Board of Scientific Counselors, Office of Infectious Diseases

Food Safety Modernization Act Surveillance Working Group

Annual Report to the Secretary, Department of Health and Human Services

2018

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BSC/OID FSMA Surveillance Working Group 2018 Report to HHS Secretary

SUMMARY

The Food Safety Modernization Act of 2010 (FSMA), signed into law on January 4, 2011, authorized the Centers for Disease Control and Prevention (CDC) to create a diverse working group of experts and stakeholders to provide routine and ongoing guidance to improve foodborne illness surveillance systems in the United States. Accordingly, in fiscal year (FY) 2012, CDC established a FSMA Surveillance Working Group (FSMA-SWG) under the Board of Scientific Counselors, Office of Infectious Diseases (BSC/OID), a federal advisory committee. This seventh annual report summarizes the FSMA-SWG's activities and recommendations during FY 2018.

The FSMA-SWG held two 2-day meetings in FY 2018, convening in December 2017 at CDC in Atlanta and again in May 2018 at The Pew Charitable Trusts (Pew) in Washington, DC, to review, respond to specific questions on, and provide guidance on foodborne illness and outbreak surveillance projects in the following areas:

- Improving governmental coordination, integration, and collaboration
- Evaluating and improving surveillance systems
- Enhancing external stakeholder collaboration and communication

The December 2017 Working Group meeting focused on responding to specific questions and providing guidance on foodborne illness surveillance data needs and approaches to measuring the public health impact of several U.S. Food and Drug Administration FMSA regulations.

The May 2018 meeting focused on a review and discussion of the opportunities and challenges of the increasing use of culture-independent diagnostic tests. The meeting was held as part of the 2018 Forum on Culture-Independent Diagnostics: Charting a Path for Public Health meeting, which was sponsored by CDC, Pew, the Association of Public Health Laboratories, the Council of State and Territorial Epidemiologists, and The Ohio State University.

The Working Group applauded recent increases in funding for food safety infrastructure, but the issues addressed in this report emphasize the need for continued resources for these activities.

BSC/OID FSMA Surveillance Working Group 2018 Report to HHS Secretary

INTRODUCTION

This report describes the fiscal year (FY) 2018 activities of the Food Safety Modernization Act Surveillance Working Group (FSMA-SWG) of the Board of Scientific Counselors, Office of Infectious Diseases (BSC/OID), a federal advisory committee at the Centers for Disease Control and Prevention (CDC). This Working Group was established in FY 2012 under authorization by the Food Safety Modernization Act of 2010 (FSMA). Membership comprises 21 experts representing local, state, and federal governments; academia; industry; and consumer groups (Appendix 1).

During FY 2018, the Working Group reviewed activities, responded to specific questions, and provided guidance on how foodborne illness surveillance could be improved by measuring the public health impact of FSMA regulations and addressing the challenges of the increasing use of culture-independent diagnostic tests (CIDTs). The Working Group also reviewed, discussed, and provided guidance on several other CDC FSMA-related projects to enhance foodborne surveillance. For reference, previous topics covered by the Working Group are summarized in Appendix 2.

BACKGROUND

Each year, an estimated 48 million people in the United States (1 in 6 Americans) get sick, 128,000 are hospitalized, and 3,000 die from (largely) preventable foodborne diseases.[1,2]

Foodborne illness is costly. According to a 2015 study,[3] 15 pathogens alone are estimated to cost $15.5 billion in the United States per year. This includes medical costs (doctor visits and hospitalizations) and productivity loss due to illness and time lost from work as well as premature death. Globally, the World Health Organization (WHO) estimated that each year as many as 600 million, or almost 1 in 10 people in the world, fall ill after consuming contaminated food. Of these, an estimated 420,000 people die, including 125,000 children under the age of 5 years.[4]

Public health surveillance is necessary for improving food safety. Timely detection and control of foodborne disease cases and outbreaks can directly reduce their public health impact; identify new food safety hazards; and enable investigators, regulators, and the food industry to learn more about ways to prevent these diseases.

Foodborne illnesses and outbreaks are reported and investigated at the local and state levels. These investigations help identify and prevent foodborne illness in local/state jurisdictions and provide essential information for national public health and food safety systems. CDC compiles information from local and state agencies and works with them to identify and link outbreak-associated illnesses, leading to identification of contaminated foods and management and control of outbreaks. Outbreak data are collected, analyzed, and shared with many stakeholders. Data from these outbreaks serve as a foundation for action by CDC, regulatory agencies, the food-producing industry, and others interested in improving food safety.

Foodborne disease and outbreak surveillance data aggregated by CDC are essential for many functions, including informing evidence-based policies, effectively assessing public health risk, and developing prevention messages for food safety improvements. These data are relied upon by other government regulatory agencies and analyzed by the media, public health, and consumer organizations that provide food safety advice to consumers and policymakers. In January 2013, CDC released the first comprehensive set of estimates of the food categories responsible for foodborne illnesses acquired in the United States from 1998–2008.[5] Building on the 2011 estimates, which showed that about 48 million people (1 in 6) get sick each year from food, these newer estimates

along with annual foodborne illness trend data from the Foodborne Diseases Active Surevillance Network (FoodNet) help regulators and industry identify the groups of foods most responsible for foodborne illness. These data also provide a historical baseline of estimates that can be further refined over time as more data and improved analytic methods become available.

Over the years, differences in data collection and reporting among states, along with issues regarding integration among various government agencies, have led to calls for improvements to ensure that foodborne illness surveillance systems provide the necessary data to assist government agencies, industry, and other food safety stakeholders in their risk-management activities.

CDC and FSMA

The Food Safety Modernization Act of 2010 provided the U.S. Food and Drug Administration (FDA) with new enforcement authority designed to achieve higher rates of compliance with prevention and risk-based food safety standards to better prevent contamination events as well as respond to and contain problems when they occur. Additionally, the law directed FDA to build an integrated national food safety system in partnership with state and local authorities. Recognizing the critical role of foodborne illness surveillance data in informing prevention efforts and CDC's expertise in this area, FSMA also directed CDC to improve governmental coordination and integration, evaluate and improve foodborne illness surveillance systems, and enhance external stakeholder collaboration.

