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Research Paper

Multistate Outbreak Investigation of *Salmonella* Infections Linked to Kratom: A Focus on Traceback, Laboratory, and Regulatory Activities

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ABSTRACT

During spring 2018, the U.S. Food and Drug Administration (FDA), Centers for Disease Control and Prevention, and state and local public health agencies responded to a multistate outbreak of gastrointestinal illnesses caused by multiple *Salmonella* serovars and associated with consumption of kratom, a product harvested from a tropical tree native to Southeast Asia. The outbreak included 199 case-patients reported by 41 U.S. states, with illness onset dates ranging 11 from January 2017 to 8 May 2018, leading to 54 hospitalizations and no deaths. Case-patients reported purchasing kratom products from physical and online retail points of service (POSs). Products distributed to 16 POSs where 24 case-patients from 17 states purchased kratom were selected for traceback investigation. Traceback revealed that the kratom was imported from several countries, the most common being Indonesia. Local and state officials collected product samples from case-patients and retail POSs. The FDA collected 76 product samples from POSs and distributors, of which 42 (55%) tested positive for *Salmonella*. The positive samples exhibited a range of pulsed-field gel electrophoresis patterns and whole genome sequence genetic heterogeneity, and 25 (60%) of 42 samples yielded at least one isolate indistinguishable from one or more outbreak-related clinical isolates. Although it does not exclude a possibility of a single contamination source, the extent of genetic diversity exhibited by the *Salmonella* isolates recovered from product samples and a lack of traceback convergence suggested that kratom was widely contaminated across multiple sites from which it was grown, harvested, and packaged. As a result of the contamination, kratom products were recalled by numerous firms (both voluntarily and mandatory). Epidemiologic, traceback, and laboratory evidence supported the conclusion that kratom products were associated with illnesses.

HIGHLGHTS

- Epidemiology investigations showed that multiple salmonella illnesses were associated with consumption of kratom, harvested from a tree native to Southeast Asia.
- Traceback investigations revealed that kratom was imported from several countries, most common being Indonesia.
- Extent of *Salmonella* genetic diversity from kratom samples and lack of traceback convergence, suggested that the products were widely contaminated.

Key words: Foodborne illness outbreaks; Kratom; *Salmonella*; Traceback investigation

The Centers for Disease Control and Prevention (CDC) estimates that nontyphoidal *Salmonella* causes about 1.2 million illnesses, 23,000 hospitalizations, and 450 deaths in the United States every year and that food is the exposure source for about 1 million of these illnesses *(4)*. During spring 2018, federal, state, and local public health and regulatory partners responded to a multistate *Salmonella* outbreak linked to kratom with unusual levels of diversity, as evidenced by pulsed-field gel electrophoresis (PFGE) and whole genome sequencing (WGS) analyses. The outbreak was first detected when a cluster of people infected with *Salmonella* I 4,[5],12:b:– was identified in the CDC PulseNet database. During the investigation, states and the U.S. Food and Drug Administration (FDA) collected both leftover and unopened kratom products to test for *Salmonella* contamination. Additional *Salmonella* serovars were identified in the kratom products. A search of the CDC PulseNet database identified ill people infected with *Salmonella* Heidelberg, *Salmonella* Javiana, *Salmonella* Okatie, *Salmonella* Weltevreden, and *Salmonella* Thompson serovars. The case-patients had reported consuming kratom.

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Kratom is a tropical tree (*Mitragyna speciosa*) belonging to the coffee family *Rubiaceae,* native to Southeast Asia. The leaves and bark of kratom are chewed, brewed in tea, smoked, or ingested as a compressed tablet or capsule *(27)*. In the United States, kratom products are primarily available as powders that can be dissolved in liquid or consumed in food *(4, 10)*.

