

Product Tracing in Epidemiologic Investigations of Outbreaks due to Commercially Distributed Food Items – Utility, Application, and Considerations

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PREFACE

PulseNet, the national molecular subtyping network for foodborne disease surveillance, has been extremely successful in detecting multi-state outbreaks due to commercially distributed food items. This success is based on the ability of molecular subtyping of foodborne pathogens to increase the specificity of case definitions used for cluster investigations. As the number of pulsed-field gel electrophoresis (PFGE) patterns submitted to PulseNet by public health laboratories has grown, so has the number of documented PFGE subtype clusters that might represent multi-state foodborne disease outbreaks. The success of PulseNet, however, has challenged the epidemiologic capacity and approaches used to investigate this growing number of subtype clusters.

In these types of cluster investigations, increasing the specificity of food exposure information provided by case-patients is equally as important as increasing the specificity of the case definition. Tracing the distribution pathway of suspect food items to production source may be the only way to obtain the food exposure specificity necessary to identify the outbreak vehicle. The effective use of product tracing as part of the epidemiologic investigation has been demonstrated in numerous foodborne disease outbreaks. However, the approaches and systems used to conduct product tracing in this context have not been standardized, and the application of this critical tool has not kept pace with the growing number and complexity of cluster investigations. Public health protection can be greatly enhanced if product tracing is more consistently and effectively applied in cluster investigations.

This document attempts to summarize the rationale for conducting product tracing as part of epidemiologic investigations, how product tracing fits in with the rest of an investigation, how it can be conducted most efficiently and effectively, and barriers to its use. It includes potential roles of key organizations and recommendations for communication and coordination among the multiple agencies that are typically involved in these types of investigations. A comprehensive review of outbreak detection and investigation methods is not possible here; for more details, the reader is referred to the *Guidelines for Foodborne Disease Outbreak Response* (CIFOR 2014).

Local and state agencies, including public health, environmental health, and agriculture agencies, are a primary focus of this document because this is where data collection for all outbreak investigations must begin in earnest. However, because most pertinent outbreaks will be multi-jurisdictional, the federal public health and regulatory agencies also are primary intended audiences; they also are critical collaborators and must support the concept of product tracing as an important part of epidemiological investigations for the process to be carried out most effectively.

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EXECUTIVE SUMMARY

The number of multi-state pulsed-field gel electrophoresis subtype clusters of foodborne pathogens (e.g., *Salmonella enterica*, *E. coli* O157:H7) identified by PulseNet has grown in recent years, and investigations of these clusters are becoming increasingly complex. Traditional analytic epidemiologic investigation methods based on subject interviews (e.g., case-control studies) are often not sufficient to identify and confirm the vehicle of outbreaks caused by commercially distributed food items. Consequently, product tracing has emerged as an increasingly important part of the epidemiologic process for the identification of a foodborne outbreak vehicle.

The overall goal of product tracing to aid an epidemiologic investigation is to determine whether a food item consumed by multiple case-patients in a cluster has a source or distribution point in common. Product distribution patterns are determined to add specificity to exposures and therefore assess the plausibility of one or more vehicles.

The decision about when product tracing is warranted in an epidemiologic investigation, and for what food item(s), depends on the timely collection and evaluation of detailed epidemiologic data. Depending on the retail source and distribution network, epidemiologists, environmental health specialists, and investigators from regulatory agencies may all assist in the traceback effort. Product tracing may be initiated by epidemiologists following up on individual cases. When it is apparent that a concerted tracing effort is warranted to advance the investigation, the epidemiologist(s) should engage the regulatory authority that inspects or regulates the involved establishment(s).

With the number of agencies potentially involved, it is essential to maintain clear lines of communication in order to coordinate efforts efficiently. A lead epidemiologist investigator should be designated who can represent all cooperating epidemiology agencies. This lead investigator is the logical person to request that a regulatory agency conduct a product trace.

The appropriate epidemiologist investigator(s) should provide a written statement describing the outbreak in detail for the regulatory agencies, including the specific evidence and rationale for launching the tracing effort. Once documentation is provided to the appropriate regulatory agencies, a meeting or conference call between the public health investigators and the involved regulatory agencies should be conducted to go through the information in detail, so that questions may be answered and a firm plan agreed upon.

Exposures to trace should be prioritized based on: the likelihood that the exposure is truly the exposure of interest for a case-patient; the availability of clear, documented details on the exposure; whether or not other case-patients share specific commonalities (e.g., ate at the same restaurant, shopped at the same grocery store, reported the same brand or variety of the suspect food item); and geographic and/or temporal dispersion of case exposures.

Conducting a product trace on any given exposure is conceptually straightforward: it is determining and documenting the producer, manufacturer, supplier, and distribution pathway(s) for the food item(s) of interest. A key goal in a traceback is to determine if there is a supplier or

other point in the distribution chain in common. The investigator doing the trace should generally start by talking to the manager who orders food at the facility that provided the food to the case-patient. Make sure the manager is clear on the specific meal/purchase date(s) of interest (these dates are provided by the epidemiologic investigators based on the food purchase dates provided by case-patients).

A great deal of useful information often can be provided by a food manager during a 10-minute phone conversation; this information can be sufficient to move the investigation forward even if additional investigatory efforts are not possible or feasible. However, as the manager is providing information on the suppliers of the food item of interest, the investigator should also request written (or ideally electronic) documentation of that information—typically invoices from the distributor corresponding to the shipment(s) most likely associated with sale of the suspect food item and corresponding bills-of-lading. Because the purpose of these tracebacks is to provide detailed exposure information for the epidemiologic investigation, the speed of the traceback is critical. Thus, gathering information by fax and/or e-mail in addition to telephone is likely to be more efficient than dispatching inspectors to gather physical records from each establishment.

As the data are being gathered, a flow chart or diagram should be made illustrating the distribution pathways and timeline from the exposures that were traced. Agencies conducting the traces should regularly share updates on the traces with the lead epidemiologic investigators using this data presentation format. Product tracing data are best interpreted through a joint analysis by the epidemiologist investigators and the regulatory agencies that conducted the traces. These entities should be in constant communication throughout the process and agree on how the product tracing data relate to the rest of the epidemiologic, laboratory, and environmental assessment information.

To begin building a functional network and system for conducting product traces as part of epidemiologic investigations, epidemiology agencies should develop a contact list for all potential regulatory agencies that could be asked to conduct an epidemiologic trace and a protocol for engaging these collaborators in such an effort. Ideally, relationship building should be conducted ahead of time and entail development of joint protocols, MOU's, etc. (However, the absence of such protocols or MOU's should not preclude or impede the conduct of product traces.) Each regulatory agency should develop its own specific response protocol for conducting a product trace in this context.

During an epidemiologic investigation, the most crucial aspect of an effective product trace is speed; therefore, the timeliness of investigations is more important than complete standardization. Process recommendations made in this document should not be used by any agency to develop rigid criteria or to require detailed justifications or priority schemes from another agency before it will participate in a product trace as part of the epidemiologic investigation. Rather, these recommendations should be used to increase the application, speed, and efficiency of product tracing in outbreak investigations.

I. Background: Current Issues in Investigations of Outbreaks due to Commercially Distributed Food Items

Outbreaks due to commercially distributed food items are being documented more frequently in the United States; outbreaks that are large in scope and/or widespread in distribution are now a regular occurrence (Barton Behravesh et al. 2011; Cavallaro et al. 2011; Gieraltowski et al. 2013; Neil et al. 2012). These outbreaks have led to intense scrutiny of food safety and foodborne outbreak investigations by the media, the public, the food industry, food industry regulators, public health investigators, and government policy makers.

The epidemiology of foodborne disease in the United States is constantly changing. A wider variety of foods is available to more consumers more of the time, including exotic or "out-of-season" fruits and vegetables. There is continuous change in the array of processed foods available as well. A greater number of meals are consumed away from home. To meet changing food preferences and demand, the food industry has developed new food production, processing, and distribution technologies and practices, resulting in extremely complex food systems. Food choices are virtually unlimited, and single food items or meals can contain many individual ingredients originating from numerous states and countries. Fragile foods, such as produce, can now be efficiently grown, harvested, packaged, and transported to the United States from distant countries. Mass food production and broad distribution mean that introduction of contaminants into the system can readily lead to large, geographically widespread outbreaks. Such contamination events can occur anywhere from farm to table.

Outbreaks caused by food items that are commercially distributed to a broad geographic area often are multi-jurisdictional in nature. Such outbreaks may be caused by any number of pathogens, including bacteria, viruses, and parasites, but the most common pathogens causing these outbreaks are *Salmonella enterica* and *E. coli* O157:H7. This document will focus on these two pathogens as a model, but most of the principles discussed would apply to other pathogens as well.

Outbreaks due to *Salmonella* and *E. coli* O157:H7 are typically detected through pathogen-specific surveillance, which involves submission of bacterial isolates from clinical laboratories to public health laboratories, and subsequent traditional or molecular subtyping. Therefore, the first challenge in any investigation is the completeness and timeliness of isolate submission and subsequent subtyping. Performance is highly variable in different jurisdictions, due in part to resource constraints. Nevertheless, PulseNet, the national molecular subtyping network for foodborne disease surveillance, has detected an ever-increasing number of multi-state subtype clusters in recent years (Tauxe 2006).

While incomplete laboratory accession and characterization can be a problem, the rate-limiting steps in investigations are frequently associated with the epidemiologic follow-up of recognized subtype clusters. This can be attributed to a number of factors, including resource constraints to handle the growing number of recognized clusters, disparate political structures, competing priorities, experience, and different cluster detection and investigation methods used in different jurisdictions. Many investigations are hampered by lack of timely

follow-up with reported cases and inadequate collaboration among local, state, and federal jurisdictions. Moreover, investigations are often more complex than they used to be. New and unusual outbreak vehicles are being recognized. Some outbreaks are due to single ingredients of complex food items; these components ("stealth vehicles") can be difficult for cases to recognize or recall. Some vehicles are frequently eaten with other foods (e.g., tomatoes and lettuce eaten together in Mexican food or sub sandwiches; cantaloupe and honeydew together in fruit salads); such combinations of ingredients in commonly eaten foods limit the utility of traditional analytic tools. Even widespread outbreaks may comprise few cases in any single jurisdiction. This frequently results in a lower prioritization of cluster investigations in many jurisdictions, which in turn blunts the aggressive response often necessary to solve an outbreak.