Signed into law on January 4, 2011, FSMA authorized CDC to create a diverse working group of experts and stakeholders to provide routine and ongoing guidance to improve foodborne illness surveillance systems in the United States and to provide advice on the criteria for the designation of five Integrated Food Safety Centers of Excellence (CoEs). In response, the FSMA-SWG of CDC's BSC/OID was created, with BSC/OID member Dr. James Hadler of Yale University's School of Public Health serving as Chair from November 2011 through December 2013; BSC/OID member Dr. Harry Chen, former Commissioner of the Vermont Department of Health, serving as Chair from January 2014 to November 2017; and BSC/OID member Dr. Timothy Jones, State Epidemiologist of the Tennessee Department of Health, serving as Chair from December 2017 to the present.

According to FSMA legislation regarding improvement of foodborne illness surveillance systems, areas for working group discussion and provision of guidance are

> "(A) the priority needs of regulatory agencies, the food industry, and consumers for information and analysis on foodborne illness and its causes;
>
> (B) opportunities to improve the effectiveness of initiatives at the Federal, State, and local levels, including coordination and integration of activities among Federal agencies, and between the Federal, State, and local levels of government;
>
> (C) improvement in the timeliness and depth of access by regulatory and health agencies, the food industry, academic researchers, and consumers to foodborne illness aggregated, de-identified surveillance data collected by government agencies at all levels, including data compiled by the Centers for Disease Control and Prevention;
>
> (D) key barriers at Federal, State, and local levels to improving foodborne illness surveillance and the utility of such surveillance for preventing foodborne illness;
>
> (E) the capabilities needed for establishing automatic electronic searches of surveillance data; and

(F) specific actions to reduce barriers to improvement, implement the Working Group's recommendations, and achieve the purposes of this section, with measurable objectives and timelines, and identification of resource and staffing needs."

This annual report to the Secretary, Department of Health and Human Services, (required by FSMA) highlights the FSMA-SWG's activities and recommendations in FY 2018 and summarizes priority areas for focus in the coming year.

WORKING GROUP ACTIVITIES—FY 2018

During its seventh year, the FSMA-SWG met twice, once at CDC in Atlanta and once at The Pew Charitable Trusts (Pew) in Washington, DC, to consider several recent and ongoing developments in foodborne illness surveillance that are key to maintaining and improving surveillance systems. The December 2017 meeting focused on exploring what CDC and state foodborne illness surveillance data could be used to evaluate the impacts of FSMA, and providing CDC updates on priority initiatives (e.g., the Interagency Food Safety Analytics Collaboration [IFSAC], CIDTs, whole genome sequencing [WGS], FoodNet and its associated population survey, improvement in surveillance data transfer from states and within CDC). The May 2018 meeting focused on identifying CIDT issues and knowledge gaps and generating potential solutions in public health practice, surveillance, and technology. These topics and Working Group discussions are summarized below. Previous annual reports and topics reviewed are listed in Appendix 2 and posted on the BSC/OID FSMA-SWG website.

I. Potential Use of Foodborne Illness Surveillance Data to Evaluate FSMA *(Discussed at the December 2017 FSMA-SWG Meeting)*

Background on FSMA Implementation

FSMA is the most sweeping change in FDA food safety authority in more than 70 years. The main themes of FSMA include prevention, enhanced partnerships, import safety, inspections, compliance, and response.

FSMA rules and implementation approach

FDA is implementing FSMA in three phases. Phase 1 consisted of developing regulations, guidance, and policy. Phase 2 includes designing strategies to promote and oversee industry compliance, and identifying performance metrics to measure success. Phase 3 involves transitioning industry strategies and metrics from design to operations and then evaluating success. In addition, as part of the planning process, FDA established multiple workgroups with operations and policy experts working together to develop a framework and multi-year implementation plan for ensuring compliance with FSMA regulations.

During FSMA Phase 1 implementation, FDA issued seven proposed rules, which are now all final and published (Table 1).

Table 1. FDA Final Rules

Regulation	Proposal	Final
Preventive Controls (Human Food)	Jan 16, 2013	Sept 17, 2015
Preventive Controls (Animal Food)	Oct 29, 2013	Sept 17, 2015
Produce Safety	Jan 16, 2013	Nov 27, 2015
Foreign Supplier Verification Programs (FSVP)	Jul 29, 2013	Nov 27, 2015
Third-Party Certification	Jul 29, 2013	Nov 27, 2015
Sanitary Transport	Feb 5, 2014	Apr 5, 2016
Intentional Adulteration	Dec 24, 2013	May 27, 2016

The framework and multi-year implementation plans that FDA developed for each of the rules encompass outreach, technical assistance, and training as well as data collection and analysis, performance goals and measures, inspections, compliance, and enforcement. FDA has placed an emphasis on (1) development of training for firms and regulators; (2) establishment of technical assistance networks (TAN) to provide central, consistent sources of outreach and technical assistance for industry and regulators; and (3) targeted education and outreach for firms.

Industry experience with FSMA preventive controls

The most significant change to industry resulting from the FSMA Preventive Control (PC) regulations has been improved documentation and improved or updated training, which have had a greater impact on medium and small companies than on large companies. Fewer changes were necessary for companies that prioritized hazard management prior to FSMA. Large companies have tended to have more robust food safety practices and environmental monitoring in place and thus had to make minimal changes to their food safety programs and testing in response to FSMA. However, many medium and small companies needed to make significant changes, and as such were given more time to implement the rules.

Since FSMA implementation, FDA inspections have become more collaborative; however, there are some emerging concerns on the part of industry. For example, taking photographs without permission has been a recent concern, but smart phones have made cameras ubiquitous. Additionally, some FDA inspectors have interpreted guidance as a requirement rather than a recommendation (e.g., Appendix 1 of Hazard Analysis and Risk-Based Preventive Controls for Human Food). Industry expects to learn more since it is still early in FSMA implementation.