Kratom and its alkaloids are regulated as controlled substances by many countries, including European Union member states such as Denmark, Latvia, Lithuania, Poland, Romania, Sweden, and France, along with the United Kingdom, Malaysia, Thailand, Myanmar, Australia, and New Zealand *(7, 11, 20)*. Although listed as a "drug and chemical of concern" by the U.S. Drug Enforcement Administration (DEA), kratom is not scheduled under the U.S. Federal Controlled Substances Act or monitored by national drug abuse surveys at this time, but it has been banned in several states *(20)*. In the United States, kratom is generally sold online and in smoke shops, gas stations, other retail outlets, and private homes. At this time, there are no FDA-approved uses for kratom. In 2018, federal, state, and local health and regulatory partners investigated a multistate outbreak of gastrointestinal illnesses caused by multiple *Salmonella* serovars linked to exposure to kratom and kratom-containing products. Based on epidemiologic, traceback, and laboratory evidence, contaminated kratom was identified as the probable vehicle of illnesses. As a result, product recalls were conducted (both voluntary and mandatory). This was the first multistate *Salmonella* outbreak in the United States to be linked to consumption of kratom products.

In a 2018 to 2019 online cross-sectional survey of 59,714 adult respondents, a past-year estimated kratom use prevalence of 0.8% was found, with users tending to have more serious substance abuse profiles than nonusers or users of cannabis, alcohol, or cigarettes *(16)*. In a retrospective analysis of the American Association of Poison Control Center's National Poison Data System from 2014 to 2019, it was found that kratom use has increased over time in the United States *(8)*.

MATERIALS AND METHODS

Epidemiologic investigation. In December 2017, CDC PulseNet, the national molecular subtyping network for foodborne disease surveillance, detected a cluster of 14 *Salmonella enterica* serovar I 4,[5],12:b:– human infections indistinguishable by PFGE. State labs performed the PFGE analysis and uploaded the gel images to CDC PulseNet. Health and regulatory officials in several states and the FDA collected leftover kratom products from case-patients and unopened kratom products from POSs and distributors to test for *Salmonella* contamination. *Salmonella* serovars including Heidelberg, Javiana, Okatie, Thompson, and Weltevreden were identified in kratom products, and a search of the CDC PulseNet database identified ill people infected with these additional *Salmonella* serovars. With product testing and epidemiologic evidence, the outbreak case definition was expanded to include the additional illnesses caused by *Salmonella* Heidelberg, *Salmonella* Javiana, *Salmonella* Okatie, *Salmonella* Thompson, and *Salmonella* Weltevreden, each serovar indistinguishable by PFGE *(4)*. The final outbreak case definition included laboratory-confirmed case-patients who had reported exposure to kratom, with illness onset dates between 11 January 2017 and 8 May 2018 *(4)*.

Product jurisdiction within the FDA. The FDA has the authority to regulate kratom products that fall within the FDA's jurisdiction, such as when a kratom product meets the definition of a drug per 21 U.S. Code 321(g), food per 21 U.S. Code 321(f), or dietary supplement per 21 U.S. Code 321(ff)(1) *(18)*. To determine a specific product's classification and jurisdiction within the FDA, the FDA and state and local government officials collected packaging and label information from patients, online, and/or physical point of service (POS) locations, as well as other potential evidence of intended use. The information was first reviewed by the FDA's Center for Food and Safety and Applied Nutrition (CFSAN) Office of Compliance and subject matter experts of CFSAN Dietary Supplement Programs to determine whether the products were dietary supplements or conventional food. If there were disease treatment claims or other evidence of intended use as a drug, the product was referred to the FDA's Center for Drug Evaluation and Research Office of Compliance for review and follow-up. At this time, there are no FDA-approved uses for kratom.

Traceback investigations. Traceback investigations were completed through collaborative efforts of the CDC, the FDA, and state and local government officials. Outbreak-associated case-patients were selected for traceback if they reported purchasing kratom products from online or physical POS locations. Each case-patient had a reported illness onset within 3 days after exposure to kratom and reported product purchase before becoming ill. The case-patients and associated POSs were geographically well distributed to minimize bias and increase the confidence in any identified convergence *(4, 12, 14)*.