Recent experience underscores that traditional analytic epidemiologic investigation methods (e.g., case-control studies) are often not sufficient to identify and confirm the vehicle of outbreaks caused by commercially distributed food items because of imprecise exposure characterization. The number of cases identified may not be sufficient for an analytic study to find a statistical association, especially when the types of suspect foods being reported by cases are commonly consumed (e.g., cheese, lettuce, tomatoes, ground beef). Similarly, combinations of foods reported by cases often prevent the clear identification of the true food vehicle. Even where traditional methods do eventually work, delayed success limits the value of many investigations.

The opportunity to abate an ongoing food safety threat makes foodborne outbreaks public health emergencies that deserve a high priority. In addition to removing contaminated food from the marketplace and directly preventing outbreak-associated illnesses, determining the root cause of an outbreak is critical in preventing similar outbreaks in the future. Successful foodborne outbreak investigations allow the identification of new vehicles and production practices that compromise food safety, documentation of the continued importance of well-established outbreak vehicles, and confirmation of risk factors identified through case-control studies of sporadic cases. The media attention given to outbreaks represents a valuable opportunity for public health communication and education. The food industry learns from documented outbreaks that result in source investigations, and may change practices as a result. Finally, political interest in food safety is generated, which can result in changes to regulations, statutes, and program funding. For these reasons, foodborne disease outbreaks require timely and effective responses.

II. Product Tracing as Part of Epidemiologic Investigations

A. Introduction

When commercially distributed food items cause outbreaks, the stages of the corresponding epidemiologic investigations are generally as follows: 1) cluster identification; 2) hypothesis generation; and 3) hypothesis evaluation. Features of hypothesis generation and hypothesis evaluation often are combined to expedite investigations (CIFOR 2014; Meyer et al. 2008). Hypotheses about potential sources may be suggested by previous experience with the agent, the age, gender or geographic distribution of cases, and preliminary interviews with cases.

This hypothesis generation may identify one or more food items that are suspected to be a possible vehicle and require further epidemiologic evaluation. When the results of epidemiologic studies clearly associate illness with consumption of a suspected food item, the food item is implicated as the source of the outbreak.

A well-known use of food product tracing¹ is to pinpoint the origin of a food item after it has been identified as an outbreak vehicle by epidemiologic methods or laboratory testing. Such tracebacks facilitate the removal of implicated food from the marketplace as well as help identify and ultimately mitigate the factors that originally led to contamination of the food. Tracebacks conducted under these circumstances are usually referred to as regulatory tracebacks.

However, product tracing has emerged as an increasingly important part of the epidemiologic process for the identification of a food outbreak vehicle. Product tracing used as part of epidemiologic investigations to help identify an outbreak food vehicle has been referred to by a number of names, including “epidemiologic”, “informational”, “investigative”, “hypothesis-generating”, and “hypothesis-confirming” tracing. These types of designations can be confusing, because the traceback process is basically the same during an epidemiologic investigation as it is after a food vehicle has already been identified (albeit with special considerations during investigations – these will be discussed throughout this document). Furthermore, tracebacks can be conducted along a continuum of points in an investigation, and when a traceback transitions from being primarily for epidemiologic purposes to more of a traditional use can be unclear. For these reasons, this document will avoid use of designations such as “regulatory” or “epidemiologic” tracebacks.

The use of product tracing as part of epidemiologic investigations is not a new concept; rather, it has been used effectively in investigations for years (Gupta et al. 2007; Hedberg et al. 1992, 1999; Laine et al. 2005; Miller et al. 2012; Naimi et al. 2003; Shah et al. 2009; Sodha et al. 2011; Van Beneden et al. 1999). However, because of the growing number of multi-state PFGE subtype clusters identified by PulseNet and the increased complexity of investigations in recent years, product tracing is necessary to identify the outbreak vehicle in more investigations.

Broadly stated, the purpose of product tracing in an epidemiologic investigation is to contribute to the investigation by determining whether a food item(s) consumed by multiple case-patients in a cluster has a source or distribution point in common (Figure 1). Product distribution patterns are determined to assess the plausibility of one or more vehicles; determining distribution patterns adds specificity to exposures being evaluated. When specificity is added to both the case definition (as provided by molecular subtyping) and exposures, outbreak investigations are much more likely to be successful.

¹ Product traces/tracing, traces/tracing, and traceback are all used synonymously in this document.

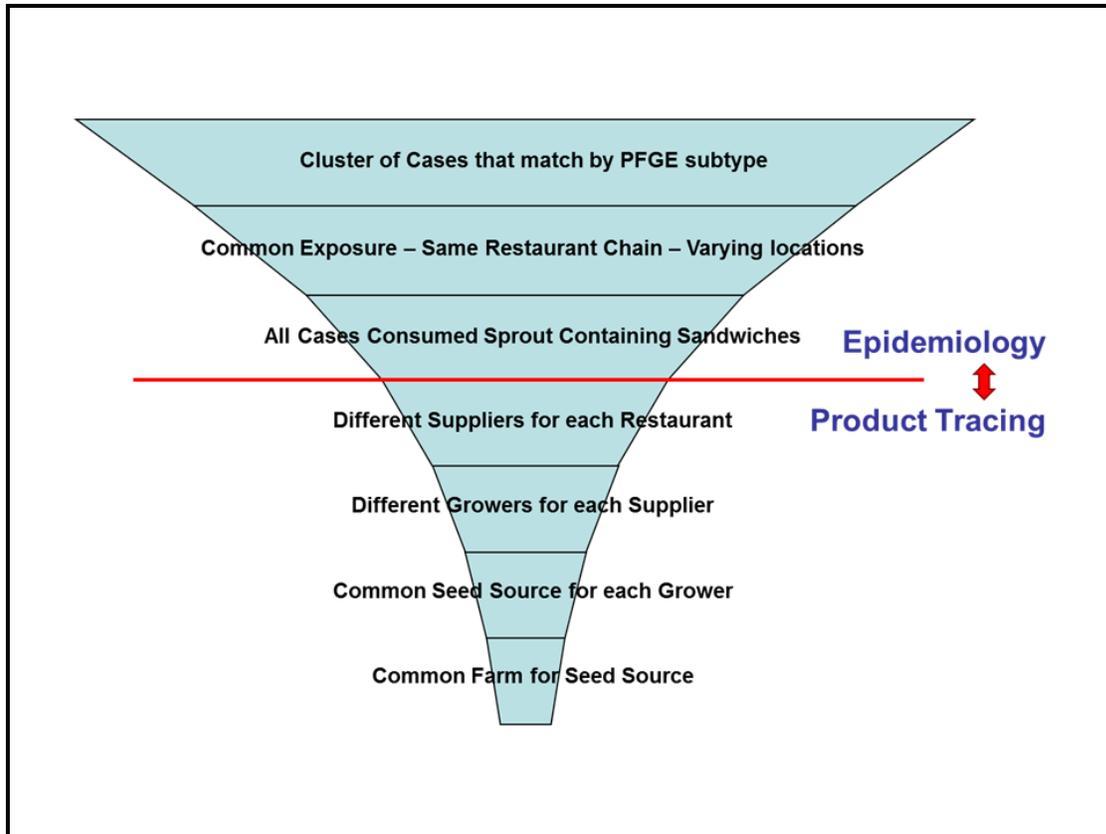


Figure 1. General example of product tracing conducted as part of an epidemiologic investigation (from an outbreak of salmonellosis associated with alfalfa sprout consumption).

For example, tomatoes are a frequently eaten food item for which consumers often can only identify a retail grocery or restaurant source and not specific brand information. Because at any given time there are likely to be many widely dispersed production sources feeding retail distribution, it is necessary to trace the distribution of tomatoes in order to properly associate a particular source of tomatoes with the outbreak. In a multi-state outbreak investigation of *Salmonella* Braenderup infections in 2003, an initial case-control study showed that cheese, lettuce, and tomatoes eaten at restaurants were all associated with illness (Gupta et al. 2007). Only through interviewing restaurant managers to identify specific varieties of these food items eaten by cases and controls did it become apparent that Roma tomatoes were the outbreak vehicle; tracebacks conducted as part of the epidemiologic investigation confirmed the association by identifying a single packer. In two other outbreaks of salmonellosis, investigators incorporated the source of tomatoes eaten by cases and controls into case-control studies; the results clearly implicated tomatoes from a single packer (Hedberg et al. 1999).

Product tracing used as part of epidemiologic investigations is conducted relatively early in the process, before epidemiologists are completely sure of the vehicle. Product tracing can have a critical impact at a variety of different points in an investigation. At times, product

tracing may be the only way to identify or confirm an outbreak vehicle. In addition, it can substantially accelerate identification of a vehicle beyond what could be accomplished using traditional methods alone. It can be used in conjunction with initial case-patient interviews to help generate (or rule-out) hypotheses. Product tracing results can be incorporated into analytic studies (e.g., evaluate a possible association with Food X from Producer Y). Finally, it can be an important tool to corroborate (or refute) an association with a food vehicle that has been identified by traditional investigation methods. Statistical associations that are found between a food product and illness may reflect a causal link but might also reflect confounding, combined consumption with the actual vehicle, bias, chance, or other factors. Therefore, it is critical that tracing of the suspected food product (backward and forward) confirms that it is a plausible vehicle. Conversely, at times a statistically significant association between a food product and illness is not achieved even when the food product is indeed an outbreak vehicle. This can happen when a formal analytic study is not done, the number of outbreak cases is low, the food vehicle is an unrecognized ingredient, and/or there are high background rates of exposure to the food product of interest. In these circumstances, increasing exposure specificity through product tracing is often critical to corroborate suspicions.

In 1995, an outbreak of *Salmonella* Newport infections manifested simultaneously in Oregon and British Columbia—with no cases in between or elsewhere (Van Beneden et al. 1999). Alfalfa sprouts (not then widely recognized as a “usual suspect” vehicle) were suspected by epidemiologists to be the source, but fewer than 35% of cases reported sprout consumption. Epidemiologists traced the sprouts and identified a seed lot in production that had gone only to growers in Oregon and British Columbia, thereby explaining the distribution of cases.