Overview of FDA's current thinking approach

As the FSMA rules were being finalized and published, FDA's focus shifted to planning for implementation and measuring progress. FDA is using a results-oriented approach to develop measures to demonstrate achievement of outcomes. The approach first defines long-term outcomes (e.g., what do we want to achieve in 5 years) and identifies activities to achieve these outcomes. Then, risk-informed, direct, and practical

performance measures are determined to measure and monitor if outcomes were achieved. As FSMA implementation continues, these outcomes and activities will be assessed for continued appropriateness and relevance. Outcomes for PC, Produce Safety, and Import Controls have been drafted, but are being further evaluated for feasibility and data limitations. In addition, activities and performance measures for each of these outcomes are still being drafted.

Measuring Public Health Impact of FSMA on Foodborne Illness

The Pew Charitable Trusts—metrics

Pew and the Robert Wood Johnson Foundation are co-sponsors of the Collaborative Food Safety Forum. This workgroup has identified the following challenges to the FSMA implementation metrics:

1. Many factors impact public health outcomes.
2. Short- , medium- , and long-term measures are needed.
3. Not all metrics may be relevant across food types.
4. There are multiple relevant metrics: inputs, processes, outputs, and outcomes.
5. Data are imperfect, limited, and subject to reporting lags.

FSMA implementation should be evaluated using a web-metrics approach that includes public health metrics, industry performance metrics, FDA performance metrics, and industry segment–specific metrics. Public health metrics should center on reducing illnesses linked to FDA-regulated foods. Industry performance metrics should have a prevention-based focus, demonstrating a strong food safety culture. FDA performance metrics should directly track FSMA implementation, while industry metrics should be specific to a particular rule (e.g., produce, preventive controls, and the FSVP).

Review of food categorization schemes

Classifying foods implicated in outbreaks can allow public health and food industry professionals to target prevention efforts for pathogens and commodities. CDC has used the Painter commodity categorization scheme to categorize foods implicated in foodborne disease outbreaks since 2009. IFSAC, established in 2011, coordinates efforts by FDA, the U.S. Department of Agriculture (USDA)/Food Safety and Inspection Service (FSIS), and CDC to generate estimates of foodborne illness source attribution and inform food safety policy. One of IFSAC's latest projects included expanding the food categorization scheme used by CDC to include more specific and useful food categories for regulatory agencies and stakeholders. To update the existing scheme, subject matter experts were consulted within CDC, FDA, and USDA/FSIS to identify new commodity categories, discuss proposed revisions, and provide expertise regarding the specific foods to be assigned to each category to ensure the new categorization scheme meets regulatory agency needs. A comprehensive food glossary was also developed to accompany the proposed commodity categorization scheme to illustrate the placement of specific foods into each commodity category. This effort resulted in the IFSAC Food Categorization Scheme, which consists of five hierarchical levels: (1) overarching food group; (2) major food type; (3) sub-specific food type; (4) food subtype varieties; and (5) specific processing, preparation, or consumption type. The IFSAC food categories reflect many of the food product definitions used by FDA and FSIS. The IFSAC Food Categorization Scheme may help to improve efforts for measuring the public health impact of FSMA; however, a high number of foods are unclassifiable (e.g., complex foods), and the unavailability of data at the lower levels may make classification of outbreaks into FSMA-regulated versus not FSMA-regulated groups challenging.

Considerations about data-driven approaches to measuring the public health impact of FSMA

FDA early approaches

Current surveillance systems such as FoodNet provide excellent data on the incidence of disease for several key foodborne pathogens; however, when evaluating FSMA, it is beneficial to look at illnesses that can be directly traced to FDA-regulated foods that are covered by the different FSMA rules. Outbreak data can provide this information on an ongoing basis for the entire country. However, outbreak data are limited in that they represent only a small fraction of overall foodborne illness, have surveillance bias such as analysis done on non-representative data, and have regional/year-to-year variability in how they are reported. In addition, in determining what outbreak data to use in analyses, considerations include

- Multistate vs. single-state outbreaks
- Selection of pathogens
- Aligning food categorization scheme and rules
- Point-of-contamination information
- Single vs. complex food vehicles

A number of approaches have been used to measure the public health impacts of food safety regulations, including (1) counting the number of outbreaks or number of outbreak illnesses, (2) estimating the overall disease burden in the population (based on outbreak data), and (3) statistical analysis to test a hypothesis of whether illnesses have been reduced after an intervention. Regardless of the approach, it is important to consider public health measures in the context of other FSMA measures and alternate hypotheses for apparent trends in outbreaks or outbreak illnesses. Continued CDC–FDA collaboration is needed to effectively evaluate the public health impacts of FSMA.

Trends over time (leveraging an IFSAC method)

Previous IFSAC work conducted to evaluate temporal trends in foodborne outbreaks and illnesses laid the foundation to focus on a simple Bayesian model for the current project. This project evaluates modeling techniques to produce estimates of foodborne outbreak and illness trends at the pathogen and food category level, and assess changes over time in foodborne illness outbreaks and illness for the four IFSAC priority pathogens. The new model developed in this current project (1) uses untransformed count data, (2) includes flexibility to capture real changes while remaining resistant to the influence of outliers (thin plate splines), (3) accounts for uncertainty and allows for evaluation of short- and long-term trends, and (4) can be used for similar scenarios or other pathogens of interest. One of the limitations is the granular ability to model specific foods and pathogens. Future directions may include incorporating epidemiological factors from the IFSAC P13 project, point of contamination, or other count data.

CDC early approaches

CDC's Enteric Diseases Epidemiology Branch has performed preliminary analysis using the Foodborne Disease Outbreak Surveillance System database focusing on produce and to some extent processed foods. The analysis involved selecting pathogens and foods, using multistate outbreak data, counts of outbreaks, and number of illnesses per outbreak. Additionally, produce items were not included if they were not covered under the Produce Safety Rule, and outbreaks that could be attributed to an ill food worker were not included. Consistent with the ill food worker approach, outbreaks of norovirus were also not included. Determining which IFSAC food categories to include in the analysis for processed foods was more challenging than for produce. Ensuring data are specific to the regulation, having adequate data to monitor change over time, and the approach to incomplete and unknown data are among the many factors to contemplate. A multi-disciplinary effort and continued CDC–FDA collaboration are needed.