The FDA performed traceback investigations at 16 POSs involving 24 case-patients. Thirteen POSs were associated with single case-patients, two were associated with two case-patients, and one was associated with seven case-patients. The case-patients became ill and were lab confirmed with an outbreak *Salmonella* serovar within 14 days after kratom purchase. The investigators collected records, including receipts, invoices, bills of lading, packaging labels, and product declaration documents from case-patients, POSs, and distributors, and they noted handling and processing practices, including product turnaround time. Some documents contained purchase dates, varieties, brands, lots, amounts, distributors, and countries of origin. Where records were unavailable, the investigators collected traceback information through interviews and e-mails with case-patients, POSs, and distributors.

Laboratory investigations. During the investigation, FDA, state, and local government officials collected leftover kratom samples from case-patients and unopened samples from POSs and distributors to test for the presence of *Salmonella* species. Samples were also collected from locations not associated with case-patients, including POSs 17 and 18 and distributors 28, 29, and 30, as a result of state, local, and FDA active surveillance activities. Specific laboratory results from state and local health departments are not included herein but were mentioned in the FDA's public communications and did support recall efforts *(23)*. The FDA samples were collected following the *Investigations Operations Manual,* including maintaining a chain of custody *(26)*. Samples were screened at the FDA's regulatory laboratories for the presence of *Salmonella* using the Vidas Salmonella (SLM) Assay Kit (AOAC 2004.03) or Vidas SLM Easy Assay Kit *(1)*. For

Salmonella-positive isolates, a confirmatory test was performed following the procedures outline in the FDA's *Bacteriological Analytical Manual (21)*. The isolates were classified using the Kauffman-White scheme, following Difco Laboratories, the Statens Serum Institute, and the CDC's and manufacturer's package inserts for *Salmonella* antisera and quality-control antigens *(2, 9)*. Antimicrobial susceptibility testing was performed using a Trek Sensititre panel that included 14 antimicrobial agents and Trek and National Antimicrobial Resistance Monitoring System methods *(13)*. No further analysis was performed for samples that had screened negative.

The genetic relatedness of *Salmonella* isolates was assessed using WGS. Sequence data were submitted to the National Center for Biotechnology Information (NCBI) Sequence Read Archive and incorporated into the NCBI Pathogen Detection database. Closely related isolates were identified based on single nucleotide polymorphism (SNP) cluster membership in the NCBI Pathogen Detection database *(5)*. Isolates that were not members of a SNP cluster were regarded as not closely related to isolates in the database. Analyses were performed on groups of closely related isolates using CFSAN SNP Pipeline version 2.0 with default parameters *(6)*. Phylogenetic trees were constructed using GARLI version 2.01.1067 (searchreps = 10), a computer program that performs phylogenetic interference *(28)*. Interpretations of genomic relatedness were based upon SNP distance, tree topology, and bootstrap analysis in accordance with the framework outlined in Pightling et al. *(15)*.

RESULTS

Epidemiologic investigation. As of 24 May 2018, 199 individuals had been identified with gastrointestinal illnesses meeting the outbreak case definition. The case-patient clinical isolates, collected from 41 states, included *Salmonella* I 4,[5],12:b:− ($n = 83$) and *Salmonella* Heidelberg ($n = 6$), *Salmonella* Weltevreden ($n = 6$), *Salmonella* Thompson ($n = 59$), *Salmonella* Okatie ($n = 28$), and *Salmonella* Javiana ($n = 17$) serovars. Ages ranged from less than 1 to 75 years with a median of 38 years, and 48% of case-patients were female. The illness onset dates ranged from 11 January 2017 to 8 May 2018. There were 54 hospitalizations and no deaths. Of 199 case-patients, 103 were available and interviewed with an outbreak-specific questionnaire, and 76 (74%) of those interviewed reported kratom consumption *(3)*.

Traceback investigation. The FDA's traceback investigation determined and documented distribution, production chain, and source or sources of kratom distributed to the POSs during the outbreak. Using product declarations, records, e-mails, and interview information collected from case-patients, POSs, and distributors, a traceback diagram was assembled to document the distribution of kratom products to POSs from distributors and foreign suppliers (Fig. 1). Case-patients reportedly purchased kratom products from seven online and nine physical retailers. The seven online retailers were linked to 14 (58%) of 24 case-patients. POSs 1 and 2 offered online and physical retail sales. POS 9 was both a retailer and a distributor (distributor 14), selling to other distributors. The nine physical retailers were linked to 10 (42%) of 24 case-patients. In addition to selling at physical retail, POS 16 was a distributor (Fig. 1), and 12 of the 16 POSs had received kratom imported from Indonesia. Although kratom (*M. speciosa*) is native to Southeast Asia, traceback revealed kratom also entered the United States from Canada, the United Kingdom, Thailand, and other unspecified countries.