The reality of multi-jurisdictional investigations is that the conclusion by epidemiologists that a product trace is warranted sometimes conflicts with policy or legal considerations, resource constraints, and different philosophies held by regulatory agencies; consequently, needed traces often are not done for these reasons. This document is an attempt to frame a process for initiating and conducting a product trace as part of an epidemiologic investigation, to define potential roles and responsibilities of involved agencies, and to improve communication among product tracing collaborators. The ultimate goal is to improve the efficacy and timeliness of foodborne outbreak investigations through the more widespread and efficient use of product tracing.

B. Deciding when to use Product Tracing in an Epidemiologic Investigation

Successful investigations often require imagination and innovation to identify the source of the outbreak, and product tracing is often an integral part of a well-conducted epidemiologic investigation. In general there are a number of conditions that, when they all occur, indicate that some form of product tracing might be useful as part of the investigation:

1. There is a pulsed-field gel electrophoresis (PFGE) or other molecular subtype cluster of cases that likely represents a common source outbreak;
2. Cases occur in multiple locations or jurisdictions (particularly if they occur in multiple states);
3. Interviews of case-patients reveal no obvious common exposure that can explain the outbreak, suggesting that the outbreak vehicle is a commercially distributed food item; and
4. A vehicle cannot be clearly implicated with traditional epidemiologic, laboratory, and environmental investigation methods alone.

The decision about when product tracing is warranted as part of an epidemiologic investigation, and for what food item(s), depends on the timely collection and evaluation of detailed epidemiologic data. Product tracing can be labor-intensive and has implications for the involved food industry partners; this underscores the importance of gathering and evaluating the appropriate epidemiologic information in order to focus the investigation as narrowly as possible.

To help recognize when product tracing might be appropriate in an investigation, investigators should use available information from early in the cluster investigation, including:

1. Case demographics;
2. Temporal and geographic case distribution; and
3. Results of exposure interviews.

Case demographics can often yield important clues to the outbreak vehicle. For example, if a high proportion of case-patients are female and the median age is from 20 to 50 years, investigators should first consider produce items such as leafy greens, tomatoes, or sprouts. Geo-temporal case distribution patterns can also yield important clues. For example, cases occurring within a few days or weeks suggest a product with a short shelf life (e.g., produce). A wide geographic distribution of cases, for which travel does not supply a common source, usually implies a widely distributed product. Sporadic cases of illness occurring over weeks and months and in multiple locations may suggest a commercially distributed product with a long shelf life (e.g., peanut butter).

The most critical component of epidemiologic investigations is the exposure interview of case-patients. The key to obtaining actionable information for product tracing is to interview as many of the cluster case-patients as possible, as soon as possible (to minimize recall loss), with detailed exposure questions; this should be done until compelling patterns emerge. The

more specific the exposure information (i.e., purchase/consumption location, brand, or variety of foods consumed), the more quickly strong hypotheses are likely to emerge. Standardization of questionnaires across jurisdictions is optimal but not always feasible early in an investigation. Regardless of the questionnaire that is initially used, case-patients often need to be re-interviewed as part of the hypothesis-evaluation process. This may need to be done to ascertain additional details on exposures once they are targeted for specific follow-up, or once a suspect food item(s) has been identified, to objectively ask all cluster cases about that specific food item(s).

There are a number of circumstances in which product tracing is almost always warranted as part of an epidemiologic investigation:

1. Case clusters are associated with multiple restaurants or institutions (e.g., long-term care facilities, college cafeterias) such that the restaurant/institution exposure has a high likelihood of representing the exposure of case-patients to the outbreak vehicle;
2. A statistical association with a food item is identified through an analytic study but uncertainty about the finding exists due to concerns about combined consumption with other food items, the possible involvement of stealth vehicles, or the occurrence of other factors about the outbreak presentation that do not align with the statistically implicated vehicle;
3. Statistical associations are found with multiple food items, and the statistical analysis cannot clearly implicate one; and
4. A borderline statistical association relating to the primary hypothesis of interest is identified, especially from a study with a small number of cases.

Product tracing can be applied effectively in other outbreak circumstances as well. One example is when a high proportion of case-patients report eating one or more particular types of food, and that proportion is appreciably higher than expected based on previous food consumption data or common knowledge. The plausibility of these associations can be quickly assessed with a binomial probability model² and real or estimated background exposure frequencies. If observed exposure frequencies are greater than seem statistically likely, product distribution information should be quickly obtained. This approach is particularly important when these foods are known (or plausible) vehicles of the pathogen in question.

Another example is when a high proportion of case-patients shop at the same retail store (either the same exact location or the same chain), and that store has a membership or shopper card program. It can be beneficial to retrieve purchase histories corresponding to

² The binomial probability model can test the observed consumption rate of a food item among cases against known or estimated background consumption rates of that food item, i.e., one can estimate how likely it is that one would get the observed number of cases reporting an exposure given a known or estimated background exposure rate. A worksheet to calculate binomial probabilities is available at

<http://public.health.oregon.gov/DiseasesConditions/CommunicableDisease/Outbreaks/Gastroenteritis/Pages/Outbreak-Investigation-Tools.aspx>.

foods consumed by case-patients during the week prior to illness onset. This approach provided the break in a *Salmonella* Montevideo outbreak that was ultimately associated with pepper spice. Open-ended interviews conducted by Centers for Disease Control and Prevention (CDC) epidemiologists early in the investigation revealed that the majority of case-patients had consumed Italian-style meats, including salami (C. Barton Behravesh, CDC, personal communication). Most mentioned a variety pack with three or four types of sliced meat but could not recall the brand. However, many of the cases shopped at Retail Chain X. Epidemiologists from the Washington State Department of Health obtained Retail Chain X membership numbers for seven case-patients and retrieved their purchase history information. Five of the seven had purchased exactly the same product—a Brand Y variety pack of three Italian-style meats (Gieraltowski et al. 2013). This finding quickly led to the confirmation of this product (and others produced by the same company) as a vehicle in this outbreak. Pepper spice was later implicated as the ultimate source of the outbreak.

It is impossible to write objective criteria that will encompass all (or even most) outbreaks where product tracing would be worth pursuing during an epidemiologic investigation. All outbreaks are different in their presentation, and preliminary investigations differ in the amount, detail, quality, and timeliness of case-patient exposure data that they produce. Ultimately, the decision on whether a product trace might be useful in an investigation is based on an assessment of the cumulative available data by the lead epidemiologist investigator(s). For multi-state outbreaks, this often involves conference calls and collaborative data evaluation by multiple health departments and the CDC. It also typically includes consulting and gathering information from regulatory and industry collaborators. Like any part of an outbreak investigation, this is a fluid process; the focus of tracing efforts can change rapidly and unpredictably as more data become available.

C. Application

1. Initiating a Product Trace as Part of an Epidemiologic Investigation

1a. Identifying Regulatory Agency Collaborators and Establishing Clear Lines of Communication

Once compelling common food histories are documented, the need for product tracing is usually apparent. That recognition may come abruptly or gradually, and not necessarily at the same time to all investigators. However, the distinction is not that important. In most instances, product tracing begins in earnest with the interviewing of food establishment (e.g., grocery store, restaurant, institution) managers and distributors to trace a suspect food item to a common distribution node or its supplier pathways.

Depending on the retail source and distribution network, epidemiologists, environmental health specialists, and investigators from regulatory agencies may assist in the traceback effort. Tracebacks may be initiated by epidemiologists following up on individual cases. When it is apparent that a concerted tracing effort is warranted to move the epidemiology investigation forward, investigating epidemiologist(s) should engage the regulatory authority that inspects or regulates the involved establishment(s), typically a local or state

environmental health agency or a state department of agriculture. In many instances, more than one agency will be involved. For example, a restaurant may be inspected by a local health department, but it may receive food from a wholesaler inspected by the state agriculture department. Often (and preferably), regulatory agencies will have had some informal advance notice about investigations of potential interest to them before more formal invitations to collaborate. This includes the federal agency that regulates the suspect food product, most often the United States Food and Drug Administration (FDA) or the United States Department of Agriculture Food Safety and Inspection Service (USDA FSIS). If distribution of the suspect food crosses state lines (which commonly is the case), the appropriate federal agency may need to be directly involved in the tracing process.

With the number of agencies potentially involved (Figure 2), it is essential to maintain clear lines of communication in order to coordinate efforts efficiently. A lead epidemiologist investigator should be designated who can represent all cooperating epidemiology agencies. This lead investigator is the logical person to request that a regulatory agency conduct a product trace. For multi-state outbreaks, this could be a CDC epidemiologist, or it could be an epidemiologist in a state or large local health department that is leading the investigation. If different from the overall lead investigator, epidemiologists that will act as the contact for each involved regulatory agency should be clearly identified. This may be a different person for each regulatory agency. For example, a state health department epidemiologist may be the contact for local health departments and the agriculture department in the same state, whereas a CDC epidemiologist or a state health department epidemiologist may be the contact person for the FDA or USDA.

1b. Providing an Outbreak Summary and Request for a Product Trace to Regulatory Agencies

Collaborative sharing and evaluation of information by public health and regulatory agencies is critical to the effectiveness of multi-jurisdictional investigations. The appropriate epidemiologist investigator(s) should describe the outbreak in detail for the regulators, including the specific evidence and rationale for launching the product tracing effort. Written information such as text narratives, graphs, and/or line lists should be provided and updated regularly. A text summary detailing the evidence supporting tracing of a given food exposure should be provided. This summary should also indicate the process used to assess all food exposures and the evidence that other foods are not likely to be involved (especially if they are common vehicles for that particular pathogen). Regulatory agencies may request a copy of the form used to interview case-patients. The summary should also include a ranked list of case exposures that should be followed. For example, a case exposure would usually be ranked higher if it is part of a restaurant subcluster or if the case had only a single, well-documented (e.g., through receipt or shopper card records) exposure to the suspect item. Regulatory agencies should contribute to prioritization of case exposures to trace based on exposure locations and the likelihood of obtaining good product tracing data. For example, some major food retailers have developed more robust electronic traceability systems and can quickly access and provide data to regulators; these higher quality data can help focus initial tracing efforts by ruling in or out specific lots or shipments of interest.