Discussion/Guidance

Discussion

The Working Group's discussion included the following observations:

- Assessing FSMA Implementation
    - Outcome measures using human illness are a high bar to prove a relationship to the FSMA rules.
    - Ideally, data from some level of ongoing environmental and product testing would be available to compare with a baseline.
    - It is difficult to use illness data. Thus, measuring outbreak data and how it affects implementation of the rules may be the best option from a human disease aspect. Several members thought outbreak data were important even with their limitations to use as a metric.
    - WGS will be a "game changer." Illness rates and outbreaks should be looked at regionally, and inspections and sampling for specific foods and pathogens should be targeted where indicated by the outbreak data.
- Consider industry's potential contribution to measuring FSMA
    - From an industry perspective, since large companies did not need to make many changes to become FSMA compliant, they may not be the best place to look for impact. Small and very small businesses have not been impacted yet, since they have more time left to adopt the rules.
    - Further investigation is needed to understand whether the outbreaks and illnesses are associated with larger or smaller food companies. However, there is a large gap between large and small companies and the resources they have access to.
    - Industry has the capacity to reduce the level of pathogens; sharing what industry is finding and looking for concerning reductions in levels over time may be useful.
    - Industry could measure the number of events that happen before a product is distributed. These "close calls" are currently not recorded because they are not reported to FDA.
    - Mapping supply chains, supplier sources, and prevalence of pathogens may be helpful. Supply chain transparency can help with traceback and traceforward investigations that may lead to the source of an outbreak. Industry is working on this effort with technology like Block Chain.
    - Industry may have critical information that could be used to fill knowledge gaps during outbreak investigations. For instance, one company may not purchase product from a particular vendor because they have positive samples, but another company may buy that positive product.
    - Industry testing data alone may not be the best source to measure impact. There is a misconception that industry has a lot of testing data that they are choosing not to share with public health. Also, industry may be resistant to share the positive results they have because they do not always lead to a public health impact, but can lead to recalls and litigation. Litigation can tie the hands of the companies that want to do the right thing.
        - Government protections similar to those used for the vaccine industry may be worth considering.

- Public health should work with industry to develop better measures for FSMA success. This may include identifying successful prevention of hazardous products from entering the marketplace and the number of employees per FDA-regulated facility trained in PC and having qualified individuals (and similar measures for Produce Safety and FSVP).
- Using outbreak data is more important in determining how industry conducts risk assessment/analysis than how impactful the rule is. However, outbreaks are just a small portion of the overall public health implication.

- Examine the effect of other epidemiological factors on measuring the impact of FSMA
  - Further analysis of data from sporadic cases, such as determining the genotype of cases and attributable fraction related to an outbreak vehicle, could be useful. Additionally, analyses that use the population who seeks healthcare as a denominator may provide additional context and greater understanding of cases.
  - More emphasis is needed on the amount of a pathogen in a product rather than a dichotomous positive/negative. The impact of FSMA may be demonstrated by measuring lower levels of pathogen rather than lower proportion of positive samples.
  - Reports by industry under the Reportable Food Registry are a good data source for measuring FSMA impacts.
  - Attribution data could be used to measure the impact of FSMA, especially if it could be matched with food industries that implemented more standards.
  - It is difficult to measure changes that are the result of FSMA because there are other factors, such as the use of CIDTs and WGS, that are potentially increasing the number of detected illnesses and outbreaks. Additionally, not all foods and not all pathogens are relevant to FSMA, and changes in these areas cannot be attributed to the increased regulation.
  - Baseline testing of foods of high risk might be available from industry. Understanding the impact of changes in production processes on outbreaks is essential in quantifying the impact of FSMA. For example, documenting production practices that changed and resulted in less contamination may be useful.
  - Regulatory agencies should focus on eliminating risk factors. Additionally, looking for critical sources, targeting certain pathogens, and addressing them legislatively would have more long-term impact on public health. For example, using policy/legislation to remove sprouts and raw milk from the marketplace would help quantify the impact of FSMA.
  - Understanding why the outbreak happens and identifying contributing factors and whether or not these factors are reduced over time may be a way of identifying the impact of FSMA using outbreak data. For example, with FSMA there should be improved training for staff, which should lead to a reduction of outbreaks being caused by a lack of training. Another approach would be to assess the timeline for detection and response, or evaluate two or three food-pathogen combinations to see what factors may have changed over time.
  - Although the number of outbreaks (or the ones linked to a source) are small, a decline in those numbers would be meaningful and easily understood by the public. CDC should quantify the impact of better detection methods to help explain to the public why there are increases in cases.

- More objective metrics are needed; outbreak data are only a small portion of foodborne illness data. USDA/FSIS has measured some objectives using baseline testing data. FDA should also develop prevalence data for pathogens in specific foods. Some FDA metrics may be flawed due to variability in practices among the inspectors themselves.
- The number of recalls should be monitored to see if there is a reduction following regulation implementation. Additionally, the proportion of FDA recalls that are due to pathogens compared with all recalls (i.e., pathogen, foreign object, and allergen recalls) could be monitored to observe change.
- The number of product positives could be compared with the number of human positives to see if there is a correlation.

- Increase capacity in states
  - It is not just important to identify more outbreaks. Public health agencies should also collect better data during outbreaks, including contributing factors and environmental antecedents. Part of the challenge is the large number of unsolved outbreaks and outbreaks not attributed to a source (or having contributing factors). CDC should continue state capacity-building efforts (e.g., the work of CoEs, FoodCORE [Foodborne Diseases Centers for Outbreak Response Enhancement], OutbreakNet Enhanced [OBNE]) to enhance outbreak detection and response activities at the state/local level, including providing training and funding to states to collect data that can be attributed to FSMA.
  - It is important to understand barriers at the state/local agencies that could be affecting their ability to solve outbreaks. Other issues that may be helpful to investigate include (1) what is the state and local capacity?; (2) how many epidemiologists per million people would be ideal?; and (3) is there a regional breakdown of where a source is not being identified, and is that related to a capacity issue?

