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

2014

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BSC/OID FSMA Surveillance Working Group 2014 Report to HHS Secretary

SUMMARY

The Food Safety Modernization Act of 2010 (FSMA), signed into law on January 4th, 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, the Centers for Disease Control and Prevention established a FSMA Surveillance Working Group (FSMA-SWG) under the Board of Scientific Counselors, Office of Infectious Diseases (BSC/OID). This third annual report summarizes the FSMA-SWG's activities and recommendations during FY 2014.

The FSMA-SWG held two 2-day meetings at CDC in FY 2014, convening in December 2013 and again in May 2014 to review, respond to specific questions on, and provide guidance on foodborne illness and outbreak surveillance projects in the following areas:

- improving surveillance of foodborne illness and outbreaks caused by norovirus
- improving antimicrobial resistance surveillance for foodborne illnesses, primarily focusing on the use of data from the National Antimicrobial Resistance Monitoring System (NARMS)
- advancing several CDC FSMA-related projects to enhance foodborne disease surveillance

The issue of foodborne illness and outbreaks caused by norovirus was identified as an important emerging area, with national significance. Even though norovirus disease is not primarily foodborne, noroviruses are the most common cause of foodborne illness in the United States, responsible for >50% (5.5 million cases per year) of all foodborne disease cases due to known agents. While the disease is rarely life threatening, the sheer numbers of foodborne disease cases caused by norovirus leads it to be ranked second in food-associated disease hospitalizations (26%) and fourth in deaths (~150 annually). The virus is also likely to be a significant cause of foodborne illness of unknown etiology. It is highly infectious and transmissible, persistent in the environment, and resistant to virtually all control measures used in food processing and sanitation/disinfection. Based on discussions and available information, the FSMA-SWG advised the following actions:

- Resources for foodborne norovirus surveillance should be targeted to enhance training, detection, investigation, reporting, and education and to support national surveillance networks
    - Targeted studies are needed to improve illness detection, to evaluate the utility of environmental and food testing, to answer key questions about foodborne transmission to improve attribution estimates, and to target mitigation activities
- Continued research is needed to develop and license sanitizers, disinfectants, and vaccines with established efficacy to control norovirus

As these activities more forward, further study will be necessary to identify specific risk groups that should be targeted for these prevention and control efforts.

Recent trends in the resistance of foodborne pathogens to antibiotics used to treat serious foodborne infections have raised important public health concerns. In a 2013 report (Antibiotic resistance threats in the United States, 2013; http://www.cdc.gov/drugresistance/threat-report-2013/), CDC described the overall danger to public health from antibiotic resistance of 17 pathogens, including 4 transmitted commonly through food: 2 with animal reservoirs and 2 with human reservoirs. During its discussions, the FSMA-SWG recognized the

importance of NARMS data in tracking antimicrobial resistance trends, targeting areas for policy intervention, and meeting stakeholder data needs. The Working Group provided additional guidance on

- collecting clinical and antimicrobial susceptibility data from new sources
- implementing whole genome sequencing and metagenomics to address future data needs
- improving and facilitating interpretation and use of different types of antimicrobial surveillance data for stakeholders

In the course of its work, the Working Group repeatedly noted the importance of national and state/local surveillance for foodborne illness and emphasized that the data gathered from this surveillance are critical for detecting outbreaks and identifying new vehicles for foodborne illness; monitoring the safety of the food supply; and directing risk-based food safety efforts by CDC, the Food and Drug Administration (FDA), and the U.S. Department of Agriculture (USDA). Further, the Working Group noted the recent loss of capacity at state and local levels due to broad budget cuts and underscored the need for additional resources to build on and better integrate existing surveillance systems and fill existing and emerging data gaps. The Working Group is pleased that initial funding was appropriated in 2014 to help move forward the important tasks authorized by FSMA, but continues to be concerned about the lack of attention to adequate funding levels for the programmatic efforts uniquely directed by CDC and implemented by state and local health departments to meet the enhanced surveillance requirements. Finally, the Working Group also stressed that foodborne illness surveillance and outbreak investigations to determine root causes lead to better hazard analysis and more targeted food safety controls at food production, processing, and distribution levels. The absence of this information undermines the effectiveness of preventive control programs mandated by FSMA for the food industry.

BSC/OID FSMA Surveillance Working Group 2014 Report to HHS Secretary

INTRODUCTION

This report describes the FY 2014 activities of the Food Safety Modernization Act Surveillance Working Group (FSMA-SWG) of the Board of Scientific Counselors, Office of Infectious Diseases (BSC/OID), 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 2014, the Working Group reviewed, responded to specific questions, and provided guidance regarding 1) foodborne illness and outbreaks caused by norovirus and 2) antimicrobial resistance surveillance for foodborne illnesses. The Working Group also reviewed, discussed, and provided guidance on several other CDC FSMA-related projects to enhance foodborne surveillance. For reference, a summary of selected CDC activities conducted in FY 2014 to address FSMA is included 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]

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 (http://www.cdc.gov/foodsafety/outbreaks/multistate-outbreaks/outbreaks-list.html; http://www.cdc.gov/foodsafety/fdoss/index.html). 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 policy, effectively assessing policy and 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 policy makers. 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 (http://www.cdc.gov/foodborneburden/attribution-1998-2008.html).[3] Building on the 2011 estimates, which showed that about 48 million people (1 in 6) get sick each year from food, these estimates and annual foodborne illness trend data from FoodNet (http://www.cdc.gov/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 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 are providing the necessary data to assist government agencies, industry, and other food safety stakeholders in their risk-management activities (http://www.cspinet.org/foodsafety/outbreak_report.html; http://cspinet.org/foodsafety/riskymeat.html).

CDC and the Food Safety Modernization Act (FSMA)

The Food Safety Modernization Act of 2010 (FSMA) 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 and BSC/OID member Dr. Harry Chen, Acting Secretary, Vermont Agency of Human Services, from January 2014 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, which FSMA requires, highlights the FSMA-SWG's activities and recommendations for FY 2014 and summarizes priority areas for focus in the coming year.

WORKING GROUP ACTIVITIES – FY 2014

During its third year, the FSMA-SWG met twice at CDC to consider several recent and ongoing developments in foodborne illness surveillance that are key to maintaining and improving surveillance systems. Focused discussions were held on two primary issues: 1) foodborne illness and outbreaks caused by norovirus and 2) antimicrobial resistance surveillance for foodborne illnesses. These issues and working group discussions are summarized as follows.

I. Foodborne illness and outbreaks caused by norovirus – Discussed at December 2013 FSMA-SWG meeting

Background

Although norovirus is not primarily foodborne, these viruses are the most common cause of foodborne illness in the United States, responsible for >50% (5.5 million cases per year) of all foodborne disease cases due to known agents. While the disease is rarely life threatening, the sheer numbers of cases caused by norovirus (Box 1) lead it to be ranked second in food-associated disease hospitalizations (26%) and fourth in foodborne-associated deaths (~150 annually). The virus is also likely to be a significant cause of foodborne illness of unknown etiology. In comparison with person-to-person transmission, foodborne norovirus outbreaks are less often associated with the epidemic (GII.4) strain; have less winter seasonality; affect younger individuals (<65 years of age); and tend to be less severe in terms of hospitalizations and deaths.

Most foodborne norovirus outbreaks are small, localized, and not known to be multistate in nature; associated with modest morbidity and little mortality; and usually investigated by state and local health authorities. These efforts are supplemented by and in part coordinated with three U.S. surveillance systems:

- The CDC-National Outbreak Reporting System (NORS; www.cdc.gov/nors/), which conducts epidemiologic surveillance for enteric disease outbreaks.
- CaliciNet (http://www.cdc.gov/norovirus/reporting/calicinet/), a network of federal, state, and local public health laboratories, which uses sequence-based typing to characterize norovirus outbreaks.
- The New Vaccine Surveillance Network (NVSN; www.cdc.gov/surveillance/nvsn/), which gathers active, population-based surveillance data for pediatric acute gastroenteritis at hospitals and emergency departments.

Box 1. Aided by increased epidemiological surveillance, mathematical modeling, and advances in diagnostic testing, recognition of the public health significance of human norovirus has increased dramatically over the last 15 years. Information from these sources has provided a better (and unexpected) picture of norovirus disease burden, epidemiology, and patterns of transmission:

- *Overall, 19–21 million cases of norovirus infection occur in the United States each year, causing 570-800 deaths.*
- *Viruses belonging to one genotype—GII.4—are responsible for the majority of norovirus outbreaks, most of which occur during the winter months in healthcare facilities, where they are transmitted from person to person, causing elevated rates of hospitalization and death in persons greater than 65 years of age.*
- *Noroviruses are now recognized as the leading cause of enteric disease outbreak-associated hospitalizations and deaths in the United States. According to CDC- NORS data for 2009-2010, norovirus is responsible for 65% of enteric disease outbreaks, 79% of illnesses, 41% of hospitalizations (36% due to Salmonella), and 84% of deaths associated with enteric disease outbreaks*
- *The majority of these outbreaks occur in healthcare facilities (64%), but about 19% occur in association with food service establishments*

Enhancement of surveillance systems is in progress. For example, NORS will include improved data upload and accessibility through a new system, NORSDirect. CaliciNet is in the process of certifying additional laboratories to supplement the 28 certified to date; the program is also using next-generation sequencing to better characterize and predict emerging norovirus strains. Enhanced outbreak reporting will be undertaken through NoroSTAT (www.cdc.gov/norovirus/reporting/norostat/)—the Norovirus Sentinel Testing and Tracking Network, a sentinel

surveillance network of state health departments. Of note, there is wide variability in state-based NORS norovirus reporting, with annual reporting rates ranging from a low of <0.9 to a high of >5.5 outbreaks per million population. Some states do not report at all.