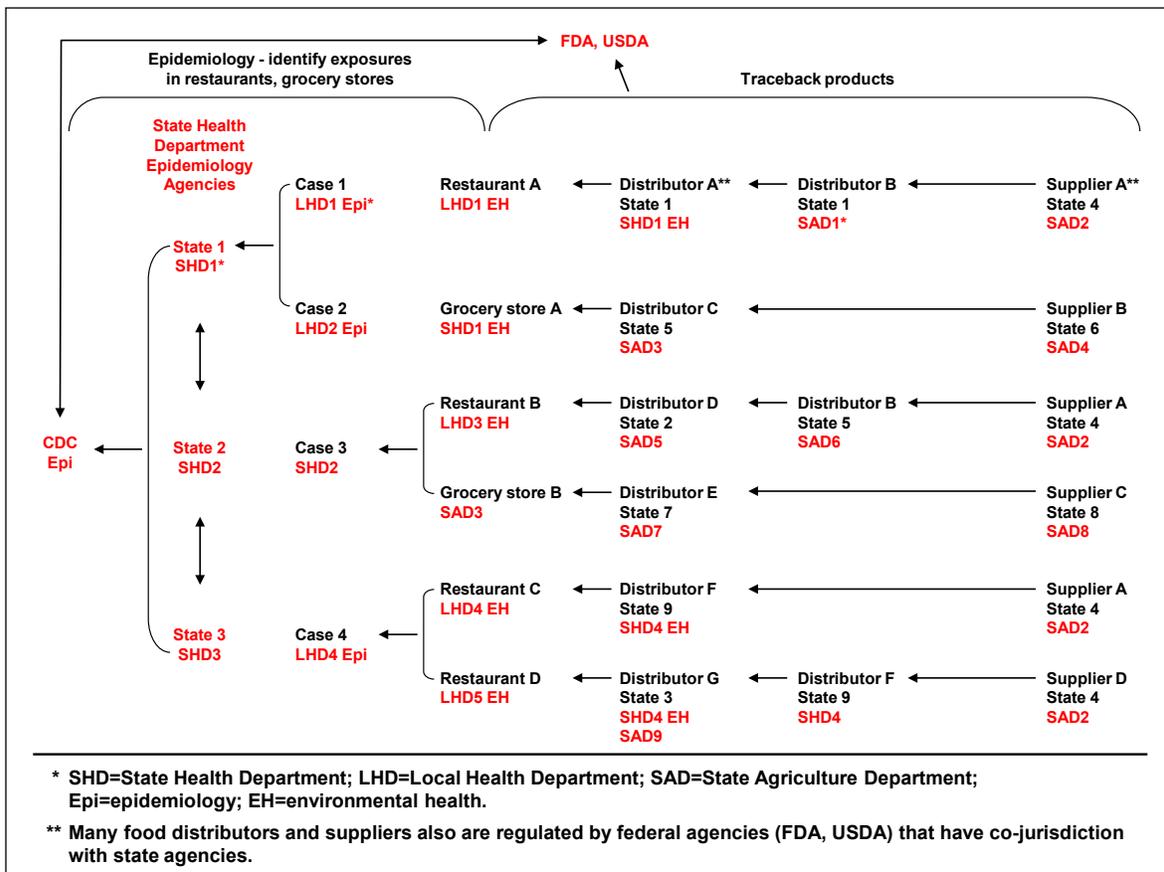


Figure 2. Hypothetical example of agencies involved in product tracing of 6 exposures from 4 cases in a multi-jurisdictional foodborne disease outbreak. Food distribution pathways are shown in black and investigating agencies are shown in red.

Once documentation is provided to the appropriate regulatory agencies, a meeting or conference call between the public health investigators and the involved regulatory agencies should be conducted to go through the information in detail, so that questions may be answered and a firm plan agreed upon. A clear understanding of the epidemiological data by the investigating regulatory agency is imperative to the broader success of the product trace. First, regulatory agencies can often provide information about their regulated product (e.g., seasonality, distribution patterns, historical perspectives) that helps assess whether a given product is a plausible vehicle. Second, existing knowledge about the product and initial tracing findings often influence the direction of further tracing efforts. The brainstorming that takes place during these discussions can identify or clarify key actions that will facilitate a rapid and focused investigation. It also may be advantageous for local/state/federal regulatory agencies to involve the affected industry partner early on. Cooperative industry collaborators can often provide important information about food product identities, formulations, manufacturing practices, and distribution patterns that can assist in product tracing efforts. Industry collaborators often notify their supply chain partners ahead of contact by a regulatory agency. This can initiate more timely data collection and reporting, and data might be available to investigators sooner.

1c. Providing Food Exposure Details to Regulatory Agencies for a Product Trace

When a food item(s) exposure of interest is identified for product tracing, the following details should be provided to the appropriate regulatory agency to optimally advance the investigation:

If the food is a retail (grocery store) item

- i) store name, address, phone number;
- ii) type of food (as specific as possible);
- iii) brand name;
- iv) variety name;
- v) UPC or PLU numbers;
- vi) other product information on packaging (e.g., lot code, “best by” or “use by” dates);
- vii) purchase date (try to verify with receipt);
- viii) if the store has membership or shopper cards, get the card number (and get permission to share it with the appropriate regulatory agency); and
- ix) if there is any product left from the same package as was eaten prior to illness, or if packages that were purchased at the same time are available (this is a good time to ask if the product or packaging can be obtained).

If the food is a restaurant item

- i) restaurant name, address, and phone number;
- ii) menu item that includes the food;
- iii) purchase/consumption date (verify with receipt); and
- iv) recipe/ingredient list for menu item.

Model forms have been created to help remind epidemiologists to collect these critical data to the extent possible (typically through follow-up interviews) (Appendix 1).

If the food was eaten at an institution (e.g., long-term care facility, college cafeteria, prison)

- i) institution name, address, and phone number;
- ii) menu item that includes the food;
- iii) recipe/ingredient list for menu item;
- iv) type of food (and brand/variety if known);
- v) consumption date; and
- vi) menu for the week before illness (from the institution).

When cases are associated with institutional settings or restaurants, it is logical to use the institution rather than the individual case as the unit of observation. Cross-referenced lists of suppliers and food items at different institutions may be difficult or impossible to assess statistically, but they can help focus commercial product investigations. In addition, institutional exposures are often of interest before there are specific target foods. For example, if it is known that Patient A was exposed at Institution X and Patient B was exposed at Institution Y, records on all foods served at Institutions X and Y can be collected and compared for commonalities. It was this process that led to identification of peanut butter

as the source of the large nationwide *S. Typhimurium* outbreak during 2008-2009 (Cavallaro et al. 2011).

1d. Prioritizing Exposures to Trace

Exposures should be prioritized based on:

1. The likelihood that the exposure is truly the exposure of interest for a case-patient;
2. The availability of clear, documented details on the exposure (e.g., receipts, shopper card information, bank statements);
3. Whether or not other case-patients share specific commonalities (e.g., ate at the same restaurant, shopped at the same grocery store, report the same brand or variety of the suspect food item);
4. Geographic and/or temporal dispersion of case exposures;
5. The likelihood that a case exposure (single case or subcluster) represents a different “leg” in the supply chain that might provide convergence upstream; and
6. The likely quality of the product tracing information available at the suspect exposure location.

Individual case-patients may have had multiple exposures to a type of food during the week before they became ill. This could represent multiple independent purchases from multiple vendors. To maximize the benefits of a product trace, it is important to identify the high-value cases with the “cleanest” possible histories: unambiguous onset and a single, well-documented exposure. For example, exposures for cases that are part of subclusters in individual restaurants or institutions should receive highest priority. If the case is not part of a subcluster but has only one exposure to the food item of interest, then that exposure should receive high priority. Consideration should be given to include cases from disparate geographic locations; tracing a food item back through different distribution pathways to a common source generally is more valuable and gives greater credence to the end result than when traces document the same exact distribution pathway to that common source. Similarly, consideration should be given to include cases whose exposures likely represent different product distribution pathways, regardless of geography. For example, an independent Mexican restaurant will likely receive its product through a completely different supply chain than a fast-food chain Mexican style restaurant even if they are located in the same city; therefore, it would be most valuable to include both types of exposure locations in product trace investigations.

Importantly, if product tracing results are to be incorporated into a case-control study, by definition product traces of appropriate exposures reported by controls will need to be traced as well. This will represent significant additional effort on behalf of the regulatory agency conducting the trace, but may be necessary to determine the true exposure of interest.

The responsibility of prioritizing exposures to trace falls upon the lead epidemiologist investigator, in consultation with the regulatory agency responsible for the trace. This task is not one that should take much extra time; in most instances, case-patient exposures can

quickly be placed in a fluid priority list on an ongoing basis as information on each new individual case becomes available.

2. Conducting the Trace

This section is not intended to provide a technical step-by-step process for how to conduct a traceback. Other resources are available that provide this level of detail (AFDO 2014; FDA 2014).

Conducting an actual product trace on any given exposure is conceptually straightforward: it is determining and documenting the producer, manufacturer, supplier, and distribution pathway(s) for the food item of interest. The investigator performing the trace should generally start by talking to the manager who orders food at the facility which provided the food to the case-patient. The first thing the investigator should do is explain the purpose of gathering the information. This explanation should include a description of the outbreak and why the food item of interest is being investigated. This is often accomplished by faxing or e-mailing the manager a letter with the above information, prior to or in conjunction with talking with that manager. The investigator should make it clear that the food item has not been implicated yet, and that the tracing efforts may ultimately help implicate or rule-out the food item as being the source of the outbreak. Make sure the manager is clear on the specific meal/purchase date(s) of interest (these dates are provided by the epidemiologic investigators based on the food consumption or purchase dates provided by case-patients).