Guidance

Based on these discussions, the Working Group highlighted the following recommendations:

- Improve the quality of sporadic illness as well as outbreak data
- Understand the effect of other factors (e.g., CIDT, WGS, investigative methods, better detection) on epidemiologic changes
- Engage industry and its wealth of information (e.g., supply chain and supplier source information, prevalence of pathogens at baseline and following interventions using best practices, “near misses” that avoided release of contaminated product) to measure the effects of FSMA rule implementation
- Increase capacity in states (not just funding, but informatics, training, surge capacity, etc.)
- Improve sharing of data between public health agencies, regulators, and industry
- Continue to improve collaborations and partnerships between public health agencies, regulators, industry, consumers, and academia

II. CDC Updates *(Discussed at the December 2017 FSMA-SWG Meeting)*

Some of IFSAC's accomplishments in 2017 include the release of the IFSAC 2017–2021 strategic plan and corresponding action plan, informing new partners about IFSAC's work, responding to requests, and initiating and completing multiple projects. IFSAC held a webinar on December 17, 2017, to present one of its key accomplishments, the 2013 foodborne illness source attribution estimates for four priority pathogens.

- IFSAC previously developed a new method for estimating foodborne illness source attribution for four priority pathogens based on outbreak data: *Salmonella*, *Escherichia coli* O157, *Listeria monocytogenes*, and *Campylobacter*.
- IFSAC published the 2012 estimates in a short report in 2015. More technical aspects of the study will be published via a manuscript.

CDC's focus is on foodborne illness rather than food safety regulation; however, information collected from outbreak investigations helps drive prevention policy. CDC is building laboratory and epidemiology capacity across the country to improve outbreak detection and investigation, which will improve prevention and control efforts. By the end of 2017, nearly 100% of state public health laboratories will have a sequencer and personnel trained to operate it. This will lead the way for making WGS routine for public health surveillance of enteric bacteria. CDC is also working to improve epidemiology support through the FoodCORE and OBNE programs, which currently fund 33 states (approximately 88% of the U.S. population).

FoodNet launched the new cycle of the Population Survey in December 2017. This survey was previously conducted in 2006–2007 to estimate the burden of acute gastrointestinal illness in the United States and to assist with hypothesis generation during cluster and outbreak investigations. The new cycle will update the data used for these purposes and includes modernized methods. FoodNet is also conducting surveillance of CIDTs to quantify the trend away from culture. Cases with only CIDT results are becoming an increasingly larger portion of cases reported to public health. Data from FoodNet's surveillance will inform interpretation of incidence rates and strategies for adapting to the changing diagnostic environment. With the expanding use of WGS, antimicrobial resistance information will be included as part of the data collected in FoodNet.

CDC conducts epidemiologic surveillance for select pathogens to detect outbreaks, identify emerging threats and trends, identify sources of illness, and monitor the impacts of public health interventions. Current low-tech surveillance operations are slow, potentially inaccurate, laborious, and expensive. Public health personnel need to be able to link epidemiologic and laboratory data in real-time because this impacts the time it takes to detect an outbreak and the number of outbreaks that are able to be solved and lead to regulatory action. At present, real-time data entry and case-linking is done only for *Listeria* because the current manual methods would overwhelm staff if expanded to other pathogens. To address this issue, CDC is upgrading its enteric case databases and is working to develop a system where states can send surveillance data to CDC electronically for real-time upload without the need for duplicate entry. This method is being piloted with four states through HL7 message mapping, but investments need to be made in state informatics capacity in order for this process to work nationwide.

III. 2018 Forum on Culture-Independent Diagnostics: Charting a Path for Public Health *(Attended in lieu of the May 2018 FSMA-SWG Meeting)*

Overview

Clinical diagnostic microbiology is undergoing one of the most significant technological revolutions since the time of Pasteur. DNA technology is making it possible for physicians to quickly obtain more information about what is making their patients sick without the need for time-consuming culture-based testing. Public health surveillance programs rely on clinical microbiology data for a variety of functions, such as detecting outbreaks, monitoring trends, and informing policy. Adapting practices to the new types of data is essential for public health to maintain its critical functions and to make full use of this expanded potential. The 2018 Forum on Culture-Independent Diagnostics was convened at the Pew headquarters in Washington, DC, to bring together subject matter experts to help public health forge a path in the CIDT era. Because of the importance of the topic, the FSMA-SWG attended the meeting in lieu of one of its biannual meetings.

Background

Foodborne disease is largely preventable, but prevention requires information about the foods that are making people ill and the means by which the foods become contaminated. The programs for tracking and managing specific diseases such as salmonellosis, campylobacteriosis, and pathogenic *E. coli* diseases have been based on patient culture reports from physicians and clinical microbiology laboratories. "Isolates," or samples of the bacteria grown as part of the culture process, are sent to public health agencies and play a critical role in disease monitoring, outbreak detection, and outbreak investigation. As the increasing use of CIDTs replaces the use of culture, public health agencies must make a wide range of adjustments to the methods and policies.

Over the years, the lessons learned from outbreak investigations conducted by state and local health departments, CDC, FDA, and USDA have triggered safety improvements by industry for a wide range of foods such as leafy green vegetables, tree nuts, vine vegetables, melons, flour, beef, poultry, eggs, spices, cereal, peanut butter, and ice cream. PulseNet, a collaboration of 83 local, state, and federal laboratories in all 50 states, has been the primary detection mechanism for large multistate outbreaks involving commercial products. A 2016 economic analysis showed that PulseNet prevents at least 270,000 cases and one half billion dollars in costs and productivity losses per year.[6] PulseNet works by conducting "DNA fingerprinting" on illness-causing bacteria (pathogen "isolates") from patients who have become ill with *Salmonella, E. coli, Listeria*, or other bacteria. Matching DNA fingerprints among multiple cases in a similar timeframe triggers an outbreak investigation, as patients with matching isolates may have consumed the same contaminated food, even if they are physically located in different parts of the country. This process depends on patients seeking medical care, physicians ordering diagnostic tests, and clinical laboratories finding a pathogen and sending an isolate to their local PulseNet laboratory. For the past several years, PulseNet has become even more effective as pulsed-field gel electrophoresis (PFGE), the older "DNA fingerprinting" method, has been replaced by WGS. Both PFGE and WGS depend on isolates.