The products were marketed in many forms, such as pills, ground or loose leaves, or powder. Powder package sizes ranged from 28 g to 1 kg. Packaging, labels, brands, and formulations varied from a powder in plastic unlabeled bags or bins to prepackaged and labeled containers with brand and ingredient information. Many online POSs accepted credit card payments, whereas others only accepted wire transfers, cash on delivery, or cryptocurrency. Some POSs also sold other botanical products, consumer goods, empty capsules, and encapsulation machines. The lack of identifying finished product and raw material ingredient information, as well as lack of transactional records, made it difficult for case-patients to identify which type of kratom product was purchased and for investigators to consistently determine whether a product available at a firm was the same lot purchased by the case-patient.

At POS and distribution levels, there were no documented product turnaround, shelf life, use-by, or expiration time frames. There was no standard product nomenclature or description, and there were variations in names, spellings, and formulations. Kratom from multiple suppliers had been comingled and repackaged, with no record of lot numbers or written handling procedures. Some online firms displayed product descriptions, consumer preparation guidance, recommended dosages, uses, and user experience testimonials, including marketing kratom as psychoactive, whereas others listed little to no information about the intended use of the product. Many POSs and distributors had no physical addresses, and some used commercial delivery service mailboxes as their contact location. Many online distributors operated Web sites through proxy registrations or withheld domain name registrant information. No records were available at 13 (81%) of 16 POSs and 23 (85%) of 27 distributors to determine amounts, verify distribution, or determine countries of origin.

Based on the available records and information, the products at POSs and distributors were imported from multiple countries, including Canada, the United Kingdom, Indonesia, Thailand, and unknown countries. Eighteen of 24 (75%) case-patients purchased products from POSs whose kratom products traced back to Indonesia and other countries. Kratom products sold at POSs 1 and 2 were traced back as exclusively imported from Indonesia. For 5 of the 27 distributors, no records or information was available to identify from which countries the kratom was imported. For suppliers identified in countries where kratom is native, no farm or harvest location or manufacturing information was available.

Laboratory investigation. Of 76 kratom product samples collected and analyzed by the FDA, 42 (55%) tested positive for *Salmonella*. Of the 42 positive samples,