A great deal of useful information often can be provided by a food manager during a 10-minute phone conversation; this information can be sufficient to move the investigation forward even if additional in-person investigatory efforts are not possible. However, as the manager is providing information on the suppliers and shipments of the food item of interest, they should provide written (or ideally electronic) documentation of that information—typically invoices from the distributor corresponding to the shipment(s) that could be associated with sale of the suspect food item, and corresponding bills-of-lading. If a local agency is simply retrieving invoices and bills-of-lading for another agency to conduct the trace, ensure that the invoices reflect all food shipments and/or in-cash purchases that could have been used on the meal/purchase date of interest. The timeframe for document collection is commodity specific (shelf stable vs. perishable products) and should be defined accordingly. When in doubt, expand the time frame in question.

Food service establishments generally try to adhere to a “First-In-First-Out” (FIFO) practice when rotating inventory. Speaking with the manager of a facility is a critical initial step in understanding how food items are used in a retail setting (e.g., ordering practices, turnover rate, storage), but it is equally important for the field investigator to interview “line-level” staff to confirm that stated policies match reality. Determining if variations to a firm’s stated FIFO policies exist is of utmost importance since the initial most-plausible exposures will guide and focus the rest of the trace investigation.

After this has been accomplished, the investigators need to talk to the previous entity that handled the food item in the supply chain; most often a distributor for the facility. The

objective is to determine and document where the distributor obtained the product, and so on until the source of the food and production date is identified. If appropriate and possible, the farm and field should be identified as well. Some firms may have records going back more than one step back in the supply chain, and it would be advantageous to have these early on even if they represent preliminary data. Supporting documentation in the form of invoices, bills-of-lading, production records, and other pertinent documents should be collected at all levels of distribution to document the movement of the food throughout the entire distribution system. It is often most efficient and rapid for the same state regulatory agency to conduct the entire trace of a single exposure. However, even if a single agency conducts the entire trace, as the distribution pathways cross jurisdictional boundaries, each pertinent regulatory agency should be notified and engaged in a discussion of roles in continuing the trace.

The product tracing process needs to be accomplished quickly if it is to be successful in helping identify the food vehicle of an outbreak. Thus, gathering information by telephone, fax, or e-mail is likely to be more efficient than dispatching inspectors to gather physical records from each establishment. Establishing firm deadlines for information requests is critical to the timeliness of the investigation. It is important to convey the urgency of the request to parties who may be unfamiliar with the routine. Requesting that documents be provided in hours, rather than days, will help ensure that necessary data are available from each point in the trace in a timely manner. If an entity in the supply chain is slow in providing information following multiple requests, it may be necessary to send a field investigator to the facility to collect the relevant documents.

As the data are being gathered, the agency conducting that portion of the investigation should create timelines, flow charts, or diagrams illustrating the distribution pathways of the exposures that were traced (see Figures 3-6 for examples). Ideally, these documents should contain dates associated with key elements such as individual shipment dates, lot codes, date of receipt of product, etc. This will be a dynamic document that can help guide the trace investigation and should be updated as new cases of illness are identified and new product distribution information becomes available. Most of the data that are collected will be in the form of invoices and other documents. Converting these text-based documents into a visual representation (such as a flow chart or diagram) will greatly aid the investigator in seeing spatial and temporal links that may be harder to discern when only comparing paper records. In outbreaks in which the network of food producers and distributors is particularly large and complex, it may not be practical to process, analyze, and visualize all information without computerized tools. During the German STEC O104:H4 outbreak in 2011, investigators developed a new relational database for analysis of voluminous traceback data and visualized connections using network graphs (Weiser et al. 2013). Regardless of the size of the outbreak, agencies conducting the traces should regularly share updates on the traces with the lead epidemiologic investigators using visual data presentation formats.

(continued on page 24)

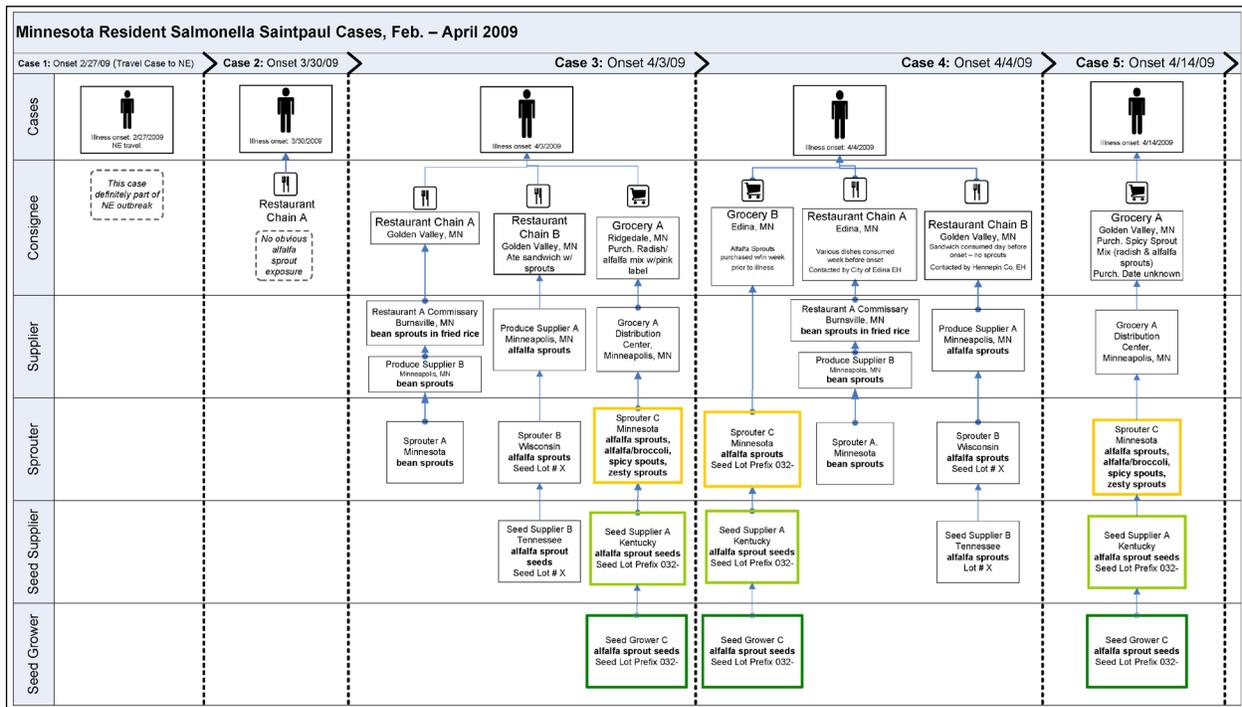


Figure 3. Example of a diagram illustrating exposure distribution pathways documented during a traceback (from an outbreak of salmonellosis associated with alfalfa sprout consumption [Safranek et al. 2009]; Minnesota Department of Agriculture).

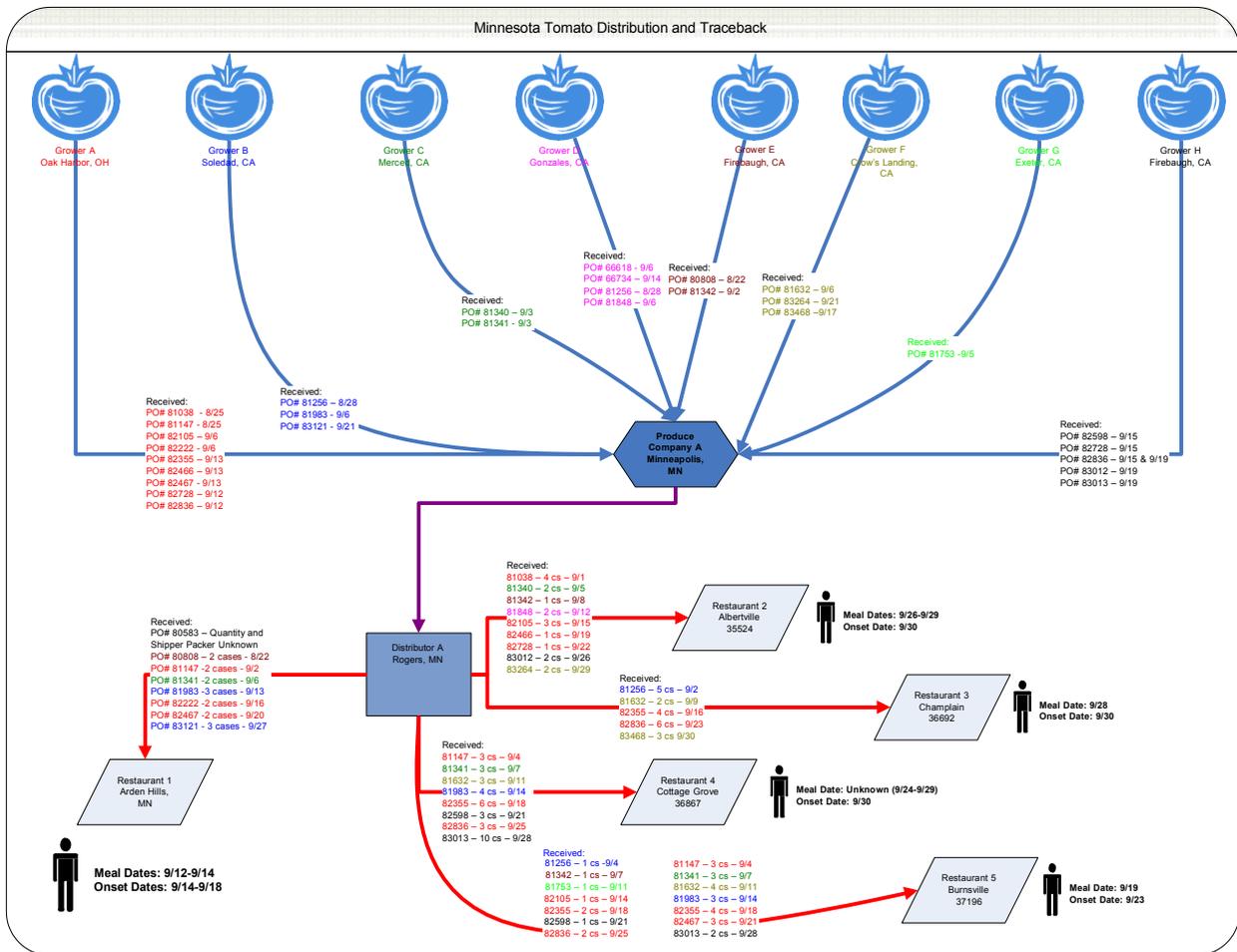


Figure 4. Example of a diagram illustrating exposure distribution pathways documented during a traceback (from an outbreak of salmonellosis associated with tomatoes [Barton Behravesh et al. 2012]; Minnesota Department of Agriculture). In this example, tomatoes from Grower A were implicated as the source of the outbreak (Note: tracebacks were done for cases in multiple states – this diagram reflects only cases in Minnesota).