Although CIDTs have been emerging in clinical microbiology for over 30 years, it wasn't until the 2010s that FDA cleared "syndromic panels" to simultaneously test for many pathogens, including bacteria, viruses, and parasites. These panels streamlined clinical laboratory processes, saving time and potentially money. The panels also provided data to physicians more rapidly than culture methods. In 2012, syndromic CIDT use was still rare, but it was already clear that the use of this type of testing would rise rapidly as the market matured. In anticipation of this trend, CDC, the Association of Public Health Laboratories (APHL), and the Council for State and Territorial Epidemiologists (CSTE) organized a "Forum on Culture-Independent Diagnostics" to chart a path for public health and to preemptively address expected issues and disruptions. The FSMA-SWG

attended the 2012 CIDT Forum and commented on the importance of CIDTs in its annual reports for FY 2013–2017.

2018 CIDT Forum Goals and Composition

By 2018, the trend toward CIDTs had accelerated and was starting to impact both negatively and positively on a number of public health surveillance activities. Through a collaborative effort, CDC, APHL, CSTE, Pew, and The Ohio State University organized a 2nd Forum on Culture-Independent Diagnostics to build upon the 2012 meeting and the intervening 6 years of experience with CIDT trends.

As with the introduction of any transformative technology, the introduction of CIDTs into the medical marketplace is causing wide-ranging effects, including immediate enhancement of clinical medicine and public health but also widespread disruption of existing systems. To more effectively harness the potential of CIDT technology and address its disruptive impacts, the 2018 Forum bought together leaders and subject matter experts from clinical microbiology, medicine, epidemiology, molecular biology, health law, policy, economics, and medical/laboratory regulation who represented government, academia, and the medical device industry. The Forum focused on public health aspects, and its goals included (1) increasing awareness among participants about the scope of the problem, current impacts, and likely impacts; (2) evaluating current efforts to address CIDT issues in public health and identify knowledge gaps; and (3) brainstorming new ideas and potential solutions. To achieve these goals, the Forum included plenary sessions to familiarize participants with all of the major topics, along with three tracts to explore subject-specific issues, including (1) public health practice, (2) strategies for preserving isolate-based surveillance until CIDT-compatible surveillance mechanisms are in place, and (3) technological approaches to characterize pathogens for public health activities without the need for culture.

The FSMA-SWG attended the 2018 CIDT Forum in lieu of its biannual meeting and provided the observations and guidance listed below. Of note, the BSC FSMA-SWG recommends that CDC develop an action plan that CDC and stakeholders can use to guide efforts and ensure continued foodborne illness surveillance into the future.

Discussion/Guidance

Public health practice

Adapting reportable enteric disease case definitions to include CIDTs

Local, state, federal, and international case definitions have been based on culture. Since an increasing percentage of total cases are now diagnosed by CIDT and not culture, there is concern that cases would not be reported if alternate definitions are not allowed, leading to inaccurate measures of burden and trends. Without accurate data, it will be difficult to measure the effectiveness of public health control programs and inform policy and the public. CIDTs have varying performance characteristics, and trends may not exactly align with culture data. Further, CIDTs may be used differently from culture (i.e., ordered more or less frequently or for different uses), which may alter the denominator used for detecting and analyzing trends. The Working Group recommended the following:

- Case definitions should be synchronized with current diagnostic practices, including CIDTs, and not be so complex as to discourage reporting.
- CDC should continue monitoring the uptake of culture-independent testing by clinical labs and the impact of such testing on the number of isolates available for WGS testing to identify outbreaks.
- Studies should be conducted to fill knowledge gaps in how results from culture-independent testing and culture compare for tracking disease incidence.

- In anticipation of further development of CIDT technology (e.g., genotyping), case definitions and reporting of CIDT results should be updated in accordance with their intended use—taking into consideration the different functions and needs of primary care providers and clinical laboratories (diagnosis and treatment) versus health department epidemiologists and reference laboratorians (public health surveillance and response).

Surveillance interpretation issues using CIDT data

CIDT syndromic panels provide information on multiple agents for which practical tests were not previously available. This new data stream provides surveillance opportunities to public health as well as challenges in interpretation. For example, frequent pathogen co-detections are being reported with CIDT use, even in asymptomatic individuals, but current surveillance systems are not designed to effectively track, use, or interpret these data. Also, non-Shiga toxin-producing *E. coli* infections (e.g., ETEC [enterotoxigenic *E*. *coli*], EPEC [enteropathogenic *E*. *coli*], EAgEC [enteroaggregative *E*. *coli*], and EIEC [enteroinvasive *E*. *coli*]) are now being reported to clinicians through the use of CIDTs, but their significance is unknown. The Working Group recommended the following:

- Additional studies should be conducted to determine pathogen-pathogen interactions and to assess the clinical and public health relevance of co-detections being detected with CIDT panels.
- Studies should be conducted to assess the public health significance of other non-STEC *E. coli* infections and the significance of positive CIDT results in asymptomatic individuals.
    - ETEC, in particular, is now frequently being reported among cases without an international travel history. This represents a new surveillance opportunity to better understand the epidemiology of ETEC.