Based on recent CDC surveillance reports, new information is available on the significance and dynamics of norovirus transmission through the food chain:

- Historically, molluscan shellfish, fresh produce, and ready-to-eat foods (those subject to significant human handling without a terminal heating step) have been associated with norovirus outbreaks. These categories constitute many different food items. Based on evaluation of NORS data from 2001-2008, for a large proportion of these outbreaks (56%) one or more specific foods could not be identified. For 28% of outbreaks, a complex (multi-component) food or "multiple foods" were implicated. In only 12% of cases was a "simple" (single component) food implicated.
- Among simple foods, leafy greens ranked first, followed by fruits/nuts and molluscan shellfish. In many cases, the source of the norovirus contamination of these foods was unknown, but, when identified, it occurred most often during preparation and service for the former two commodities and during production for mollusks.
- The most common venues identified for foodborne norovirus outbreaks were restaurant/deli (62%); caterer (11%); private home (10%); and banquet, grocery store, school, other (11%).
- The food handler is a key factor in foodborne transmission of norovirus. In outbreaks in which a source of contamination could be found, the food worker was the implicated source 70% of the time (www.cdc.gov/vitalsigns/norovirus/).
- The collective body of evidence suggests that norovirus contamination commonly occurs during food preparation and service rather than during production and processing—a finding which suggests that strategies to prevent norovirus outbreaks should involve modification or regulation of food preparation practices.

Many features of norovirus make it a particularly efficient infectious disease agent, highly infectious and transmissible:

- Symptomatic individuals shed virus in the feces in massive amounts (frequently $>10^6$ genome copies/g). Lower but still significant levels of virus are shed in vomitus. At the same time, infectious doses are extremely low (20-1,000 particles). A small amount of stool (for instance, 1 g) from a single infected individual can result in thousands of infectious doses.
- Infected individuals shed virus in the stool for days to weeks after resolution of symptoms, and can also shed asymptomatically. This means that individuals without apparent disease can still serve as a source of infection for others or a source of contamination for food.
- Host genetic factors influence susceptibility to norovirus. While different individuals may be susceptible to different noroviruses, every individual would likely be susceptible to one or more viruses over the course of a lifetime. Since immunity appears to be short lived (no more than a few years), and provides little cross-protection against genetically diverse noroviruses, most individuals will likely remain susceptible to norovirus infection for life.
- Noroviruses mutate rapidly, and new epidemic GII.4 strains emerge every 2-3 years, displacing previous predominant GII.4 viruses.
- There currently is no vaccine available for norovirus, although phase III trials are beginning for one formulation. Efficacy is unknown, as is the degree of cross-protection against multiple strains. It will likely be at least 5 years before a vaccine is commercially available. Periodic reformulation of the vaccine may be necessary to protect against newly emerging viruses.

Many attributes also make norovirus an efficient foodborne pathogen, with the only exception being an inability to grow or multiply in foods. Consequently, it can be difficult to prevent norovirus contamination and/or inactivate the virus if present in foods or the environment. For example:

- There is strong evidence that norovirus can persist for days to weeks on environmental surfaces; weeks to months in foods; and even years in contaminated waters.
- The virus is resistant to most commonly used food preservation methods (e.g., low temperature, extremes of pH, preservatives, drying conditions). Further, the virus shows some degree of elevated resistance to many food processes, including heat, high pressure, and ionizing radiation. It is also resistant to most sanitizers and disinfectants used at commonly recommended concentrations (e.g., ethanol, quaternary ammonium compounds, chlorine). CDC recommends the use of 1,000-5,000 ppm hypochlorite for the disinfection of contaminated surfaces, concentrations impractical for the food sector. In the United States, soap and water, not hand sanitizers, are recommended for hand hygiene to prevent norovirus.

Despite a dramatic increase in our understanding of norovirus over the last two decades, there remains an important limitation to the progress of the science. Specifically, human norovirus cannot be cultivated *in vitro*, nor is there a practical animal model for its study. Thus, there is no way to "grow" the virus, resulting in a variety of issues affecting our capacity to detect and understanding noroviruses:

- Detection must be non-culture based. The most common detection method used is reverse transcription quantitative PCR (RT-qPCR). Broadly reactive RT-qPCR methods exist, and can be effectively used on clinical samples (where virus concentration is very high). Virtually all state health departments routinely use these methods, and follow them by amplicon sequencing for strain genotyping.
- Despite the utility of RT-qPCR for virus detection, only a few routine clinical diagnostics are commercially available in the United States. In addition to technical challenges, barriers to development of commercial diagnostics include failure by patients to seek medical attention and the lack of a specific clinical treatment aside from rehydration therapy. In short, there is little incentive for formal diagnosis, which creates significant limitations for surveillance.
- Detection of norovirus in food and environmental samples is much more complicated than in stool. The virus concentrations are lower; the virus cannot be enriched (grown) to increase numbers; and sample matrices are more diverse. The general approach for detection in foods is to concentrate the virus from the sample; extract the nucleic acid; and amplify by reverse transcription PCR (RT-PCR). These issues and approaches result in a more complicated protocol, with relatively poor assay sensitivity and specificity. In the absence of cultivation, confirmation of presumptively positive samples is difficult. The International Organization for Standardization's (ISO's) certified methods have recently emerged (for bottled water, leafy greens, raspberries, and shellfish), but they are cumbersome and not widely used in the United States.
- Detection of viral RNA by RT-qPCR does not confirm that an infectious virus has been identified. Viral RNA can persist even after norovirus has been inactivated.
- In the absence of cell culture of noroviruses, it is necessary to rely on surrogate viruses that can be cultured to predict human norovirus behavior in the environment and its response to various inactivation strategies. Some of these surrogates (e.g., feline calicivirus [FCV]) do not behave in the same way as human noroviruses, but others (e.g., murine norovirus, Tulane virus) show inactivation patterns that more closely mimic human norovirus, although results should be interpreted cautiously.

Questions Presented to the Working Group and Subsequent Discussions/Guidance

1. How can norovirus illness and outbreak surveillance, investigation, and data collection be improved?

Discussion: As a function of relatively recent efforts, much more is known about foodborne norovirus disease burden and epidemiological attribution.[1-3] Yet, many unanswered questions remain that could be addressed using enhanced epidemiological systems and studies. Specific needs include

- More reliable estimates of norovirus foodborne disease burden, both epidemic and endemic
- Better characterization of how much endemic illness is attributed to foods relative to other transmission routes
- Better characterization of attribution by food type, venue, etc.
- Description of the epidemiology of foodborne norovirus illness in person/place and time.
- Understanding of how and where the virus is transmitted in the food chain to enable more focused prevention and control efforts
- More robust data on disease incidence in various sensitive subpopulations, particularly the elderly and young children
- Validated real-time indicators of community norovirus activity

Addressing all these issues is not possible using the current epidemiological systems, even with enhancements. Hence, it is necessary to prioritize resources based on the most pressing questions to be answered. These circumstances are exacerbated by the fact that the vast majority of foodborne norovirus outbreaks are small, localized, associated with modest morbidity and little mortality, and frequently not identified or reported. While CDC provides guidance for investigation of suspected foodborne disease outbreaks as well as prevention of, control of, and response to norovirus outbreaks, there is considerable variability among jurisdictions in how these outbreaks are investigated. As a result, wide variability exists in reporting rates through the NORS system. In addition, the degree and rigor undertaken in norovirus foodborne outbreak investigation and reporting is significantly dictated by state resources, which have been decreasing. Taken together, these issues currently limit the utility of outbreak surveillance data. Yet CDC, as a national agency, can aid in increasing knowledge of the epidemiology of foodborne norovirus disease by supporting the efforts of the state and local authorities, and supporting targeted studies and systems designed to answer key surveillance questions.

Guidance: The Working Group agreed that resources for foodborne norovirus surveillance be used to address pressing issues in a targeted manner. Support to state and local authorities should be provided for

- training and education on the importance of foodborne norovirus surveillance
- increased reporting
- developing more standardized outbreak investigation and reporting protocols focusing on issues such as best practices for assessing norovirus exposures, for proper sample handling and collection, and for communicating to various venues and populations

The Working Group stated that measures to strengthen existing national surveillance tools and systems should be continued, including NORS (improved data download and accessibility, NORSDirect) and CaliciNet (continued training and certification of additional states).

Resources should be provided to conduct targeted studies to evaluate the role/utility of various activities to enhance the detection of norovirus outbreaks, including

- sentinel surveillance in a few states (NoroSTAT)
- complaint-based systems
- syndromic surveillance

2. What are the utility and future prospect for norovirus testing in environmental and food samples for outbreak surveillance?

Discussion: Successful detection of virus contamination in a food can be extremely helpful. But, as described earlier, testing foods and environmental samples for norovirus contamination is very difficult. Because human norovirus cannot be cultivated *in vitro*, we rely on non-culture-based detection methods, with all their disadvantages (e.g., lack of an isolate, issues associated with viability/infectivity). This testing difficulty is exacerbated by a variety of factors including

- very low levels of virus contamination
- multiple sample matrices
- cumbersome and inefficient sample preparation steps
- residual matrix-associated inhibition
- poor assay sensitivity and specificity
- lack of standardization

Consequently, both false-positive and false-negative results are common. Confirmation by sequence analysis is difficult when virus contamination levels are low. Collection of environmental samples during an outbreak investigation might help in managing norovirus contamination, particularly on environmental surfaces.