Restaurant	Days Prior to Meal Date Shipper/Packer Received at Restaurant												
	0	1	2	3	4	5	6	7	8	9	10	11	12
Restaurant 1 - Case 1 Meal Date - 9/12							Grower C 81341 2 cs				Grower A 81147 2 cs		
Restaurant 1 - Case 2 Meal Date - 9/14		Grower B 81983 3 cs							Grower C 81341 2 cs				Grower A 81147 2 cs
Restaurant 1 - Case 3 Meal Date - 9/13	Grower B 81983 3 cs							Grower C 81341 2 cs				Grower A 81147 2 cs	
Restaurant 1 - Case 4 Meal Date - 9/13	Grower B 81983 3 cs							Grower C 81341 2 cs				Grower A 81147 2 cs	
Restaurant 1 - Case 5 Meal Date - Unknown (9/16?) Onset Date - 9/19	Grower A 82222 2 cs			Grower B 81983 3 cs							Grower C 81341 2 cs		
Restaurant 2 - Case 6 Meal Date: 9/26 Onset Date: 9/30	Grower H 83012 2cs				Grower A 82728 1 cs			Grower A 82466 1 cs				Grower A 82105 3 cs	
Restaurant 2 - Case 6 Meal Date: 9/27 Onset Date: 9/30		Grower H 83012 2cs				Grower A 82728 1 cs			Grower A 82466 1 cs				Grower A 82105 3 cs
Restaurant 3 - Case 6 Meal Date - 9/28 Onset Date - 9/30						Grower A 82836 6 cs							Grower A 82355 4 cs
Restaurant 2 - Case 6 Meal Date: 9/29 Onset Date: 9/30	Grower F 83264 2 cs			Grower H 83012 2cs				Grower A 82728 1 cs			Grower A 82466 1 cs		
Restaurant 4 - Case 7 Meal Date: Unknown (9/27?) Onset Date: 9/30			Grower A 82836 3 cs				Grower H 82598 3 cs			Grower A 82355 6 cs			
Restaurant 5 - Case 8 Meal Date: 9/19 Onset: 9/23		Grower A 82355 4 cs				Grower B 81983 3 cs			Grower F 81632 4 cs				Grower C 81341 3 cs

Figure 5. Example of a diagram illustrating shipments of tomatoes into restaurants in Minnesota prior to case exposures at those restaurants (from an outbreak of salmonellosis associated with tomato consumption [Barton Behravesh et al. 2012]; Minnesota Department of Agriculture). This data presentation format complements that shown in Figure 4 and helped implicate tomatoes from Grower A as the source of the outbreak. Of note, shipments from the implicated grower were typically not the most recent shipment into the restaurant prior to the meal date, and sometimes were the 3rd most recent shipment.

(continued from page 19)

A product trace done as part of an epidemiologic investigation may not be prohibitively resource intensive. An investigation to reconstruct the distribution pathways of one or two food items from a single point of sale may take between 8 and 24 person hours to make all the telephone requests and collect all paperwork electronically and create a flow diagram. If local or state jurisdictions cannot spare the resources to conduct timely data collection for a particular trace investigation, a number of alternatives may be available. For example, state agencies (public health or regulatory) may be able to step in and assist local health departments. State agencies may be able to help neighboring states; several state agriculture departments have received funding for and are developing rapid response teams, in part for investigating outbreaks. These teams could be used as a regional resource for these types of investigations. District or national FDA or USDA FSIS staff may also be available to collect data, even at points of service. Cross-jurisdictional investigations could benefit by pre-establishing MOUs for traceback investigations (between local and state entities or between states themselves).

3. Interpreting Product Tracing Data

Product tracing data are just one of the many sources of information that should be considered in an outbreak investigation. Investigators must use all available information to construct a coherent narrative of what happened and why. Results of product traces must be integrated with results of analytic epidemiologic studies, food worker interviews, environmental health assessments, facility inspections, and food product and environmental testing. It is sometimes necessary to incorporate results of product tracing into analytic studies.

Product tracing data are best interpreted through a joint analysis by the epidemiologist investigators and the regulatory agencies that conducted the traces. These entities should be in constant communication throughout the process and agree on how the product tracing data relate to the rest of the epidemiologic information.

Bear in mind that not every reported exposure will trace back to a single point of manufacture or distribution. There are a number of potential explanations for this. One is that the given exposure may not have been the one that really caused that case's illness; histories are often inaccurate or incomplete. In addition, irregularities in record keeping or product handling may result in identification of the wrong distribution pathway. In any event, one should not expect all traces to converge even if the outbreak vehicle has been correctly identified—much as experienced investigators are never surprised when <100% of cases recall eating the implicated food. ***Minor inconsistencies are common and may be ignored, but investigators should be wary of explanations that depend upon implausible scenarios. Large numbers of inconsistencies may indicate that alternate hypotheses need to be considered.***

D. Considerations

1. Special Needs for Product Tracing when Conducted as Part of an Epidemiologic Investigation

There is no fundamental distinction between product tracing conducted as part of an epidemiologic investigation versus product tracing used in support of regulatory action; where they differ is usually in the point of the investigation at which tracing is conducted, the extent of record collection and documentation, and often who is doing the work.

Product tracing used during an epidemiologic investigation is a means to obtain more specific exposure information to help identify an outbreak vehicle; it is another tool in the tool box of epidemiologists.

Product traces conducted after a food vehicle has already been conclusively implicated are generally carried out under defined protocols. This is particularly true for federal regulatory agencies, which have strict policies and procedures for such activities. In this circumstance, traces are often very time-consuming, which may limit their epidemiological utility but produce a meticulously documented file that may be essential for subsequent legal action and root-cause analysis. Conversely, product traces conducted as part of epidemiologic investigations are more variable in terms of the types of data that are collected, more flexible in terms of methods that can be used, and less constrained by official policies and procedures (because they are not initially conducted in the context of regulatory action involving a particular food item). Consequently, product tracing as part of an epidemiologic investigation typically can be conducted much more quickly but still in a way that advances an investigation.

Tracing conducted as part of an epidemiologic investigation comprises a variety of activities, which might include a 10-minute phone call with an industry contact to ascertain the relatedness of food products from two different retail sources, the comparison of food purchase histories obtained using cases' shopper cards, or the comparison of purchasing records for multiple institutions where cases were potentially exposed. The common thread is using information about product distribution to elucidate potential epidemiological connections between cases. Often there is more uncertainty underlying these types of tracebacks. Did these cases (or institutions) buy any products in common? Did this sprouter buy seed from the same lot as that one? In brief, is there a plausible product distribution scenario that fits the other epidemiologic data?

At times, product traces conducted as part of epidemiologic investigations more closely resemble the more traditional traces conducted after a food vehicle has already been conclusively implicated. In these instances, the optimal trace includes collection of written documentation (e.g., bills-of-lading) of all steps in the trace. However, in the trace, key food distribution pathways can be identified quickly by investigators through communication with the appropriate industry contacts (often via phone call); specific direction by the investigator enables industry contacts to quickly supply appropriate specific documentation of the pathways of interest. This is in contrast to more traditional regulatory traces, in which a comprehensive review of records and

product handling practices at each node must be evaluated. The time required for this process limits its utility for epidemiologic investigations.

2. Concerns, Potential Pitfalls, and Challenges

2a. Timeliness

The usefulness of pathogen-specific surveillance in preventing ongoing transmission of disease from contaminated food, especially perishable commodities, is directly related to the speed of the investigation process. Therefore, when product traces are required to help identify or confirm an outbreak vehicle, they need to be done quickly.

The detailed recommendations in this document regarding a more consistent product tracing process as part of epidemiologic investigations, when it can be used, data elements to be gathered and shared, potential roles and responsibilities of different agencies, and communication processes have been given to increase the understanding of product tracing in this context and to optimize its use. This document outlines an optimal sequence of processes that may not always be practical to follow completely. This document **should not** be used by any agency to develop rigid criteria, or to require detailed justifications or priority schemes from another agency before participating in a product trace during an epidemiologic investigation. Furthermore, attempts to strictly follow the processes described in this document **should not** slow down an investigation. The most crucial aspect of an effective product trace is speed, and the intent of this document is to increase the timeliness of investigations rather than decrease it; timeliness is more important than complete standardization.

Even if an outbreak appears to be over, identifying the vehicle and source of contamination is still extremely valuable, and the speed of traces and other investigative efforts is still important in accomplishing this.

2b. Participation by Multiple Local, State, and Federal Agencies, and Coordination of Efforts

A successful product trace often requires the collaboration of numerous agencies (Figure 2) which may have competing priorities, different resource constraints, and significantly varying levels of experience at this type of work. In addition, some jurisdictions may have only one or two cases in a given cluster and may not give the investigation a high priority. As a consequence, coordination of product tracing efforts can be a challenge. That said, the fact that these outbreaks are multi-jurisdictional can also be an advantage from a product tracing standpoint; triangulation from disparate geographic areas to the same food producer can constitute exceptionally strong evidence that a particular food is indeed the vehicle. Even single cases from a given state can be exceedingly important in these types of investigations (Laine et al. 2005; Miller et al. 2012). Therefore, every attempt should be made to engage all involved states, even those with few cases.

Not all regulatory agencies may have the same legal authority to access product distribution records. Most state authorities generally have broad authority to collect and review records. Prior

to the passage of the Food Safety Modernization Act (FSMA), Section 414(a) of the FD&C Act provided access to records relating to food that was reasonably believed to be adulterated and present a threat of serious adverse health consequences or death to humans or animals. FSMA expands FDA's access to records beyond records relating to the specific suspect article of food to records relating to any other article of food that the FDA reasonably believes is likely to be affected in a similar manner. In addition, FDA can now access records if FDA believes that there is a reasonable probability that the use of or exposure to an article of food, and any other article of food that FDA reasonably believes is likely to be affected in a similar manner, will cause serious adverse health consequences or death to humans or animals. Coordination between agencies to determine which agency may have the strongest regulatory authority to collect and review records should be considered during a product trace investigation.