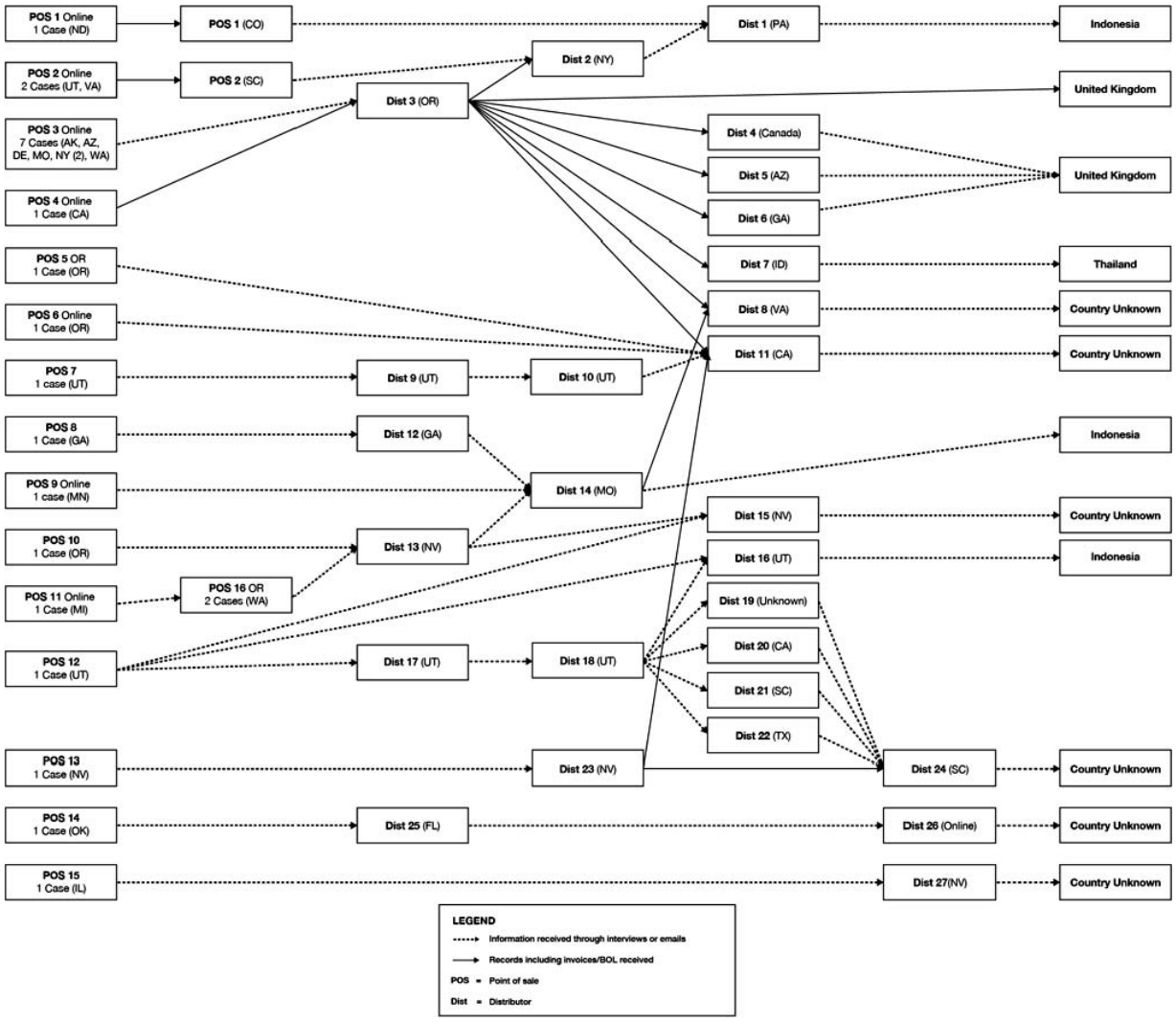

FIGURE 1. *Traceback diagram showing kratom products from points of service associated with case-patients through distribution to suppliers with countries of origin.*

25 (60%) were determined to be outbreak-related by WGS and or PFGE. Overall, 22 (52%) samples were determined to harbor strains representing more than one *Salmonella* serovar. In addition, 16 (72%) of 22 samples with more than one *Salmonella* serovar were outbreak related (Table 1).

The positive samples were collected from six POSs and eight distributors (Table 1). Although POSs 17 and 18 and distributors 28, 29, and 30 were not associated with case-patients, 10 samples were positive with *Salmonella* serovars related to the outbreak by PFGE or WGS, implying that the contaminated kratom was distributed outside the case-patient–associated POSs and distributors. When products tested positive for *Salmonella,* the responsible firms were informed of positive results. Most firms voluntarily recalled the affected products, and the FDA published a list of products that tested positive for *Salmonella,* including, where known, the retailer and/or known labeled distributor of the product on its Web site *(23)*.

In addition to voluntary recalls, the FDA issued a mandatory recall order on 2 April 2018. This was after the FDA determined that there was reasonable probability that all food products containing powdered kratom manufactured, processed, packed, and/or held by one firm were adulterated under section 402(a)(1) of the Federal Food, Drug, and Cosmetic (FD&C) Act and that use of or exposure to such products would cause serious adverse health consequences to humans or animals. The firm opted to not voluntarily recall after the FDA provided it with an opportunity to voluntarily cease distribution and recall the products. The FDA has the authority to mandate a recall when a responsible party chooses not to voluntarily recall when the criteria under section 423 of the FD&C Act are met. The FDA can use its mandatory recall authority when it determines that there is a reasonable probability that an article of food (other than infant formula) is adulterated under section 402 of the FD&C Act or misbranded under section 403(w) of the FD&C Act and that there is a reasonable probability that use of or exposure to such food will cause serious adverse health consequences or death to humans or animals *(25)*. This was the FDA's first time issuing a mandatory recall order, and at the time of this publication, this remains the only time the FDA has issued a