Guidance: The Working Group concluded that while advancements in testing may soon present different options, at present, routine testing of foods for norovirus contamination is currently not feasible or advisable. They advised that if testing is done, results should be interpreted with caution. In some situations, food-testing data—as well as testing of environmental samples—may be useful, particularly in support of prevalence studies and outbreak investigations.

3. How can we improve the data collected to inform source attribution?

Discussion: Recent CDC publications have shed more light on the most important "simple foods" associated with norovirus transmission.[3] However (aside from molluscan shellfish), very little is known about how and when those foods become contaminated (i.e., pre-harvest, harvest, manufacturing, retail, food preparation). In addition, little is known about the prevalence of virus contamination. CDC data also show that the vast majority of outbreaks are caused by complex or combined foods/dishes served in retail-type establishments. In these cases, the food component from which the contaminant originated is almost always unknown. And while it is clear that the food handler plays a critical role in contamination, the relative importance of certain food-handling behaviors and practices is also unknown. Yet, this sort of attribution information is crucial in implementing control measures and/or regulatory actions. More research is needed to identify the factors that most significantly impact the risk of norovirus contamination and disease along the farm-to-fork chain.

Guidance: The Working Group stated that U.S. Department of Health and Human Services (HHS) agencies should work together to design and implement focused studies to answer key questions about foodborne transmission of norovirus. These answers can be used to improve attribution estimates and identify targeted mitigation strategies. The most pressing issues for such studies include

- Environmental assessments to determine
  - Points in the food chain at which a product is contaminated (i.e., production, manufacturing, food handling)
  - The proportion of contamination that occurs pre-retail
  - The role of aerosolization of vomitus in contamination of foods
- Epidemiological attribution studies to learn more about
  - Sources of norovirus contamination of foods

- Implicated foods, particularly for multiple-vehicle outbreaks
- Intensive investigation of outbreaks in high-risk settings to identify contributing factors and potential control measures

The Working Group agreed that in-depth studies should be undertaken in a few states to assess the proportion of norovirus illness that is due to contaminated food or contact with ill food workers in retail settings. The goal is to identify the riskiest foods and the role of food preparation techniques (e.g., food worker hygiene, sanitation and disinfection) and food characteristics on outbreak risk. To achieve this goal, it will be necessary to link multiple foodborne illness surveillance systems (e.g., CaliciNet and NORS).

4. What role would a norovirus vaccine (and better sanitizers/disinfectants) have in controlling foodborne disease, and which groups should be targeted? What are the implications of better controls for surveillance?

Discussion: The Working Group was briefed on two potential norovirus prevention and control strategies: improved sanitizers/disinfectants and vaccination. A synopsis of the current U.S. scientific consensus on these strategies is provided in the norovirus background section. Norovirus is recalcitrant to most available sanitizing and disinfecting agents when they are used at manufacturer recommended or regulated concentrations. Improved anti-norovirus surface compounds could theoretically reduce disease burden by preventing transmission via fomites. The availability and use of hand sanitizers with specific anti-norovirus activity could have a major impact on person-to-person (and perhaps foodborne) transmission. Clearly, many sectors could be positively impacted (e.g., healthcare, schools, cruise lines, and retail food establishments), but development of new products faces a number of issues. Development costs are high for a historically low-margin industry. A major issue involving hand sanitizers is the requirement for completion of the FDA New Drug Application process to claim anti-norovirus efficacy, which is cost-prohibitive. Surface disinfectants are easier to license because they can claim anti-norovirus activity based on their action against the cultivable surrogate FCV, but in most inactivation experiments in the laboratory, FCV does not behave in the same manner as human norovirus. The efficacy of hand sanitizers against norovirus needs to be more clearly established.

Vaccines are in development and are currently entering Phase III trials. To date, their short- and long-term efficacies are not well established. It will likely take at least 5 years before a vaccine might be commercially available. Challenges to vaccine development and efficacy include genetic drift and cross-protection against multiple strains, which potentially may require periodic (2-3 years) reformulation. Vaccination would likely be recommended for subpopulations at risk for more severe disease (e.g., the elderly), for healthcare staff, and for food workers, but may also be implemented as a routine childhood immunization.

Guidance: The Working Group stressed the need for continued research to develop and license sanitizers, disinfectants, and vaccines with established efficacy to control norovirus. As these products develop, further study will be necessary to identify specific risk groups to target for these prevention and control efforts.

Conclusions

Norovirus is highly infectious and transmissible, persistent in the environment, and resistant to virtually all control measures used in food processing and sanitation/disinfection. Epidemiological surveillance remains critical to improving our understanding of foodborne transmission of norovirus, and identifying ways to prevent it. The Working Group's deliberations and conclusions were based on current knowledge. Members stressed that implementation of their guidance would help reduce the burden resulting from this leading cause of foodborne disease.

II. Antimicrobial resistance surveillance for foodborne illnesses – Discussed at May 2014 FSMA-SWG meeting

Background

Recent trends in the resistance of foodborne pathogens to antibiotics used currently and in the recent past to treat serious foodborne infections, have raised significant questions and concerns of public health importance (Appendix 3). CDC recently reported on the overall danger to public health from antibiotic resistance of 17 pathogens, including 4 transmitted commonly through food, with 2 having animal reservoirs and 2 human reservoirs.[4] CDC estimated that each year, approximately 441,000 antibiotic-resistant illnesses and 66-70 deaths occur in people ill from infections caused by the enteric pathogens *Campylobacter*, non-typhoidal *Salmonella*, *Salmonella* Typhi, and *Shigella* (Appendix 3, Table 3.1). The CDC report confirmed that the maintenance and protection of a number of antibiotics that are effective in treating human foodborne illness can now be considered under threat, and that conducting surveillance for antimicrobial resistance of foodborne pathogens is essential for formulating evidence-based policies that assure protection of existing medically important antibiotics, implementing practices that ensure best use of existing antibiotics, and identifying needs in the development of new ones.

NARMS is the only national public health surveillance program that monitors the susceptibility of enteric bacteria to antimicrobial agents of medical importance to help assess the impact of veterinary antimicrobial use on human health. To achieve this mission, NARMS conducts the following[5]:

- monitors trends in antimicrobial resistance among enteric bacteria activities from humans (overseen by CDC), retail meats (overseen by FDA), and food production animals at slaughter (overseen by USDA/Food Safety and Inspection Service [FSIS])
- disseminates timely information on antimicrobial resistance in pathogenic and commensal organisms to stakeholders in the United States and abroad to promote interventions that reduce resistance among foodborne bacteria
- conducts research to better understand the emergence, persistence, and spread of antimicrobial resistance
- provides data that assist FDA in making decisions related to the approval of safe and effective drugs for animals.[6] FDA coordinates the overall integrated tri-agency program, which is based on the use of common test platforms, standardized test methods and interpretations, standardized agent panels, and sharing of test results of strains.

In annual agency-specific reports published online[7,8] (2012 most current by CDC as of the May 2014 FSMA-SWG meeting), NARMS reports trends in the resistance to antimicrobials of human and veterinary medical importance for two important enteric pathogens—non-typhoidal *Salmonella* (across all species and retail meats) and *Campylobacter* (in humans, chickens, chicken breast meat, and ground turkey), and for two indicator bacteria, generic *Escherichia coli* and *Enterococcus,* in retail and food animal isolates (to detect emerging resistance and resistance genes that could potentially be transferred to pathogenic bacteria). NARMS also tests human isolates of the pathogens *Shigella, Salmonella* Typhi, *E. coli* O157, and *Vibrio* (other than *V. cholerae*). More recent reports publish findings for the previous 10 years only.

The reports describe sampling methods; overviews of findings with a focus on new findings and highlights for the year of report; test results for all pathogens, including resistance to individual agents and to multiple antimicrobials; patterns of antimicrobial resistance and changes in resistance patterns observed; detailed tables and graphs for susceptibility test results by pathogen (including common *Salmonella* types) and year; annual resistance percentages for 10 years; and minimum inhibitory concentration (MIC) distributions for isolates from the current year. CDC recently enhanced its annual report to provide online interactive data displays, which allow users to visualize resistance trends by pathogen and antimicrobial agent. Since 2003, NARMS has jointly

published an Annual Executive Report, which presents data in an integrated format, allowing readers to easily compare data from different sources, and also incorporates online interactive data display features.[8]

Use of NARMS data to protect food safety

FDA has used data from NARMS to change how antimicrobials are used in agriculture, most notably through withdrawing the approval of fluoroquinolones for use in poultry; prohibiting extra-label use of fluoroquinolones and cephalosporins in cattle, swine, chickens, and turkeys; and issuing the agency's final guidance on the judicious use of medically important antimicrobials in food-producing animals.[6] CDC and USDA/FSIS have used NARMS data to investigate foodborne outbreaks. Non-governmental organizations (e.g., Center for Science in the Public Interest) have used NARMS data in conjunction with other data to conduct their own analyses to advocate for public health strategies and action (e.g., antibiotic resistance associated with foodborne outbreaks).[9] CDC has worked with partners to use NARMS data, linked to other databases (e. g., NORS and PulseNet [http://www.cdc.gov/pulsenet/]), to conduct attribution analyses to better understand the sources of enteric infections. Details are presented in Appendix 3.

Previous reviews of and recommendations to improve NARMS

The Working Group acknowledged and concurred with the findings of several previous reviews conducted of NARMS, which documented strengths and areas for improvement (Appendix 3, Table 3.2). The Working Group observed that several of the recommendations made during these previous reviews had been addressed; however, in addressing the questions posed by CDC, the Working Group identified additional improvements to advance the effectiveness and usefulness of NARMS (see sections below).