In some states, public health departments have not formed the working relationships with their state and local regulatory agencies necessary for these regulatory agencies to be seamlessly involved in traces for epidemiologic purposes. In some investigations and for various reasons, including capacity limitations, regulatory agencies may not be able to help conduct a trace requested by a state agency. While engaging regulatory agencies should be the first option in initiating a product trace, the speed of any investigation should not be sacrificed if regulatory agencies are unable to participate.

A common bottleneck in product traces is gathering documentation from the initial points of service/purchase; this is often done by local health departments that have many competing priorities. These records must be collected promptly. If local staff are not available, a state or federal agency should gain permission from the local agency to collect these records. Time is of the essence.

2c. Negative Effect on Industry

One important concern in conducting a product trace is the potential adverse effect that it could have on a company or industry segment. For example, if a company's customers hear about an investigation (which is very likely to happen when one is working back from the consumer) they may stop buying product from that company. Therefore, investigators must emphasize to concerned parties that it is routine to assess many conjectural hypotheses, a process that ultimately dismisses many of these conjectures as it narrows down on the implicated product. While contacting companies before the outbreak vehicle has been officially identified may create discomfort, it is imperative that public health protection takes precedent. Almost without exception, the food industry is more than willing to cooperate and equally as committed to identifying the source of an outbreak. Gathering information by phone, fax, or e-mail, in addition to being quicker, is also a way to initiate a trace in a low profile manner.

2d. Lack of Detailed, Accurate Records

Product traces can be rendered ineffective by imprecise exposure information. Therefore, it is best to use only those exposures for which solidly documented details are available. However, even when every attempt is made to obtain precise exposure information, exposures selected for tracing sometimes are not the ones associated with the outbreak. Therefore, investigators should

not dismiss a plausible vehicle based simply on lack of convergence of one (or even more) traceback leg.

Investigations can also be stymied by poor record keeping by commercial food establishments, distributors, manufacturers, or growers. For example, in an outbreak of *Salmonella* Newport infections associated with blueberries in Minnesota (Miller et al. 2013), traditional traceback methods involving the review of invoices and bills-of-lading were initially used to attempt to identify the source of the blueberries. Based on initially incomplete evidence from a retailer (Retailer A) and the primary distributor, the invoices pointed to Wholesaler A and Grower A based on FIFO product rotation. However, when point-of-sale data were analyzed and linked to shopper-card information, a common Global Trade Item Number was identified. This information led to on-site record evaluation at Retailer A, and the discovery of additional records at this location documented the supply chain from Grower B to Wholesaler C to Retailer A, shifting the focus of the investigation from Grower A to Grower B.

While current regulations require each entity in the supply chain (farms and points-of-service excluded) to be able to identify “one-step forward and backward” traceability, in practice not all businesses are fully compliant. Moreover, these requirements do not generally require that firms maintain lot codes or “internal traceability.” The issue of internal traceability is of critical importance to the trace investigator since in the case of a repackaged food (e.g., tomatoes) or a food used as an ingredient (e.g., peanut butter), the trace can be lost if internal traceability is not maintained. FDA is currently in the rule-making process under Section 204 of the FSMA, and future rules may articulate additional specific record keeping requirements.

For every point in a trace, attempts should be made to verify information using documentation from one step upstream and one step downstream. This redundancy can be very helpful. When Wholesaler X sells to Restaurant Y, both should have documentation of the transaction, and this documentation should be in agreement (ship and receive dates, quantities, product description, etc.). Thus, incomplete records at one node will not necessarily break the trace. Despite the best efforts of all concerned, however, many traces end inconclusively. At some point the decision may have to be made to move on to more promising case exposures.

Some traces go international, which introduces another level of complexity and sometimes political sensitivity. Lack of accurate records (or legal access to them) can be an issue. That is not always the case, however, and often the importer, large distributor, or representatives of the foreign government are able to provide useful information.

2e. Confidentiality Concerns in Data Sharing

While some of the specifics vary by state, all public health agencies have laws that protect the confidentiality of identifiable case data. Absent a specific waiver from the case (or their attorney), the general rule is to withhold identifiable data from the general public, but to allow limited access to qualified public health agency partners on a need-to-know basis. Most state epidemiologists, for example, are allowed to share names, addresses, or other identifiers with their counterparts in other states or at CDC—but they should only do so if there is a specific need (e.g., CDC staff are going to call neighborhood controls for a case-control study and need to

know the case's home address, or an FDA official is going to pick up a sample at someone's home). The use of coded ID numbers on spreadsheets is generally preferred.

Going outside the realm of public health agencies requires explicit authorization by the case or their legal representative. This issue will arise when epidemiologists try to get "shopper card" sales records on a case from grocery stores—a common exercise in outbreak investigations. The case must understand and consent to the release of otherwise privileged information (e.g., Store X will have to learn that Patient Y was diagnosed with salmonellosis) before the store is approached. Any authorized release of privileged information should be as circumscribed as possible; clinical details, for example, would rarely be relevant to a records request.

In contrast to information collected about individual cases, state laws differ considerably about the confidentiality of information collected about commercial entities during outbreak investigations. In some states such information is tantamount to case data, while in others it is considered public information. Regardless, almost all states restrict the public dissemination of this information while an investigation is ongoing. Most state epidemiologists can and do readily share this kind of information with collaborating public health agencies during investigations; this kind of information can be critical to making progress. Regulatory agencies—and in particular federal agencies (e.g., FDA, USDA)—may be especially cautious in sharing this type of information because of restrictions prescribed by regulation or policy; this caution in sharing of information among investigators may be dealt with through standing confidentiality agreements between federal agencies and specific public health partners at the local and state levels. Agencies should examine their policies regarding sharing of commercial source information and attempt to identify a mechanism to share as much of this type of information as possible to the widest possible group of collaborators.

E. Examples

Example #1: Cyclosporiasis in British Columbia (*Emerg. Infect. Dis.* 2009;15:1286-88)

Shah et al. (2009) provide an excellent example of tracebacks conducted during the epidemiologic investigation of a cyclosporiasis outbreak in British Columbia. The authors do an elegant and concise job of explaining the rationale, approach, execution, and interpretation of product traces conducted as part of an epidemiologic investigation, providing a “must read” for anyone interested in this topic. In brief, case interviews, population control comparisons, and product distribution information limited suspect foods to strawberries, cilantro, and basil. Interviews of grocery store owners, restaurant managers, and distributors were used to trace the produce items to suppliers (Figure 7). The trace implicated Mexican organic basil from a particular distributor as the outbreak vehicle. Once the vehicle was identified, the authorities conducted a full traceback of organic basil by using formal documentation.

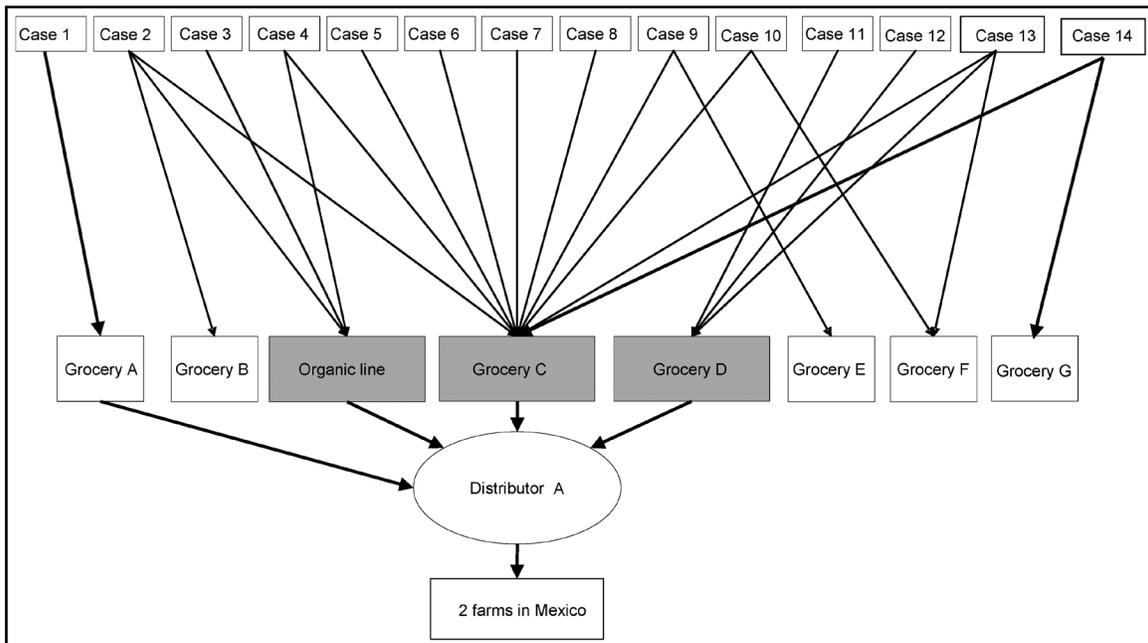


Figure 7. Traceback of basil eaten by persons with confirmed cyclosporiasis (N = 14), British Columbia, Canada, May–August 2007. From: *Emerg. Infect. Dis.* 2009;15:1286-88.

Example #2: Multi-state *E. coli* O157:H7 outbreak associated with hazelnuts (*J. Food Protect.* 2012;75:320-7)

In this multi-state outbreak of *E. coli* O157:H7 infections, tracebacks were used by state regulatory agencies to complement traditional epidemiological cluster investigation methods to confirm hazelnuts as the outbreak vehicle. Bulk in-shell hazelnut or mixed nut (including hazelnut) consumption was documented during epidemiological interviews of the first seven cases in three different states; no other strong hypotheses emerged. In part because hazelnuts had never before been identified as a source of *E. coli* O157:H7, investigators agreed that demonstrating a common source of hazelnuts was paramount to the conclusion that they were indeed the vehicle. Based on case onset dates, purchase dates, and purchase locations, regulators in Minnesota, Michigan, and Wisconsin traced product back through the supply chain. Six (86%) retail locations received the suspect hazelnut or mixed nut shipments from a Minnesota distributor, and one retailer (14%) received their products from a Wisconsin distributor. Both distributors received 100% of their bulk in-shell hazelnuts and mixed nuts from a distributor in California, and a recall of nuts from the California distributor was issued. The outbreak strain of *E. coli* O157:H7 was subsequently isolated from hazelnuts or mixed nuts in three states.