TABLE 1. *Kratom samples collected and analyzed by FDA that tested positive for* Salmonella *serovars*[a]

Firm ID[b]	*Salmonella* testing	*Salmonella* serovar(s)	Outbreak related
Dist 1	Positive	I 4,[5],12:b:−, Weltevreden	Yes
Dist 1	Positive	Javiana, Okatie, Orientalis, Thompson, Weltevreden	Yes
Dist 1	Positive	I 4,[5],12:b:−, Okatie, Orientalis, Thompson, Weltevreden	Yes
Dist 1	Positive	Weltevreden	No
Dist 3	Positive	Weltevreden	Yes
Dist 3	Positive	Thompson	Yes
Dist 3	Positive	Thompson	No
Dist 3	Positive	Okatie, Orientalis	Yes
Dist 15	Positive	Weltevreden	No
Dist 15	Positive	Javiana, Melaka, Newport	No
Dist 15	Positive	Javiana, Weltevreden	No
Dist 15	Positive	Weltevreden	No
Dist 15	Positive	I 4,[5],12:b:−, I 9,12:-:1,5, Javiana, Okatie, Rubislaw, Thompson	Yes
Dist 18	Positive	I 4,[5],12:b:−, Javiana, Wandsworth	No
Dist 18	Positive	I 30:-:e,n,z15, Okatie, Thompson, Wandsworth	Yes
Dist 18	Positive	Okatie, Virchow, Weltevreden	Yes
Dist 28	Positive	I 4,[5],12:b:−, Kumasi, Okatie, Thompson	Yes
Dist 28	Positive	Weltevreden	Yes
Dist 28	Positive	I 4,[5],12:b:−, Javiana, Orientalis, Thompson	Yes
Dist 28	Positive	Okatie, Weltevreden	Yes
Dist 28	Positive	I 4,[5],12:b:−, Javiana, Kumasi	No
Dist 29	Positive	Javiana	No
Dist 29	Positive	Weltevreden	No
Dist 30	Positive	I 4,[5],12:b:−, Okatie, Weltevreden	Yes
Dist 30	Positive	I 4,[5],12:b:−	No
Dist 30	Positive	Javiana, Thompson, Weltevreden	Yes
Dist 30	Positive	Okatie, Weltevreden	Yes
Dist 30	Positive	Okatie	Yes
POS 1	Positive	I 4,[5],12:b:−, Javiana, Okatie, Thompson, Weltevreden	Yes
POS 3	Positive	Okatie	Yes
POS 3	Positive	I 4,[5],12:b:−	No
POS 9/Dist 14	Positive	Thompson	Yes
POS 9/Dist 14	Positive	Javiana	No
POS 9/Dist 14	Positive	I 4,[5],12:b:−, Okatie	No
POS 9/Dist 14	Positive	Javiana	No
POS 9/Dist 14	Positive	Weltevreden	Yes
POS 9/Dist 14	Positive	Okatie, Thompson	Yes
POS 16	Positive	Okatie, Weltevreden	Yes
POS 17	Positive	Javiana, Weltevreden	No
POS 17	Positive	Weltevreden	Yes
POS 17	Positive	Weltevreden	No
POS 18	Positive	Okatie	Yes

[a] Each row represents a sample.
[b] ID, identifier; Dist, distributor.

mandatory recall order. Ultimately, the firm recalled all kratom powder products it had previously manufactured, processed, packed, and/or held from 4 April 2017 to 17 April 2018 *(24)*.

