomic sequence database maintained by the National Center for Biotechnology Information (National Institutes of Health, Bethesda, MD) in 2020 were found by the CDC to be genetically related to clinical isolates in an unsolved United States outbreak of listeriosis, including isolates recovered from a portobello mushroom sample in 2016 and an imported enoki mushroom sample in 2019. This genetic breakthrough catalyzed product sampling by FDA, the California Department of Public Health (CDPH), and other state partners at retail and import. This sampling led to the recovery of *L. monocytogenes* isolates from enoki mushrooms produced by one manufacturer in the Republic of Korea that were genetically related to clinical isolates. The FDA also conducted a traceback investigation that converged on the same implicated Korean manufacturer, who exported enoki mushrooms to the United States, Canada, Europe, Australia, and Southeast Asia *(33)*. This outbreak

led to FSVP inspections at three importer firms that found deficiencies in food safety verification and recordkeeping for foreign suppliers. A WL was issued to the importer of record that cited a failure to perform a hazard analysis and failure to review verification activities for completeness *(39)*. All enoki mushrooms produced by the implicated manufacturer were recalled, and the manufacturer was also placed on two import alerts. During multiple foreign enoki inspections, risks from condensation and inadequate moisture control were noted and may have been a contributing factor to contamination from *L. monocytogenes*. Import alerts remain a robust tool for FDA to ensure the safety of foods imported into the country.

2022 peanut butter *Salmonella* Senftenberg outbreak

In 2022, FDA, CDC, and state partners investigated a multistate outbreak of *Salmonella* Senftenberg illnesses linked to peanut butter. The outbreak resulted in 21 ill people and three hospitalizations reported in 17 states *(45, 68)*. There was an epidemiologic signal for peanut butter from Firm A, so FDA and state partners conducted an inspection of the facility in 2022. The facility was found to be operating in a state of disrepair, and the firm had not adequately addressed all potential avenues of product contamination, including faulty seals and equipment design which permitted water to enter into the processing equipment *(68)*. Additionally, Firm A had limitations in their finished product testing program to identify contamination. Upon re-testing, some product that had initially tested negative later tested positive as part of the firm's investigation. On May 20, 2022, Firm A agreed to voluntarily recall peanut butter produced at their facility manufactured between October 1, 2021, and May 20, 2022, which precipitated several downstream recalls, and FDA issued a WL to the firm *(53)*. While the exact source and route of the contamination was not determined, epidemiologic and traceback evidence confirmed that the peanut butter consumed by ill people was produced by Firm A.

2019-2020 clover sprout *E. coli* O103 outbreaks

In February 2020, FDA, CDC, and state and local partners investigated an outbreak of *E. coli* O103 infections linked to clover sprouts. The outbreak resulted in 51 illnesses and three hospitalizations, reported in ten states *(2, 32)*. Epidemiologic evidence analyzed by CDC indicated that clover sprouts from specific sandwich chain restaurants were a likely source of the illnesses. FDA investigators analyzed a sample of Brand A sprouts and recovered an isolate of *E. coli* O103, which matched the outbreak strain by whole genome sequencing (WGS). The isolate also matched the outbreak strain from another outbreak that took place between November and December 2019 in Iowa, which was associated with sprouts from multiple restaurants of a sandwich chain. In the earlier outbreak, *E. coli* O103 was isolated from spent irrigation water at the sprouting facility. The 2019 traceback investigation found that a common seed lot was used to grow the recalled sprouts as well as sprouts served at some of the sandwich chain restaurant locations during the 2019 and 2020 outbreaks. In response to the investigation findings, WLs were issued to two sprout growers and the operator of the sandwich restaurants *(34, 36, 37)*. The sprout growers were cited for violations of the Produce Safety Rule, including failing to discontinue use of a seed lot known to be contaminated, and failure to properly maintain and sanitize food contact surfaces and equipment.