Questions Presented to the Working Group and Subsequent Discussions/Guidance

1. Questions on use of NARMS data

In foodborne outbreak investigations

- Would it be useful to further improve linking of outbreak isolates with antimicrobial susceptibility testing data?
- Do NARMS data provide enough information on the prevalence and trends in antimicrobial resistance among foodborne pathogens isolated from humans?
- Are there changes in the current NARMS practices for submission of isolates from humans that should be considered?
- Are there supplemental/better/alternative sources of data on antimicrobial resistance among foodborne pathogens isolated from humans that could/should be used?

In understanding sources of enteric infections

- How can CDC further enhance the use of NARMS antibiotic susceptibility data, obtained from human sporadic and outbreak cases, to understand sources of enteric infections?
- How can information be collected regarding clinical outcomes of illnesses associated with antimicrobial resistant foodborne pathogens?
- How otherwise, can human isolate data collection and analysis be improved?

Discussion and Guidance for improving use of NARMS data by stakeholders

The Working Group identified several enhancements to NARMS that, if implemented, would enhance and/or increase the use and usefulness of its data by a growing number of stakeholders:

- Clarifying and providing standardized definitions for antimicrobial resistance
- Identifying new sources of data (e.g., clinical outcomes, antimicrobial susceptibility test results)
- Increasing sample size of human and retail meat samples/isolates
- Collecting food, travel, and other exposure data from patients whose cultures yielded isolates
- Comparing information on outbreak strain isolates with NARMS antimicrobial testing results
- Further enhancing the linkage of NARMS data to other relevant databases (e.g., NORS, FoodNet, PulseNet)
- Conducting epidemiologic studies to meet information needs of stakeholders; for example,
    - Studies of foodborne outbreaks yielding isolates with mixed resistance patterns
    - Continuing and enhancing attribution analyses to identify sources of enteric infections
    - Linking antimicrobial resistance and severity of human illness (including patient treatments and failures, hospitalizations and deaths), clinical risk factors, and host susceptibility
    - Assessing the public health impact of eliminating use of growth-promoting antimicrobials in food animals
    - Studying contamination versus pathogen load in organic foods
- Collecting and linking additional environmental health information to NARMS data
- Increasing use of whole genome sequencing as resources allow
- Augmenting the already strong collaborations among federal agencies and with state partners, private healthcare systems, industry, and other stakeholders

The Working Group identified several approaches that could be considered to achieve the enhancements listed above. It was noted that additional resources would be required to explore how best to access new sources of data (e.g., the NARMS program does not request submission of epidemiologic data from state health departments), to conduct antimicrobial susceptibility testing, to fulfill IT requirements, to manage data, and to build increased analytical capacity at state levels. Approaches discussed include the following:

- Explore new sources of and resource requirements for the collection of clinical and antimicrobial susceptibility data:
    - State public health and medical care systems, including hospital and clinical laboratory/data systems
    - Electronic health records when available; for meaningful use of these data, case definitions and harmonizing or taking different testing methods into account would be needed
    - Managed care reporting systems (Vaccine Safety Datalink [VSD; http://www.cdc.gov/vaccinesafety/Activities/VSD.html], the National Healthcare Safety Network's [NHSN; http://www.cdc.gov/nhsn/about.html] Antimicrobial Use and Resistance Module)
    - Health information exchanges and other data sources associated with the Patient Protection and Affordable Care Act
    - Health insurance claims data (it was noted that these data likely will be expensive and designed for billing, rather than for research, but with additional, appropriate resources, they could fill important information gaps)
    - Death certificate information (e.g., hospitalizations, deaths, and other information)
    - Regulatory food testing data, including the Electronic Laboratory Exchange Network (eLEXNET), and FDA food-related import data

- Explore how primary antimicrobial susceptibility testing could be best conducted at the state or clinical laboratory level, with results and accompanying demographic and other data sent to CDC (following the model of PulseNet), and identify additional resources that would be required.
- As resources permit, increase whole genome sequencing of every isolate and, with accompanying phenotypic and epidemiologic information on isolates, use in comparisons and linkages between environmental, food, and clinical outbreak isolates. These comparisons may help prioritize outbreak investigations and public health actions.
- Explore how antimicrobial susceptibility testing could be conducted in food production animals--preharvest/on-the-farm.

2. Questions on managing, sharing, integrating, and reporting NARMS data

- How can data integration and reporting/sharing be improved?
- Does reporting of susceptibility data from outbreaks meet data requests/needs of public health agencies and the public?

Discussion and Guidance on managing, sharing, integrating and reporting NARMS data

The Working Group discussed how to improve and facilitate interpretation and use of different types of antimicrobial resistance surveillance data for a growing number of stakeholders. They suggested greater emphasis be given to

- Ensuring messaging is focused on providing information for decision making, including influencing policy formulation at national and societal levels and decision making by consumers. Messaging will need to evolve over time to accurately put risks into context for different audiences and stakeholders. For example, messages might explain the relationship between NARMS data and the role of antibiotic resistance as a threat to modern medicine; convey to consumers the potential risks to individual and family health; and provide guidance on food purchases (e.g., providing the definition of antibiotic-free meat, considerations in determining whether to buy these products and whether these products should be promoted), on food preparation, and on the possible need and timing of when to seek medical attention in the event of illness.
    - Ensuring messages convey top-level scientific findings in plain language, communicating the risk of pathogens and resistance, including virulence to different groups.
    - Developing communications that reflect the urgency of concern (e.g., potential for doubling or tripling of levels of antimicrobial resistance and associated impacts).
- Identifying different stakeholders to determine information needs, tailor reports, and overall facilitate greater use of NARMS data
    - NARMS stakeholders range from those with societal/population-based responsibilities, to individual consumers, at federal, state, local, and tribal levels. For example, the list of stakeholders includes policy makers and program decision makers; public health officials, clinical medicine practitioners/health care providers, and other science officials; industry, including food producers, processors, retail chains, restaurants, and others along the food chain; drug sponsors; farmers; regulators; consumers and the public; and academic researchers.
- Actively engage with different stakeholders (e.g., in strategic planning exercises, needs assessments) to identify their current and future information needs to inform decision making and policy formulation. Learning what new information is needed beyond that provided currently will be critical to ensure the system collects, analyzes, interprets, and reports results in a way that will facilitate data use.
    - For some stakeholder groups, incentives (e.g., for industry) and additional resources (e.g., for state partners) will be required to ensure engagement
    - As needed, provide education and or guidance to different stakeholder groups on accessing, interpreting, and using information. Use outbreaks as learning opportunities for appropriate

interpretation and use of NARMS data by industry, the public health sector, and consumers. State and local outreach will be needed.
    - Regulatory stakeholders have identified the need to reassess and modify NARMS as needed to align with regulatory changes (cross-connecting NARMS surveillance data with regulatory needs and responsibilities) and to refine regulatory approaches (e.g., provide updated guidance on judicious use of antibiotics).
- Providing reports on a quicker timeline, balancing the need to "go live" with time needed to obtain information for annual reports

3. Questions on Global Implications of NARMS data

- How can global utilization of human antimicrobial resistance data be improved?

Discussion and Guidance: The Working Group agreed that sharing and utilizing human antimicrobial resistance data with international partners, based on standardized methods and reporting, is essential for effectively confronting this growing global problem. They commended NARMS support of the WHO Advisory Group on Integrated Surveillance of Antimicrobial Resistance (AGISAR) and increasing collaboration with the Canadian Integrated Program for Antimicrobial Resistance Surveillance (CIPARS). They mentioned WHO's network of hospitals—Health Promoting Hospitals Network—as a potential template for additional sources of data for NARMS, and commented on the sharing of whole genome sequencing among global partners, which is already providing useful, higher quality data to support global monitoring of levels, patterns, and trends of antimicrobial resistance.

4. Future Directions

The Working Group concluded its discussions by looking ahead. There will be new stakeholders and a need to learn about and meet their information requirements. Collaborations and partnerships will remain at the core of successful surveillance and research efforts to confront antimicrobial resistance of foodborne pathogens. In particular, the roles for industry, including food animal production groups, in conjunction with the public and other private sector partners, were seen as areas of growing importance. The Working Group suggested looking at industry-public health collaborations in Europe for lessons of interest to the United States. Addressing challenges would provide opportunities to advance understanding of levels of, patterns in, changes to, trends in, and sources of antimicrobial resistance of foodborne pathogens.

- **Questions: With respect to antimicrobial resistance pathogen testing, how do we prepare for the transition to culture-independent diagnostic methods and whole gene sequencing (and possible loss of pure cultures)?**

Discussion and Guidance: In particular, as the scientific diagnostic testing community continues to move fairly quickly to culture-independent methods and isolates become unavailable, NARMS will need to adapt to new technologies. Beyond whole genome sequencing methods are the challenges and immense opportunities that studies of the enteric microbiome and applications of metagenomics will bring. Although much is still unknown, some level of phenotypic testing and a better understanding of the genotype/phenotype connection will always be needed.

The Working Group suggested that a sentinel network for a few sites could be established to continue collecting and using isolates and culture-based methods, while the majority of the system eventually transitions to culture-independent methods.

With sufficient resources, whole genome sequencing has the potential to serve as the single assay of NARMS surveillance and supplant existing multiple methods that include classical serotyping, PFGE, and other strain typing methods, in vivo antimicrobial susceptibility testing, and piecemeal PCR gene detection and plasmid typing. Whole genome sequencing would also provide capability in the conduct of genome/nucleotide surveillance and would provide virulence profiles, molecular phage typing, markers for source attribution, better understanding of emerging trends, and cost savings.