DISCUSSION

The epidemiologic, traceback, and laboratory evidence collected and analyzed during this investigation demonstrated that the outbreak was caused by contaminated kratom and kratom-containing products. Traceback investigation showed that kratom was imported from multiple countries. Kratom samples, collected across various points in the distribution chain, yielded outbreak-related *Salmonella* serovars, suggesting that contamination may not have been limited to a single source, process, or activity within the distribution chain. Kratom grinding, encapsulation, bottling, and labeling occurred at various points throughout the distribution chain and were a likely contributing factor to increased risk for contamination. However, the investigation did not reveal that other botanicals were grown, harvested, manufactured, packaged, or distributed with kratom, suggesting that kratom was the source of the contamination.

Tracing positive samples and isolates identified via this outbreak investigation presented complexity. In most traceback investigations, positive samples associated with an outbreak are considered a breakthrough in identifying the

source contamination. In this situation, new positive samples tended to raise more questions regarding additional illnesses, and in several instances, new *Salmonella* serovars served to expand the definition of the outbreak, rather than aid in narrowing a list of likely contamination sources. The FDA also analyzed isolates from samples using WGS, looking for connections to similar *Salmonella* serovars. From these samples, multiple *Salmonella* serovars were identified (Table 1). Laboratory and traceback findings were combined to determine the distribution chain and origins, but no clear picture emerged. However, isolation of outbreak and nonoutbreak *Salmonella* serovars from samples that associated and did not associate case-patients suggests that kratom may be grossly contaminated.

There were numerous challenges in conducting the traceback investigation for kratom compared with other food products. The efforts to establish product jurisdiction through review of kratom packaging and label information from patients, online, POSs, distributors, and other potential evidence of intended use slowed the FDA's traceback and other regulatory activities. POSs and distributors provided little information on the product's use, manufacturing, and distribution, including the absence of expiration times, shelf life, turnaround times, and product handling processes. FDA foodborne outbreak traceback investigators rely on shipment records and information to document incoming and outgoing amounts and lot information, as well as to link shipments with case-patients, POSs, distributors, and manufacturing origin. It is possible that comingling and repackaging of products from different suppliers occurred at POS and distributor levels with little documentation. With little inventory or lot information available, there were delays in the investigation and ultimately an inability to verify available products, associated suppliers, or growing and harvest origins.

Unlike most FDA traceback investigations of products purchased from physical POS locations where illnesses can be clustered, online purchases are generally widely dispersed, with understandably little regional clustering, adding a new dimension to traceback investigations. Investigators faced challenges verifying contact information for online POSs and distributors, because Web site registration data were often inaccurate or unavailable. Online purchases posed additional traceback and regulatory challenges because of a lack of physical customer receipts and unusual physical source locations, including commercial maildrops, virtual office spaces, and even residential homes. It is atypical for the FDA to inspect or collect documents from such facilities. The FDA continues to learn how to navigate these unique investigations.

Even when the physical and online source locations were determined, it was difficult to determine and evaluate the conditions under which the products were manufactured, packaged, and distributed. The POSs and distributors had no FDA Establishment Identification numbers, which are normally issued by the FDA to identify regulated establishments or facilities for inspections. In addition, some POSs and distributors may have thought that kratom products fell outside of FDA jurisdiction or were not subject to FDA authority. Under normal circumstances, there are mutual expectations between regulators and regulated entities. When the expectations and understanding of jurisdiction are absent, inspection and document collection can be delayed or inhibited. The use of the FDA's mandatory recall authority was a reflection of the desire of the agency to take swift actions to protect the public.

Irrespective of the documented challenges, assembling the traceback information from case-patients, POSs, and distributors was an important step in attempting to understand how kratom is distributed. Despite being native to Southeast Asia, kratom associated with this outbreak was also imported from Canada and the United Kingdom to the United States. However, there is no evidence to suggest that kratom imported from nonnative countries was grown and harvested there *(17, 19)*. With lack of information on growing and primary manufacturing locations, multiple contamination sources during growing or manufacturing cannot be ruled out. With 55% of the samples collected and analyzed by the FDA testing positive for *Salmonella,* some with multiple serovars, a couple of scenarios may have occurred. There may have been widespread and multiple contamination events during growing, harvesting, and manufacturing and the possibility of comingling or cross-contamination among kratom products during distribution. This scenario is supported by (i) a lack of convergence to a common distributor, brand, supplier, country of origin, or grower; (ii) a high level of genetic diversity among *Salmonella* serovars isolated from kratom samples collected from case-patients, POSs, and distributors; and (iii) an unexpected level of genetic diversity within individual samples. It is also possible that a single source, such as a grower, region, or country, with diverse *Salmonella* contamination exists, because more than half of the positive samples contained *Salmonella* isolates representing multiple serovars. Acknowledging the limitations of the traceback, such a single source cannot be excluded.