2019 papaya *Salmonella* Uganda outbreak

In June 2019, FDA and CDC investigated an outbreak of *Salmonella* Uganda infections linked to papaya imported from Mexico. The outbreak resulted in 81 illnesses reported in nine states, including 27 hospitalizations *(67)*. The epidemiologic and traceback information collected in the investigation confirmed that the distributor from New York was the exclusive distributor of the imported papayas responsible for the outbreak. FDA requested the distributor conduct a voluntary recall of the papayas, but they initially refused to initiate the recall, based on the absence of laboratory evidence supporting *Salmonella* contamination of their papayas *(67)*. FDA contacted the distributor's wholesale customers to ensure the fruit was no longer available for sale, had been discarded, or was not further processed or frozen. Additionally, FDA and CDC issued a public notice advising the public not to consume, sell, or distribute the distributor's papayas *(27)*. The firm was issued a WL for FSVP violations, due to the firm's imported papayas being implicated in outbreaks in 2019 and 2017, in addition to a previous finding of *Salmonella* in the firm's imported papayas in 2011 *(47)*.

2020 bagged salad cyclosporiasis outbreak

In June 2020, FDA, along with CDC and state and local partners investigated a multistate outbreak of *Cyclospora* infections linked to salad products containing iceberg lettuce, red cabbage, and carrots *(31)*. The outbreak resulted in 701 illnesses and 38 hospitalizations reported in 14 states. The traceback investigation identified that both the brand name and private labels were produced by the same processing facility. This led to a voluntary recall of the product by the processor under its brand and private labels associated with multiple, large grocery store chains. The firm was issued a WL for failure to properly implement preventive controls and validate its supply chain *(35)*. Additionally, FDA investigated multiple farms identified in the traceback but could not conclusively determine the source of this outbreak. As a result of this outbreak, FDA increased surveillance sampling in the growing area.

2021 cashew brie salmonellosis outbreak

In 2021, FDA, CDC, state, and local partners investigated a multistate outbreak of *Salmonella* Duisburg, *Salmonella* Chester, *Salmonella* Typhimurium, and *Salmonella* Urbana (*S.* Urbana) infections linked to the consumption of a brand

of cashew brie, a vegan or plant-based cheese alternative. The outbreak resulted in 20 illnesses and five hospitalizations reported in four states *(13)*. Investigators from the Tennessee Department of Health and the California Department of Public Health collected product samples of the cashew brie and recovered the outbreak strain of *S.* Urbana. FDA investigated the producer's facility and collected and analyzed samples of unopened, raw cashews, which also yielded the same *S.* Urbana outbreak strain. This outbreak was likely caused by a miscommunication between supplier and manufacturer on the Ready-to-Eat (RTE) status of the cashew ingredient. The firm was issued a WL for failure to implement processes to control for the presence of pathogens in raw materials *(42)*. The producer recalled all varieties of its products *(40)*.

CONCLUSIONS

FDA recognizes that the safety of domestic and imported food supply in the United States is a shared responsibility. Since the passage of the 2011 FDA Food Safety Modernization Act (FSMA), the agency has aimed for the prevention of foodborne illness, instead of exclusively focusing on outbreaks *(62)*. The goals of the FSMA regulations are to clarify what specific steps must be taken at each point within the supply chain to avoid contamination. Specifically, firms must investigate and determine the cause of any violations and prevent their occurrence.

Food safety and monitoring is an essential responsibility of industry. Our industry partners must prevent dangerous microorganisms from contaminating processing facilities and, eventually, our food. The goal of both the Preventive Controls for Human Food and Foreign Supplier Verification Program regulations are to safeguard consumers. These regulations mandate that the operators of an establishment take precautions against contamination, including from environmental sources, and confirm that hazards are being managed. Firms could, for instance, conduct product testing and environmental monitoring to confirm that microbiological dangers have been controlled *(51)*. WGS can accompany industry's strategies to prevent foodborne illness and offers an extremely accurate DNA fingerprint that identifies pathogens from food or environmental samples. Results from WGS can be used as an industry tool to assess the persistence of a pathogen in the firm environment, evaluate the efficacy of hygienic and preventive measures, and monitor the ingredient supply chain *(7, 58)*.

Industry has the responsibility to ensure it complies with all requirements of federal law, including FDA regulations. Understanding the regulatory violations identified during an outbreak investigation may help those who manufacture and distribute the nation's food supply focus on prevention efforts and reduce the burden of foodborne illness.

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DISCLAIMER

The findings and conclusions of this report are those of the authors and do not necessarily represent the official position of the U.S. Food and Drug Administration.

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