Given the importance of antimicrobial resistance surveillance, and the challenges and opportunities ahead, the Working Group closed the discussion by recommending consideration of additional strategic planning among partners and stakeholders to identify priority information needs, activities, and resources that will keep NARMS at the forefront in providing data that are needed to effectively address the threat of antimicrobial resistance.

RESOURCES

The FSMA-SWG acknowledged that additional resources are required to evaluate the effectiveness of FDA voluntary guidance for judicious use of antibiotics by industry to reduce antimicrobial resistance, and to build on and better integrate existing surveillance systems and fill existing data gaps. There is also a critical need to build capacity at the state and local levels that have experienced severe losses in capacity, including hiring experienced foodborne epidemiology, laboratory, and environmental personnel. This effort includes the need to engage schools of public health to train the existing workforce and the next generation of state and local food safety public health scientists and practitioners. The Working Group is pleased that initial funding was appropriated in 2014 to help move forward the important tasks authorized by FSMA, but continues to be concerned about the lack of attention to adequate funding levels for the programmatic efforts uniquely directed by CDC and implemented by state and local health departments to meet the enhanced surveillance requirements.

NEXT STEPS

To provide additional guidance on these and other emerging priority areas, the Working Group will devote time at future meetings to explore priority areas in more depth and provide associated advice for future actions. These reviews will include expert presentations on current status and progress of each priority followed by a discussion on possible enhancements to improve foodborne illness surveillance in that area. Since six new members will join the Working Group in FY 2015, some of the group's time will be devoted to reviewing progress in addressing previous priority areas in addition to examining new areas in more depth during FY 2015. These topics include a review of progress in addressing several major priority areas, including

- Improving governmental coordination and integration (e.g., attribution, multistate outbreak investigation, whole genome sequencing, listeria project, etc.),
- Evaluating and improving foodborne illness surveillance tools and systems (e.g., SEDRIC multistate outbreak investigation software, CIFOR guidelines and tool kit, Integrated Food Safety Centers of Excellence, FoodCORE performance measures, addressing "orphan" diseases such as cyclosporiasis, vibrio infections, toxoplasmosis, cryptosporiasis)
- Enhancing external collaboration and communication
- Addressing new areas such as enhancing surveillance of environmental contributing factors and antecedents

In conclusion, the Working Group believes that important progress has been made in the implementation of FSMA, but that significant gaps remain that impact the quality of foodborne illness surveillance data. Ensuring states have the staff and resources to fully investigate outbreaks by identifying both the food and pathogen responsible and reporting these data to NORS, along with improvements in the integration and sharing of data, are prerequisites to the formulation, implementation, and evaluation of science-based disease prevention and control policies and to an improved overall integrated food safety system.

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Appendix 1: Surveillance Working Group

Working Group Members

Meetings held in December 2013 and May 2014

BSC Representative Members:

- Chair, thru December 2013: James Hadler, MD, MPH – Associate Professor, Yale University
- Chair, since January 2014: Harry Chen, MD – Acting Secretary, Vermont Agency of Human Services
- Member, since May 2014: Kristy K. Bradley, DVM, MPH - State Epidemiologist and State Public Health Veterinarian, Oklahoma State Department of Health

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:

- Robyn Atkinson, PhD, HCLD – Association of Public Health Laboratories
- Thomas S. Dunlop, MPH, REHS – National Environmental Health Association
- Timothy Jones, MD – Council of State and Territorial Epidemiologists
- Heidi Kassenborg, DVM, MPH – Association of Food and Drug Officials
- Mary Currier Mallette, MD, MPH – Association of State and Territorial Health Officials
- Joseph Russell, MPH, RS – National Association of County and City Health Officials
- John Tilden, Jr., MS, DVM, MPH – National Association of State Departments of Agriculture

Consumer Partner Members:

- Caroline Smith DeWaal, JD – Center for Science in the Public Interest
- Sandra Eskin, JD – The Pew Charitable Trust
- Barbara Kowalcyk, PhD – Center for Foodborne Illness Research and Prevention

Industry Partner Members:

- Catherine Adams Hutt, PhD, RD – National Restaurant Association
- Russell S. Flowers, Jr., PhD – Mérieux NutriSciences Corporation
- Joan Menke-Schaenzer – ConAgra Foods, Inc

Academia Partner Members:

- Craig Hedberg, MS, PhD – Professor, University of Minnesota
- Lee-Ann Jaykus, PhD – Professor, North Carolina State University
- John Glenn Morris, Jr., MD, MPH&TM – Professor, University of Florida

Appendix 2: Selected CDC Accomplishments in Implementing FSMA Surveillance Requirements

The Food Safety Modernization Act (FSMA) recognizes that robust foodborne illness surveillance data are needed to inform prevention efforts. FSMA directly links surveillance with prevention and highlights the need for stronger partnerships at the local, state, and federal levels. FSMA directs the Centers for Disease Control and Prevention (CDC) to

I. Improve governmental coordination and integration
II. Evaluate and improve foodborne illness surveillance systems
III. Enhance external stakeholder collaboration

CDC supports the implementation of FSMA in many ways. In fiscal year (FY) 2014, CDC increased the support for existing infrastructure for laboratory, surveillance, and outbreak response activities, while continuing the activities of the five Integrated Food Safety Centers of Excellence (CoEs).

The summary below highlights selected CDC accomplishments that support FSMA. The majority of these activities build upon existing infrastructure and labor capacity, but some are new in FY 2014 and exclusively address CDC's surveillance responsibilities under FSMA.

I. Improving Governmental Coordination and Integration

Food safety is a shared initiative among local, state, and federal public health partners. FSMA recognizes that strong coordination among partners is essential to rapidly detect food safety problems, determine where issues are occurring, and identify and use effective strategies to prevent foodborne illness. CDC is working to strengthen coordination and data sharing across government agencies and with external partners.

A. Coordinating federal, state, and local foodborne illness surveillance systems

- ***Multistate foodborne illness outbreak investigations***

  In FY 2014, CDC supported federal, state, and local health agencies to monitor between 15 and 40 clusters of potential foodborne illness per week, resulting in approximately 10 major multistate outbreak investigations (Table 2.1).

  CDC continues to improve foodborne illness and outbreak metrics through the Epidemiology and Laboratory Capacity for Infectious Diseases (ELC) Cooperative Agreement sites and by working with the Council to Improve Foodborne Outbreak Response (CIFOR) to use performance measures and associated targets as guidelines for states to use in their outbreak investigations. The council serves many professional organizations focused on state and local health department activities.

Table 2.1. Selected Multistate Foodborne Illness Outbreaks, United States, FY 2014*

Pathogen	Distribution	Vehicle
Cyclosporiasis	133 illnesses reported from 1 state	Cilantro
Salmonella Branderup	4 illnesses reported from 4 states	Nut butter
Salmonella Newport and Hartford	31 illnesses reported from 16 states	Organic sprouted chia powder
Escherichia coli O121	19 illnesses reported from 6 states	Clover sprouts
E. coli O157:H7	12 illnesses reported from 4 states	Ground beef
Listeria monocytogenes	8 illnesses reported from 2 states	Roos Foods dairy products
Salmonella Heidelberg	9 illnesses reported from 1 state	Mechanically separated chicken at a correctional facility
Multidrug-resistant *Salmonella* Heidelberg	634 illnesses reported from 29 states and Puerto Rico†	Foster Farms chicken
Salmonella Stanley	17 illnesses reported from 3 states	Raw cashew cheese
E. coli O157:H7	33 illnesses reported from 4 states	Ready-to-eat salads

***Pathogens listed in chronological order of outbreaks**
†Data through 09/12/2014

- ***CDC support of FDA implementation of FSMA***

  CDC works closely with the U.S. Food and Drug Administration (FDA) to support FSMA implementation efforts by providing expert participation in a number of FDA-led activities and workgroups. These efforts include

  - **Participating in the National Agriculture and Food Defense Strategy Interagency Workgroup.** The workgroup consults with FDA to assist in U.S. Department of Health and Human Services (HHS) clearance of the draft National Agriculture and Food Defense Strategy, which also includes an implementation plan and a coordinated research agenda.

    – FSMA Section 108 directs the development of a National Agriculture and Food Defense Strategy, where FDA; the U.S. Department of Agriculture (USDA); the Department of Homeland Security; the Environmental Protection Agency; CDC; and state, local, and tribal health authorities work together to protect the food supply from hazards that might be intentionally added to food in the United States.

  - **Serving on the Advisory Committee to the FDA Rapid Response Team (RRT) network.** The RRT network, in collaboration with FDA and currently operating in 18 states, provided an update on

CDC-related food safety activities at its annual meeting in November 2013. In February 2014, representatives presented on RRT activities at a CDC seminar. Representatives continue to present on CDC's outbreak investigation teams and protocols during monthly RRT calls. (FSMA Sections 202, 205[c], and 209)

- **Contributing to the FDA-led Biennial Report to Congress on the Food Emergency Response Network.** This report was submitted in November 2013 in accordance with FSMA Section 202[b].

- **Co-authoring a chapter led by colleagues from FDA on surveillance in the draft FSMA Biennial Report.** This chapter

  - Reviews previous food safety programs and practices
  - Outlines the success of those programs and practices
  - Identifies future programs and practices
  - Includes information related to matters described in FSMA Section 110[a] (2)

- **Participating in the Food Safety Research Report Interagency Work Group.** This workgroup developed a joint food safety and food defense research plan and report (FSMA Section 110[g]).

- **Collaborating with FDA to prepare for the biennial Conference for Food Protection.** CDC is providing expert consultation on questions related to the revision of the *Food Code*, and participated in the biennial meeting held in August 2014.