Goods imported into the United States must be declared to U.S. Customs and Border Protection, and information about the shipment, product, and related firms must be provided by the importer. Products regulated by the FDA are reviewed, and if they appear to be in violation of FDA laws or regulations, they can be refused entry into the United States. There are two FDA import alerts that identify kratom products and firms that have met the criteria for Detention without Physical Examination *(22)*. Import Alert 54-15 applies to kratom products that are dietary supplements or bulk dietary ingredients. Import Alert 66-41 applies to kratom products that are drugs and appear to be unapproved new drugs. However, lack of declaration and false declaration of kratom products are ways importers attempt to evade FDA jurisdiction and federal oversight that helps to prevent violative products from entering U.S. commerce.

Lastly, the lack of accurate and/or truthful information and records provided throughout the entire supply chain diminished the ability to identify and trace possible contamination sources during this outbreak. Besides false declarations at the time of import, it was difficult to determine the intended use of kratom products in U.S. commerce because of the absence of product names,

dosages, labels, packaging, and use instructions. The ability to correctly classify products as drugs, dietary supplements, or food is critical for determination of product jurisdiction and potential regulatory actions. These jurisdictional issues required additional time for evaluating the products, investigation, and increased interactions among functional groups, resulting in delays not normally experienced in foodborne illness outbreak investigations. Attempts to circumvent FDA authority during import, manufacturing, labeling, and distribution made it challenging to protect the public from the threat of *Salmonella* in kratom.

The FDA investigations revealed the multistate outbreak of salmonellosis from multiple serotypes of *Salmonella*—I 4,[5],12:b:–, Thompson, Okatie, Heidelberg, Weltevreden, and Javiana—were caused by contaminated kratom or kratom-containing products. Widespread *Salmonella* contamination in various forms of kratom and at multiple points in distribution indicated that initial contamination occurred before POS. Because of multiple suppliers, lack of accurate import declarations, lack of distribution and production records, and comingling at multiple distribution levels, the investigation was unable to identify a specific single country of origin for many outbreak-related POSs. Despite these challenges, the investigation resulted in several voluntary and one mandatory recall of kratom products in the United States.

Currently, it is unknown whether the kratom plant is inherently prone to contamination or contamination is a product of poor production, harvest, and postharvest processes. Although imported to the United States from other countries, kratom is native to Indonesia and cannot be ruled out as the origin of the contaminated kratom.

The lack of records and information provided to the FDA resulted in the inability to traceback products to specific processors or growers. This also inhibited the FDA from conducting onsite foreign inspections and conducting examination and sampling of imported products, as would be done in foodborne illness outbreaks traced back to foreign suppliers. Although limited, the available records and information from interviews with cases, POSs, and distributors were generally sufficient to document links with shipments countries from which kratom was imported. If kratom declared to the FDA at the time of import appears to be in violation of an FDA law or regulation, it can be refused entry into the United States. In the United States, the failure of POSs and distributors to follow good manufacturing practices during processing and packaging puts consumers at additional risk, especially when other botanical products are processed and packed at same location, because of the chances of cross-contamination. In addition to the public health concerns raised by this outbreak, there are no FDA-approved uses for kratom. Although it is important to gather more information, the data suggest that certain substances in kratom have opioid properties that expose users to the risks of addiction, abuse, and dependence, and the agency has received adverse event reports associated with kratom use.

Regardless of its pharmacology and legal status, consumers, retailers, and further processors in the United States should be aware of the prevalence of *Salmonella* in kratom products, especially given its increased use in the United States *(8)*. The outbreak highlighted the continued public health risk of *Salmonella* in kratom products and a potential need for manufacturing, distribution, marketing, and microbiological assessment studies and research.

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