Use of CIDTs for exclusion (and test-of-cure) from sensitive occupations/settings

There are strong incentives for the use of CIDTs to quickly screen persons ill with communicable diseases such as Shiga toxin-producing *E. coli* disease and salmonellosis who work in sensitive settings (such as healthcare, food service, or daycare) before their return to work. Screening with CIDTs increases the potential for reducing economic hardship to affected individuals due to its quick results. However, this is an "unintended use" for these diagnostics, and the performance characteristics of CIDTs in these circumstances are unknown. The goal of exclusion is to limit transmission, but the tests are designed to measure presence/absence of pathogen nucleic acid, not transmission potential. Nevertheless, CIDTs are already being used for this purpose in some states, and national guidance is urgently needed. The Working Group recommended the following:

- National standardized guidance for exclusion and return of enteric-positive persons working in high-risk settings should be developed.
    - CSTE offered to form a workgroup with experts from CDC and other stakeholders to develop national model practices for the states, who can then adopt or modify them. CSTE will develop an easily navigable flowchart for detecting and monitoring high-risk cases based on which tests have been ordered for each phase of exclusion.
- Long-term parallel studies of culture and culture-independent testing of ill workers subject to exclusion should be conducted to fill significant knowledge gaps in this area.
- The FDA Food Code section on exclusion of food workers, which only addresses culture-confirmed results, should be updated once the CSTE guidelines are developed.

Preserving isolate-based surveillance

Until advanced direct-from-specimen pathogen characterization assays are developed, recovery of isolates from patient specimens will be needed to maintain public health functions. Reflex culture (i.e., isolate recovery on CIDT-positive specimens) may be performed at clinical laboratories where the CIDT was used or at public health laboratories, or some combination of the two approaches can be used. For this to occur, the specimen collection methods used by the CIDTs would need to be compatible with methods that will enable culture to be performed, and laboratory resources would need to be identified. Clinical laboratories could potentially be compensated either by reimbursement or workload credit (which affects productivity calculations and allotment of staff). Either approach would require new mechanisms to be put in place and considerable communication between clinical and public health laboratories. Funding would also need to be identified for the public health laboratory option.

Issues with CIDTs and isolate recovery

CIDTs do not require pathogen viability to function, which can result in inconsistent isolate recovery.

Point-of-care testing systems that utilize rectal swabs directly inoculated into the test system also make isolate recovery impossible. The Working Group recommended the following:

- CDC should work with FDA and manufacturers to develop language that could be included with product inserts to warn users that testing should be compatible with public health reporting mandates and that the CIDT limitations may require additional specimen collection and testing.
- Modification of laboratory accreditation requirements should be considered to specifically encourage the use of whole stool specimens for isolate recovery.
- Opportunities should be identified to facilitate collaboration among the medical device industry and clinical and public health laboratories about novel collection devices and isolate recovery issues.
- More education should be provided to clinical laboratories about reporting laws and approaches to isolate recovery.

Resource and reimbursement

Reimbursement for reflex culture in clinical or reference laboratories currently requires either (a) a test order from the provider or (b) a specific Current Procedural Terminology (CPT) test code (e.g., reflex culture from CIDT for mandated public health requirements). Often, neither of these is included and laboratories must perform reflex cultures at a cost. The Working Group recommended the following:

- Codes should be developed that allow reflex culture, isolate recovery, and shipment of isolate costs to be reimbursed by third-party payers.
- Public health laboratories should be informed about potential federal funding (e.g., CDC Epidemiology and Laboratory Capacity for Infectious Diseases [ELC] Cooperative Agreement) for performance of reflex cultures.

Communication

Increased communication, education, information sharing, and collaboration with stakeholders such as healthcare institutions, labs, public health, accreditation organizations, insurers, and professional organizations (e.g., the Association of State and Territorial Health Officials [ASTHO], Academy of Health Information Professionals, providers) will be critical to identify and implement solutions to preserve isolate-based surveillance. The Working Group recommended the following:

- A communication toolkit should be developed to help engage and educate partners and critical stakeholders about the opportunities and challenges associated with CIDTs.

- Public health case studies and data related to the immediate impacts of CIDTs on foodborne illness and outbreak detection should be published more widely to increase awareness of these challenges among various stakeholders.
- Economic analysis of the cost-benefits and cost-avoidances associated with maintaining isolate-based surveillance should be conducted to inform decision makers and insurers.

Technological solutions

Characterization of foodborne disease surveillance isolates to the level accomplished by WGS is needed for outbreak detection and to monitor trends in pathogen virulence and antimicrobial resistance. There are a number of intrinsic challenges with developing assays to achieve WGS-type resolution directly from specimens, without the need for a culture step (i.e., culture-independent pathogen characterization). These challenges include (1) the complexity of the stool matrix (large variety of prokaryotic and eukaryotic DNA, including human DNA); (2) the similarity of pathogens to commensal flora, making it difficult to distinguish sequences to the specificity level required; (3) signal-to-noise ratio (especially for pathogens in low abundance); and (4) the need for rapid, low-cost, low-complexity, and potentially high-volume workflows in the resource-constrained public health laboratory environment.

CDC is currently investigating the use of highly multiplexed amplicon sequencing (HMAS, for partial cgMLST) as a short-term solution, along with shotgun metagenomic approaches for the long term. Feedback and additional ideas in this area were solicited from the Forum subject matter experts. The BSC FSMA-SWG members thought that CDC researchers were on the right track, but since few members were experts on this, the Working Group deferred to the BSC/OID Infectious Disease Laboratory Working Group to provide guidance on this topic.

RESOURCES

The Working Group applauded recent increases in funding for food safety infrastructure, but the issues addressed in this report emphasize the need for continued resources for these activities. As CIDTs and other technologies continue to rapidly evolve, public health and regulatory agencies will face substantially increased costs in responding to the transition. For example, the increasing use of CIDTs in clinical settings will shift the burden of performing reflex cultures and additional confirmatory testing to public health laboratories. Data management and translation of tremendous amounts of new types of data into formats that are meaningful to outbreak investigators and regulators will require increased investment in laboratory and informatics infrastructure. Additional research will be needed to guide the food industry and regulatory agencies in using increasingly sensitive and detailed data to find and eliminate threats at various levels in the food chain. The number of foodborne disease outbreaks being identified by new technologies is already rising and will continue to do so. Increased resources are needed to support the use of these new technologies to improve the safety of the U.S. food supply.

NEXT STEPS

Since its formation 7 years ago in 2011, the FSMA-SWG has met 14 times and completed seven annual reports for the HHS Secretary. In December 2017, nine new members began their terms to fill positions vacated by members whose terms had expired. There was considerable discussion of the value of the guidance provided thus far, ways to improve the FSMA-SWG meetings, and potential future topics.