F. Building a Functional Network and System for Conducting Product Traces as Part of Epidemiologic Investigations

1. Agency-Specific Response Protocols

Product traces conducted as part of epidemiologic investigations generally start with the investigating epidemiology agency at a state or large local health department. Therefore, these agencies should develop a contact list for all potential regulatory agencies that could be asked to conduct an epidemiologic trace and a protocol for engaging these collaborators in such an effort. These collaborators vary by state but could include state and local environmental health agencies, state agriculture agencies, and district and national federal regulatory agencies (e.g., USDA and FDA). A considerable investment on the part of a state epidemiology agency may be required in identifying key stakeholders within regulatory agencies, conveying to them the value of this concept, and getting them to commit to develop protocols and obtain appropriate training and experience. Ideally, relationship building should be conducted ahead of time and entail development of joint protocols, MOU's, etc.

Each regulatory agency should develop its own specific response protocol for conducting a trace as part of an epidemiologic investigation. This protocol should include the names of staff responsible for conducting that agency's part of the trace, how they should be notified of a product tracing request (including names and contact information of who should be notified), procedures to gather the necessary information from the involved food facility, and a mechanism for sharing the information with the requesting epidemiology agency.

Guidelines and best practices for conducting tracebacks have been developed and include, but are not limited to, the Rapid Response Team Best Practices Manual and FDA's Guide to

Traceback of Fresh Fruit and Vegetables Implicated in Epidemiological Investigations (<http://www.fda.gov/ICECI/Inspections/InspectionGuides/ucm075005.htm>). An increasing number of state and federal agencies are coordinating investigation and response efforts using the Incident Command System, which, if properly adapted to the situation, can improve multi-agency and multi-jurisdictional coordination and information sharing.

2. Training

Training and routine exercises should be conducted to develop and maintain product tracing skills. Training for product traces as part of epidemiologic investigations is particularly amenable to a practical tabletop exercise format. For example, a real-world tabletop exercise could easily be designed in which food exposures from 2 or more (as many as desired, depending on the size of the exercise) actual recently reported sporadic cases of *Salmonella* or *E. coli* O157:H7 infection could be traced. Exposures could be chosen to represent grocery store and restaurant exposures from a variety of jurisdictions, and also to ensure the involvement of a variety of local, state, and federal agencies. The traces may not go back to the same source, but that is immaterial for a training exercise.

Another training option is to conduct retrospective reviews (“hot-washes”) of recent cluster investigations, of which there are many every year. A third option is for agencies that have considerable experience in conducting product traces as part of epidemiologic investigations to develop training opportunities for those who wish to become more proficient.

Additionally, FDA offers classroom training in product tracing and has resources on their website pertaining to product tracing (FDA 2014). While this training is geared toward a fully documented trace needed for regulatory action in an outbreak, the basic concepts are the same when tracing to inform an epidemiologic investigation.

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APPENDIX

- 1. Example of a form used to capture food product information for use in product tracebacks.**

CASE INFORMATION

State Case ID Age Sex County of Residence Page 1 of Links to other cases Onset date for this case is... Onset of first symptoms Onset of vomiting/diarrhea Earliest + specimen date Does history suggest this might be a secondary case?

EXPOSURE/CONSUMPTION EVENTS (Use supplemental page if >2 defined exposures)

Source of info Exposures are... # of exposures in xxx days < onset Exposure # 1 Exposure # 2 Location

PRODUCT PURCHASE/SOURCE INFORMATION (Use supplemental page if >1 purchase or source)

Case reported Source # 1 Place Address Purchase date Source info is... Documentation

Traceback info

PACKAGE/ LOT/SAMPLE INFORMATION

Purchase quantity Original unit package Original (store) condition Leftovers Product was held in... Current sample custody Original packaging is... UPC Brand Label Package Size Production/Best By Codes Sample ID # Lab Results

EPI AGENCY CONTACT

Agency Name Phone Email

ADDITIONAL INFORMATION

State _____ Case ID _____

Page 2 of _____

Append this sheet for cases with more complex histories (e.g., multiple exposures and purchases)

Notes**ADDITIONAL EXPOSURE/CONSUMPTION EVENTS**Exposure # 3 m____/d____/yy____ Time ____ am noon ____ pm midnightLocation own home other private home restaurant institution _____Exposure # 4 m____/d____/yy____ Time ____ am noon ____ pm midnightLocation own home other private home restaurant institution _____**ADDITIONAL PURCHASE/SOURCE INFORMATION**Source # 2 store restaurant institution unknown _____

Place _____ Address _____

Purchase date 2 m____/d____/yy____ Time ____ am noon ____ pm midnight unknownSource # 3 store restaurant institution unknown _____

Place _____ Address _____

Purchase date 3 m____/d____/yy____ Time ____ am noon ____ pm midnight unknown**ADDITIONAL PACKAGE/ LOT/SAMPLE INFORMATION**Purchase #2 quantity single unit case of ____ units loose unknown _____Original unit package box bag clamshell loose unknown _____Original (store) condition frozen refrigerated room temp unknown _____Leftovers none open package (likely source) loose product (same purchase) open package (same purchase; different unit) sealed package; same purchase likely source product (no packaging) similar product _____Product was held in... freezer refrigerator room temperature Quantity available _____Current sample custody consumer _____ health dept _____ PHL _____ Ag Lab _____Original packaging available unavailable uncertain photos available

UPC _____ Brand _____ Label _____ Size _____

Production/Best By Codes _____

Sample ID # _____ Lab _____ Results positive negative pending

General Comments

This is a state-developed template; feel free to adopt or adapt it. It provides a standard format for documenting commercial product exposures in outbreak investigations once a likely vehicle is identified. This kind of information is critical for narrowing the definition of implicated product as much as possible, and may be used by regulatory agencies to attempt tracebacks.

This format should work well for most outbreaks, but may require tweaking for a given situation. At minimum you will need to specify a header for the outbreak (e.g., "Brand X pot pies, Outbreak #0706PAJPX-1c), the time interval to be covered by the exposure questions (e.g., 5 days, 7 days, 10 days before onset), and a fax number or other central collection point for completed forms.

Case Information

Do not include identifiers on this form (names, phone numbers, etc.). Indicate if there are additional pages for this case.

Case ID. Use a unique identifier such as a state PHL specimen ID or state case ID number.

Links to other cases. Known links other than presumed consumption of the same product, obviously.

Dates and Times. Get precise answers for exposure and onset times whenever possible. Estimates are OK, but try to get at least the closest hour. Prompt as needed: "What is your best guess of the time?" Don't let them get away with vague stuff like "morning" or "after midnight." Be careful with times such as "midnight" or early morning hours—which day do they mean? By "2 am Friday night," for example, do they really mean Saturday morning? Keep probing until it is unambiguous. Write down what they mean—not what they say. Consider midnight to be the *end* of the day (e.g. 11:59 pm).

Secondary cases. Indicate if the history suggests that this case may be secondary (i.e., source could be person-to-person rather than direct consumption of the product). If there was similar antecedent illness in the household or among other close contacts, even if not lab-confirmed, check this box.

Exposure/Consumption Events

Exposures in the likely exposure period. For traceback purposes, people with the "cleanest" histories are obviously preferred, but life doesn't always cooperate. Characterize the recalled exposure history as best as you can. Press to get a best recollection of the date and time of exposure; the latter is needed to calculate the incubation period.

Quality of Information. "Documented" means that there is some kind of written or electronic record to support the history. This might be a restaurant receipt, a copy of the menu from an institutional source, a food diary, or the like. It does *not* mean that you wrote down what the case told you! "Well-characterized" means that the history is pretty specific and likely to be accurate. "Poorly characterized" means that they are pretty sure that they ate it, but don't recall specific details.

Exposure # 1, # 2, etc. Fill in the details for each discrete exposure, numbering them 1, 2, 3,..., where 1 is the ultimate exposure before their onset of first symptoms. Use the supplemental page if needed. (This should be infrequent.)

Product Purchase and Source

Source. The product source refers to where the product that they consumed came from, e.g., purchased at a store, eaten at a restaurant, eaten in an institutional meal, etc. The source may be second-hand, e.g., they ate the food at a family potluck, and it was purchased by another household, in which case you'll need to ferret out the original purchase history.

Enter the name of the store, restaurant or institution (e.g., Safeway Store #5587, Wal-Mart; Polynesian Terrace restaurant, Old Folks Nursing Home) with street address and city name.

If the person consumed product that came from multiple, discrete sources (e.g., cantaloupe in a restaurant fruit salad on Monday and at home from a grocery store purchase of whole melon), number the sources sequentially and attach additional sheets to characterize each purchase.

Quality of Information. Indicate how well the purchase information is documented, and what kind of documentation there is (if any). For store shopper card information, indicate if you have obtained the relevant records from the store already ("in hand") or if the shopper merely has indicated that the purchase was made using such an account, such that the documentation is at least potentially available.

Traceback Info. If you have already garnered any traceback information, specify it here (e.g., BurgerLand gets its lettuce from Charlie's Produce, Wichita KS, with deliveries on Mondays, Wednesdays, and Fridays). Regulatory agencies will probably re-check all this information if they do a formal traceback.

Package/Lot/Sample Information

In what form was the product purchased? Was this a single box of cereal, a case of 12 packages, loose or bulk items (e.g., 1 cantaloupe, a bunch of fresh cilantro)?

Leftovers. If the consumer, restaurant, or institution has leftover product that has been or potentially could be tested, indicate the relevant specifics. If packaging is available, get the details. A digital photo is good; collecting the packaging itself is even better.

Traceback form

Sample. If leftover product has already been collected for testing, indicate here (with any results).