- **Serving on the FDA-led Partnership for Food Protection (PFP) Governing Council.** Three representatives from CDC participated in the 50-state PFP meeting in August 2014. The PFP supports FSMA Section 205(2)[c], Improving Food Safety and Defense Capacity at the State and Local Level, Subparagraphs (1)(A-F).

- **Inviting active participation by FDA representatives in the Integrated Foodborne Outbreak Response Management (InFORM) Meeting.** Held in November 2013, the meeting was tailored to public health and regulatory officials involved in foodborne outbreak response activities. Laboratorians, epidemiologists, and environmental health/regulatory personnel involved in foodborne and enteric disease outbreak responses at state, federal, and national levels attended the meeting. (FSMA Section 205(2)[c])

- ***Cholera and Other Vibrio Illness Surveillance (COVIS)***

  In FY 2014, CDC continued to oversee the COVIS electronic database as well as

  - Worked with states to improve seafood traceback information and to collect the exposure history of all cases
  - Investigated all potential clusters for possible common source food vehicles

- Developed a spreadsheet on SharePoint for states to record traceback information in real time to aid in early outbreak detection

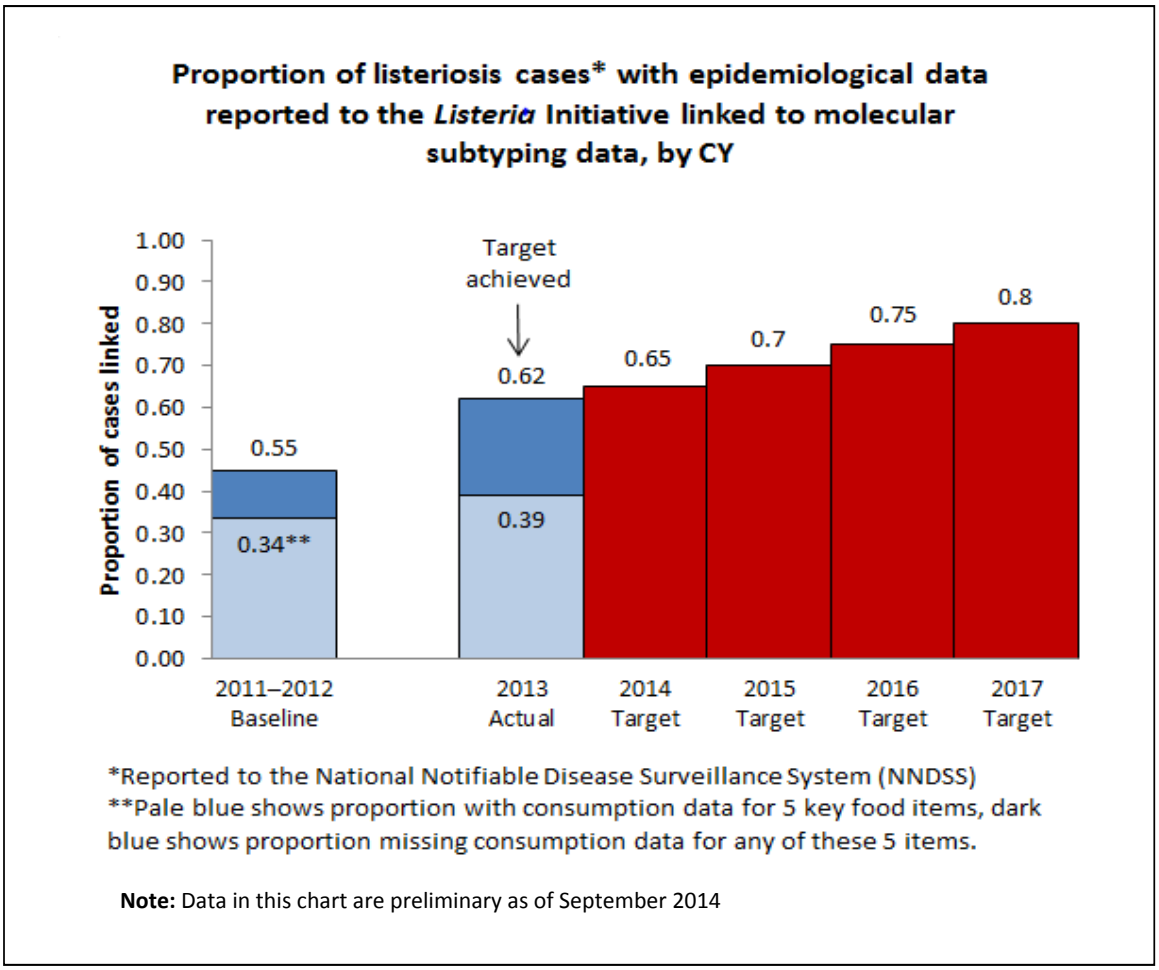
- Facilitated a national workgroup of foodborne epidemiologists to improve communication across states to aid in outbreak investigations and tracebacks

COVIS documented the emergence of a new strain of *Vibrio parahaemolyticus* in the Atlantic Ocean.[1]

- ***Listeria Initiative***

To better detect and investigate illness clusters, CDC continues to work with states to identify ways to improve the reporting of epidemiologic and laboratory data in a timely manner. In FY 2014, each state was notified of recent uploads of *Listeria* isolates to PulseNet from their state on a weekly basis to increase the percentage of isolates that had linked epidemiological data. These efforts led to improvements in *Listeria* reporting during calendar year 2013 as indicated by increases in the proportion of all listeriosis cases with linked epidemiologic and laboratory data (Figure 2.1).

Figure 2.1. Proportion of listeriosis cases* with epidemiological data reported to the *Listeria* Initiative linked to molecular subtyping date, by calendar year



Note: Data in this chart are preliminary as of September 2014

- **CDC's Advanced Molecular Detection (AMD) initiative** provided funding to improve the integration of epidemiologic exposure data with whole genome sequencing (WGS) to better detect and solve outbreaks. Specific approaches included

  - Building an epidemiologic analysis application within BioNumerics, the software system used for WGS-based surveillance to identify foods possibly associated with illness clusters using point-and-click analyses

  - Hiring an epidemiologist to aid states with open-ended interviewing during cluster investigations and building a web-based data entry system for the collection of *Listeria* data from states

  - Disseminating cluster investigation information to states through SEDRIC, the System for Enteric Disease Response, Investigation, and Coordination (a web-based platform developed by CDC and Palantir Technologies)

  As a direct result of the WGS project, a few illnesses were found to be associated with products that were then recalled. Pulsed-field gel electrophoresis (PFGE) alone would have likely missed linkages between illnesses and food products. Several of the foods implicated (stone fruits, bagged lettuce, and bean sprouts) had never been identified as *Listeria* vehicles.

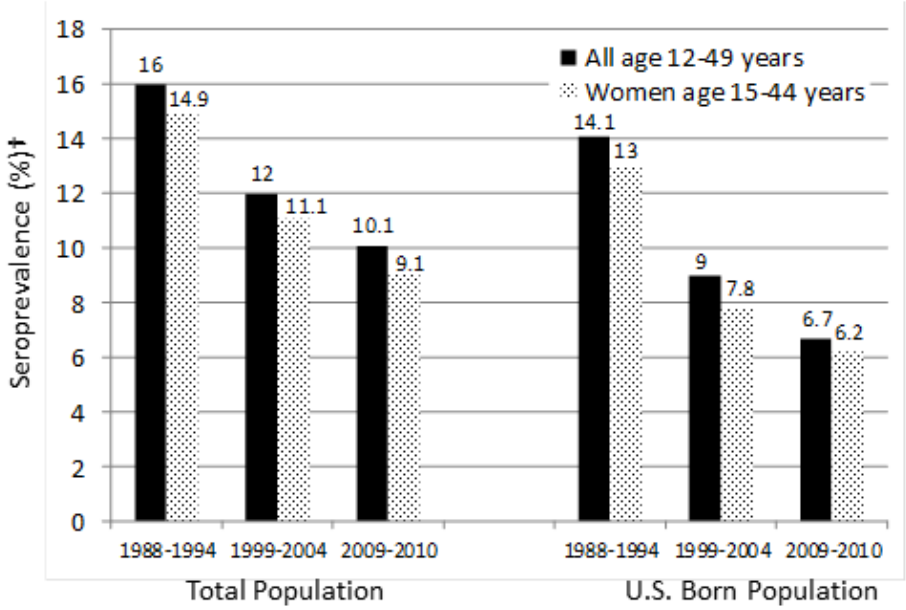
- ***Trichinellosis surveillance***

  CDC published a summary of trichinellosis surveillance data from 2008–2012 in a *Morbidity and Mortality Weekly Report* (*MMWR*) *Surveillance Summary*, which was accepted for publication in FY 2014.

- **Toxoplasma gondii *sero-surveillance***

  In 2014, CDC conducted *Toxoplasma gondii* sero-surveillance using serum samples from the 2011–12 National Health and Nutrition Examination (NHANES) Survey. This survey was a collaboration among CDC's Division of Parasitic Diseases and Malaria (DPDM), Center for Global Health, and the National Center for Health Statistics' Division of Health and Nutrition Examination Surveys. The 2009–10 *Toxoplasma* sero-prevalence data were compared with past NHANES *Toxoplasma* sero-prevalence data and were published in 2014 to visualize basic trends in a timely manner. Additional data from 2011–12 and 2013–14 are required to fully stratify the data for demographic groups and estimate the annual incidence of *Toxoplasma gondii* in various groups by gender. Figure 2.2 illustrates basic surveillance trends in the reduction of the prevalence of *Toxoplasma gondii* infections in the United States.