Based on the discussion, examples of potential future topics include

- Enhancing integrated data systems within CDC and among CDC, FDA, and USDA
- Improving root cause identification and analyses
- Addressing challenges with imported foods
- Building state capacity and associated performance measures
- Providing periodic reviews of
    - Priority areas (e.g., CIDTs, WGS, antimicrobial resistance)
    - Interagency collaborations such as IFSAC, the Interagency Foodborne Outbreak Response Collaboration (IFORC), the Interagency Collaboration on Genomics and Food Safety (Gen-FS), and FoodNet
    - Trends in priority pathogens (e.g., *Salmonella*, STEC, *Listeria*, *Campylobacter*) and ways to prevent infections
    - "Orphan" illnesses (e.g., cryptosporidiosis, cyclosporiasis, hepatitis A)
- FY 2020 use of WGS in outbreak detection and metagenomics

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APPENDIX 1: FSMA SURVEILLANCE WORKING GROUP MEMBERS

Meetings held in December 2017 and May 2018

BSC Representative Members:

Chair, Timothy F. Jones, MD—State Epidemiologist, Tennessee Department of Health

Member, Kristy K. Bradley, DVM, MPH—State Epidemiologist and State Public Health Veterinarian, Oklahoma State Department of Health (also CSTE representative, see below)

Member, Lee W. Riley, MD—Professor and Chair, Division of Infectious Diseases and Vaccinology, School of Public Health, University of California, Berkeley

Federal Partner Members:

Dale Morse, MD, MS—Centers for Disease Control and Prevention

Jeffrey Farrar, DVM, MPH, PhD—Food and Drug Administration

David Goldman, MD, MPH—United States Department of Agriculture, Food Safety and Inspection Service

Public Health Partner Agency Members:

Natalie Adan—National Association of State Departments of Agriculture

Denise M. Toney, PhD, HCLD (ABB)—Association of Public Health Laboratories

Michele DiMaggio, REHS—National Environmental Health Association

Kristy K. Bradley, DVM, MPH—Council of State and Territorial Epidemiologists (see above)

Ernest M. Julian, PhD—Association of Food and Drug Officials

Nathaniel Smith, MD, MPH—Association of State and Territorial Health Officials

Mark Bergtholdt, REHS, MPH—National Association of County and City Health Officials

Consumer Partner Members:

Sarah Sorscher, JD, MPH—Center for Science in the Public Interest

Dara Alpert Lieberman—Trust for America's Health

Karin Hoelzer, DVM, PhD—The Pew Charitable Trusts

Industry Partner Members:

Natalie Dyenson, MPH—Dole Food Company, Inc.

Scott K. Hood, PhD—General Mills

Michael J. Roberson, MS, CFS, CP-FS—Publix Super Markets, Inc.

Academia Partner Members:

Jeffrey B. Bender, DVM, MS—University of Minnesota

Michael P. Doyle, PhD—University of Georgia

Elaine Scallan, PhD—University of Colorado, Denver

APPENDIX 2: FY 2012–17 FSMA SURVEILLANCE WORKING GROUP ANNUAL REPORTS AND MEETING TOPICS

FY 2012 Annual Report

Main topics:

- Selection Criteria for Integrated Food Safety Centers of Excellence
- Interagency Food Safety Analytics Collaboration
- Improving Foodborne Illness Surveillance Systems: Focus Areas for Future Discussion

Supplementary topics:

- Overview of the Human Illness Surveillance Requirements of FSMA – CDC
- Summary of Nov 3–4, 2011 Pew Food Safety Forum's Surveillance Workshop
- Overview of Foodborne Illness Surveillance Systems and Challenges – CDC
- Overview of Multistate Foodborne Outbreak Investigations and Challenges
- Economic Analyses on FoodNet and PulseNet – CDC
- Website Improvements to Make Data More Accessible to the Public
- Improved Outbreak Reporting Mechanisms: PulseNet Portal and Palantir – CDC

FY 2013 Annual Report

Main topics:

- Culture-Independent Diagnostic Tests
- Performance Measures to Enhance Federal, State, and Local Foodborne Illness Surveillance

Supplementary topics:

- CoE Congressional Report
- Attribution of Foodborne Illnesses, Hospitalizations, and Deaths to Food Commodities
- Vital Signs and Recent Communication Updates

FY 2014 Annual Report

Main topics:

- Foodborne Illness and Outbreaks Caused by Norovirus
- Antimicrobial Resistance Surveillance for Foodborne Illness

Supplementary topics:

- Whole Genome Sequencing *Listeria* Surveillance Project
- Cyclosporiasis

FY 2015 Annual Report

Main topics:

- Governmental Coordination, Integration, and Collaboration
- Environmental Factor Surveillance for Foodborne Illnesses

Supplementary topics:

- Cyclosporiasis Surveillance
- *Vibrio* Surveillance

FY 2016 Annual Report

Main topics:

- Industry Role in Enhancing Surveillance
- Review of Proposed Plans of the Interagency Food Safety Analytics Collaboration
- Traceback Surveillance
- Integrated Food Safety Centers of Excellence
- Plans for Foodborne Antimicrobial Resistance Funding

Supplementary topics:

- Multistate Outbreak Summary
- *Shigella* Update
- Website Updates (NARMS: Now, FOOD Tool, general)
- PulseNet Cost-Benefit Paper

FY 2017 Annual Report

Main topics:

- Culture-Independent Diagnostic Tests and Their Potential Influence on Foodborne Illness Detection and Outbreak Surveillance and Response
- Genomic Testing (e.g., WGS) and Its Potential Effects on Foodborne Outbreak Investigations and Response

Supplementary topics:

- National Outbreak Reporting System (NORS) Overview and Trends
- Interagency Food Safety Analytics Collaboration Updates
- Case-Case Analyses Using Existing Surveillance Data
- Foodborne Disease Active Surveillance Network (FoodNet) Program and Recent Trends in Rates of Enteric Illness