Figure 2.2. *Toxoplasma gondii* age-standardized antibody seroprevalence trends, United States*



*Jones JL, Kruszon-Moran D, Rivera H, Price C, Wilkins PP. *Toxoplasma gondii* seroprevalence in the United States 2009–2010 and comparison with the past two decades. Am J Trop Med Hyg 2014;90:1135–9.

†P<.001 linear trend for all series. Age-adjusted to 2000 Census population.

- ***Multi-agency collaboration on real-time WGS integrated surveillance for foodborne illness and pathogens in the United States***

  In FY 2013, CDC, FDA, the National Institutes of Health (NIH), and USDA/Food Safety and Inspection Service (FSIS) collaboratively launched a nationwide demonstration of real-time whole genome (WG)-based national surveillance for *Listeria monocytogenes* infections. This effort, reported first in the FY 2013 annual report, continued to mature during FY 2014. For the first time, partner laboratories are uploading WG sequences obtained from human, food, and environmental isolates collected for foodborne disease surveillance by CDC and food and environmental pathogen surveillance by FDA and USDA/FSIS in real time (defined as < 1 week from isolate receipt) into a public database at NIH/National Library of Medicine/National Center for Biotechnology Information.

  In addition to the WG sequences of isolates, a minimal set of related metadata, essential for the interpretation and use of genomic information, are uploaded with WG sequence data. All data are immediately available to federal, state, and local public health and regulatory agencies. With the exception of a subset of clinical isolate metadata, most data are also immediately accessible to the public, including the food industry, academia, and consumers. The subset of metadata that is not available could result in inadvertent disclosure of private patient information, which is withheld in compliance with state and federal privacy and confidentiality laws and formal data-sharing agreements between CDC and state PulseNet laboratories.

  CDC, FDA, USDA/FSIS, and state and local partners have begun, on an experimental basis, to successfully use WGS data to investigate foodborne outbreaks caused by *Listeria monocytogenes*,

Salmonella, and Shiga toxin-producing *Escherichia coli* (STEC). This integrated surveillance platform is helping to identify sources of foodborne outbreaks in a timely manner, which is essential for the implementation of public health and regulatory actions to stop outbreaks as soon as possible.

- ***FoodNet surveillance***

  CDC, FDA, USDA/FSIS, and 10 state health departments participate in the Foodborne Diseases Active Surveillance Network (FoodNet) and have continued their collaboration to provide critical data[2–8] for policymakers, the scientific community, and the public. This collaboration

  - Published an April 2014 *MMWR* article with preliminary data from 2013 and featured the data on the incidence and trends of infection with pathogens transmitted commonly through food on the FoodNet website.
  - Updated data for the monitoring of Healthy People 2020 goals related to the incidence of *Campylobacter, Listeria, Salmonella*, STEC O157, *Vibrio*, and *Yersinia* infections. FoodNet also monitored the incidence of hemolytic uremic syndrome and participated in a Healthy People 2020 progress review.
  - Continued to provide quarterly reports on the incidence of *Salmonella enterica* serotype Enteritidis to support the HHS High Priority Health Goal of reducing foodborne illness in the population through a decreased rate of 1.9 cases of *Salmonella* Enteritidis illness per 100,000 by December 2015.
  - Linked data between multiple surveillance systems:
    - FoodNet and National Antimicrobial Resistance Monitoring System (NARMS)—linked for 2004–2013
    - FoodNet and COVIS—linked for 1996–2013
    - FoodNet and extended *Listeria* information—linked for 2004–2012
    - FoodNet and extended *S.* Typhi information—linked for 1996–2012
    - FoodNet and the CDC-National Outbreak Reporting System (NORS)—linked for 2011, currently being linked for 2012–2013

- **Shigella *surveillance***

  An epidemiologist hired by CDC in August 2014 has led nine multistate and assisted with four single-state shigellosis outbreaks, including one international outbreak. Outbreak case counts ranged from 7 to 365 and were detected in as many as 26 states. PulseNet assisted with identifying the majority of multistate outbreaks through PFGE patterns. NARMS testing was completed for four outbreaks (>12 isolates), and in those instances, *Shigella* was resistant to ampicillin, chloramphenicol, streptomycin, sulfisoxazole, tetracycline and trimethoprim/sulphamethoxazole, ciprofloxacin, and

azithromycin. Antibiotic-resistant shigellosis infections were found most frequently among men who have sex with men.

B. Increasing participation of public health and food regulatory agencies and laboratories in national networks

Local and state health departments serve as the foundation of food safety efforts by investigating outbreaks, conducting disease surveillance, and implementing local control measures. FSMA recognizes the critical role of local, territorial, tribal, and state agencies in a national food safety system and incorporates provisions to coordinate, integrate, and enhance surveillance and outbreak response activities at all levels.

CDC provides funding, tools, training, and strategic leadership. These enhancements are expected to

- Improve the quality of data obtained at the state and local levels
- Ensure that data are analyzed and shared quickly to aid in the rapid response to food safety gaps

CDC provides resources to enhance and integrate critical national surveillance, outbreak detection, and response networks. Scientists need strong data to quickly identify the source of outbreaks and inform prevention efforts. In FY 2014, CDC provided approximately $17 million to local and state public health departments through the ELC Cooperative Agreement and the Emerging Infections Programs (EIP) to support critical foodborne illness surveillance efforts. This funding was essential to maintain capacity to track, detect, investigate, and respond to emerging foodborne disease threats. Other activities to support national networks included

- ***Supporting enteric disease labs***
    - CDC conducted three 50-state training seminars and four 50-state informational round-table training sessions for public health and regulatory laboratories to increase knowledge and participation in the implementation of WGS efforts. CDC trained 10 public health and regulatory laboratories in sequencing methods.
    - Five state and local health agencies, along with CDC, formed a consortium to develop and test best practices for isolate recovery by state and local public health laboratories in support of PulseNet. This consortium addresses the potential threat to the survival of PulseNet due to the adoption of new culture-independent diagnostic tests (CIDTs) by clinical laboratories. CIDTs effectively support patient management, but do not produce an isolate, which is required for PulseNet to operate.
    - CDC developed a regulatory and reimbursement workgroup to identify possible solutions to the effect of CIDTs on foodborne disease surveillance systems, including PulseNet. A report from this workgroup is anticipated in FY 2015.
    - CDC launched a "No-Petri-Dish" Diagnostic Test Challenge, which offered a $200,000 prize for a novel technological solution to the problem that CIDTs do not produce isolates.
    - The national botulism laboratory team successfully installed instruments and completed in-house validation of mass spectroscopy (Endo-PEP MS) to detect botulinum neurotoxin in clinical and non-clinical specimens.

- The PulseNet web portal went live in FY 2014. This electronic analysis system, developed in collaboration with USDA, the Association of Public Health Laboratories, and Carnegie Mellon University, allows for sophisticated electronic queries, analyses, and presentation of PulseNet data.

- ***Preparing for the launch of CryptoNet***

  To improve the surveillance and outbreak investigation of cryptosporidiosis, CDC's Waterborne Disease Prevention Branch developed CryptoNet, a molecular subtyping system (similar to PulseNet) that targets *Cryptosporidium* infections. This system was tested internally during the 2009–2013 outbreak seasons and shown to be very useful in identifying outbreaks, tracking infections and contamination sources, and investigating sporadic cases. In FY 2014, several collaborating state public health laboratories, including Florida, Georgia, Maine, Colorado, Wisconsin, and Idaho, submitted outbreak and/or sporadic case samples for molecular analysis and inclusion in CryptoNet. Funding was provided to Tennessee, Maine, and Wisconsin to begin building molecular capacity for *Cryptosporidium* in the state laboratories.

- ***Establishing the Norovirus Sentinel Testing and Tracking network***

  In August 2012, CDC established the Norovirus Sentinel Testing and Tracking (NoroSTAT) network to improve the timeliness of norovirus outbreak reporting through the National Outbreak Reporting System (NORS) and CaliciNet (National Norovirus Outbreak Network). The network allows for near real-time assessment of norovirus activity. The five states in NoroSTAT (Minnesota, Ohio, Oregon, Tennessee, and Wisconsin) include approximately 33 million residents, which is 11% of the total U.S. population. These five states had the highest per capita reporting rates for norovirus outbreaks historically, and therefore were least likely to be affected by underreporting biases. State health departments that participate in NoroSTAT report suspected norovirus outbreaks through NORS and CaliciNet within 7 business days of being notified about the outbreak. NoroSTAT reporting allows norovirus strain data uploaded through CaliciNet to be rapidly linked with epidemiologic characteristics of outbreaks reported through NORS by using consistent outbreak identifiers in each system.

  NoroSTAT information can be used to
  - Quickly evaluate current norovirus outbreak activity
  - Compare previous years
  - Assess strain-specific characteristics of norovirus outbreaks, including the impact of new strains on outbreak frequency and severity

  During the first 2 years of implementation, 1,391 suspected and confirmed norovirus outbreaks were reported by NoroSTAT states. The mean reporting lag decreased from 75 days in the 3 years preceding NoroSTAT to 3 days after the network's implementation. All 1,391 outbreak reports contained all required data elements, while only 945 (71%) of the 1,322 outbreaks in the 3 years preceding NoroSTAT reported these data. The mean time required for testing and genotype reporting decreased from 36 days during the year immediately preceding NoroSTAT to 4 days after its implementation.

  Data collected through NoroSTAT reaffirm that most norovirus outbreaks occur in long-term care facilities and are spread through direct person-to-person transmission. Moreover, norovirus

outbreak reporting through NoroSTAT has substantially improved both the completeness and the timeliness of these reports.

- ***CaliciNet enhancements***

  In FY 2014, CaliciNet received uploads from 28 CaliciNet certified states and Washington, DC. Specimens from norovirus outbreaks from the remaining 22 states were typed by five regional CaliciNet support centers. A total of 1,050 norovirus outbreaks were reported in 2014, with 15.3% epidemiologically identified as foodborne.

C. Sharing surveillance information on a timelier basis among federal, state, and local agencies

- ***National Antimicrobial Resistance Monitoring System for Enteric Bacteria***

  NARMS, established in 1996, is a collaboration among state and local public health departments, CDC, FDA, and USDA. This collaboration

  - Implemented the secure web-based data system at 54 NARMS sites. States can now access the results of antimicrobial susceptibility testing as soon as they are entered in the system.
  - Contributed data to the NARMS integrated database hosted by FDA. This database captures antimicrobial susceptibility data on enteric bacterial isolates from humans (CDC), retail meats (FDA), and food animals (USDA).
  - Automated the linkage of PulseNet and NARMS surveillance systems to allow isolate-level PFGE data to be imported into the CDC NARMS database and enable analysis of resistance data by PFGE pattern.
  - Imported NARMS data into SEDRIC to allow state, federal, and outbreak response partners to visualize susceptibility data.
  - Produced interactive graphs of NARMS human isolate antimicrobial resistance data for high-priority bacteria. These graphs are posted on the NARMS website.
  - Published the susceptibility testing results of outbreak isolates in all multistate outbreak investigation web updates.
  - Secured Institutional Review Board approval for a case-patient questionnaire that allows NARMS epidemiologists to collect information from patients on exposures (e.g., foods, animal contact, travel, history of antibiotics or hospitalization) associated with resistant and non-resistant infections and the clinical outcomes of those infections.
  - Adopted a new international measure that uses Epidemiological Cut-Off Values (ECOFFs) to move towards a globally standardized method for tracking antimicrobial resistance in *Campylobacter.*

- Conducted laboratory studies to determine if resistance determinants detected in the bacterial genome via WGS can be used to accurately predict resistance phenotype.

- Developed customizable dashboards that enable rapid identification of data anomalies. Defined or emerging resistance patterns will be flagged within the NARMS data system.

- Participated in a cross-disciplinary National Institute for Mathematical and Biological Synthesis (NIMBioS) workgroup to identify conceptual approaches and analytical methods to link shifts in the use of antimicrobials and antimicrobial resistance associated with FDA's risk mitigation strategy.

- Developed a prototype for a publicly accessible web-based tool, "NARMS Watch Public," that provides isolate-level susceptibility data in the form of maps, graphs, and charts. This tool includes the capability to download isolate-level susceptibility data.

- Held a NARMS public meeting in August 2014 where newly summarized surveillance data and analyses were shared in presentations, including

  - Foodborne *Salmonella* attribution using linked NARMS, NORS, and PulseNet data

  - Clinical outcomes of resistant *Salmonella* infections using linked NARMS and FoodNet data

  - Nalidixic-acid resistance in *Salmonella* Enteritidis associated with international travel using linked NARMS and FoodNet data

  - Trends in *Salmonella* resistance using NARMS data

- ***Foodborne Disease Outbreak Surveillance System (FDOSS)***

  - In FY 2014, CDC conducted four foodborne disease outbreak webinars to improve the sharing of surveillance data and provide training to state and local health departments about foodborne disease outbreak reporting. Nearly all states participated.

  - CDC updated the Foodborne Outbreak Online Database (FOOD) with data on foodborne disease outbreaks through 2012.

  - CDC published the 2011 and 2012 annual reports for "Surveillance for Foodborne Disease Outbreaks, United States" online.

D. Identifying and proposing solutions to eliminate key barriers at federal, state, and local levels to improve foodborne illness surveillance

- ***National Center for Environmental Health Enhancements***

  - The ***National Voluntary Environmental Assessment Information System*** (NVEAIS) is a new surveillance system targeted to jurisdictions that inspect and regulate restaurants and other food venues such as banquet facilities, schools, and other institutions. The system provides an

avenue to capture underlying environmental assessment data that describe what happened and how events most likely led to a foodborne illness outbreak. NVEAIS was launched (after a delay) in April 2014 in conjunction with the e-learning training *How to Conduct a Foodborne Illness Outbreak Environmental Assessment.* Per the Division of Emergency and Environmental Health Services' communication plan, multimedia dissemination of these resources to food safety programs and the public was implemented prior to and continued after the launch of both NVEAIS and the e-learning course. Monitoring of the uptake of both these tools began in April 2014 and is ongoing. State programs participating in NVEAIS include the following state departments of health: California, Connecticut, Minnesota, New York, North Carolina, Tennessee, and Wisconsin. Local programs participating in NVEAIS include Davis County Health Department (Utah), Fairfax County Health Department (Virginia), and the New York City Department of Health and Mental Hygiene (New York). With the delay in launch, a summary of data reported to NVEAIS is expected in summer 2015.

- The ***e-Learning training on Environmental Assessment of Foodborne Illness Outbreaks*** is a free, interactive online course to help prepare individuals to serve on a team that investigates foodborne illness outbreaks in restaurants and other food service venues. Since the launch of the e-Learning program, over 1,100 national and international users have signed up for the training. Pre-test and mastery test scores show a significant increase in knowledge regarding foodborne outbreak environmental assessments. In addition to the target audience of U.S. food safety program staff, two universities have incorporated this training program into their public health curriculum: the University of New England (online; Introduction to Environmental Health course, Master of Public Health degree program) and Pace University (Westchester County, New York, Community and Environmental Health Nursing course, BS Nursing degree program).

II. Evaluating and Improving Surveillance Systems

To implement FSMA requirements to evaluate and improve surveillance systems, CDC has improved epidemiological tools and microbiological methods for obtaining quality exposure data and identifying and classifying cases. Selected CDC activities include

A. Tracking and analyzing culture-independent test use in laboratories

- ***Foodborne Diseases Active Surveillance Network***
  - Continued surveillance to measure effects of CIDTs on foodborne illness surveillance[6]
  - Continued to collect information on laboratory methods used to diagnose FoodNet pathogens
  - Continued to collect reports of infections diagnosed using CIDTs
  - Improved the multistate foodborne outbreak tracking system

- ***System for Enteric Disease Response, Investigation, and Coordination***

  SEDRIC facilitates collaborative multistate outbreak investigations of enteric disease. SEDRIC integrates relevant surveillance data sources in real time, rapidly visualizes outbreak data, provides a secure platform for partner collaboration, and manages a repository of historic surveillance and outbreak data.

  Federal and state partners actively use SEDRIC to investigate multistate foodborne disease outbreaks. Highlights from their SEDRIC use include

  - More than 225 SEDRIC users from CDC, FDA, and USDA and in all 50 states
  - Eighteen successful pilots of the SEDRIC line-list editor by state and federal partners
  - Ability by states to obtain cluster-specific outbreak information 24–48 hours faster using SEDRIC than through typical laboratory communications
  - Twenty-eight SEDRIC-specific trainings given in the last 2 years, including two trainings at national conferences, and two individualized on-site trainings for states

  Epi Info™, an online public health tool, now includes a module for deploying and collecting questionnaire data. Once integrated into SEDRIC, public health officials can collect data using the National Hypothesis Generating Questionnaire directly from ill persons during outbreaks. The questionnaire collects information on more than 300 food items and other exposure commonly associated with multistate outbreaks. The Office of Management and Budget approved the questionnaire and initial testing of a "reverse directory lookup application" to identify phone numbers to rapidly complete case control studies.

  SEDRIC is reducing the time to pinpoint how and where contamination occurred in multistate foodborne disease outbreaks. Tools developed in this framework employ an all-hazards approach to multistate outbreak response and can be evaluated in multiple real events broadly applicable to programs across CDC.

B. Developing better methods to detect, investigate, respond to, and control multistate foodborne outbreaks

- ***Foodborne Diseases Centers for Outbreak Response Enhancement (FoodCORE)***

  FoodCORE centers work together to develop new and better methods to detect, investigate, respond to, and control multistate outbreaks of foodborne diseases. Currently 10 centers participate, covering about 18% of the U.S. population.

  Key findings from FoodCORE activities in the first year of the program (Y1) from October 2010 to the end of the second year (Y2) in December 2012[9] included

- Molecular subtyping for a higher proportion of *Salmonella*, STEC, and *Listeria* isolates (86% vs. 98%), with a reduced time to complete testing from a median of 8 to 4 days
- Epidemiologic interviews with more STEC and *Listeria* case-patients (93% vs. 99%), with a reduced time to attempt interviews from a median of 4 to 2 days
- Nearly 200 environmental health assessments
- Increase in average proportion of isolates with PFGE data, as follows:
  - *Salmonella* from 82% during baseline to 98% in Y2
  - STEC from 93% during baseline to 97% in Y2
  - *Listeria* from 82% during baseline to 99% in Y2

FoodCORE centers (selected through competitive award) include departments of health in Connecticut, New York City, Ohio, South Carolina, Tennessee, Utah, and Wisconsin. Three new centers were added in August, 2014: Colorado, Minnesota, and Oregon.

- Improvement in pathogen-specific proportions of case-patients with an attempted interview, as follows:
  - *Salmonella* from 88% during baseline to 98% in Y2
  - STEC from 90% during baseline to 98% in Y2
  - On average, 100% of *Listeria* case-patients had an attempted interview during both time periods
- Average turnaround time for STEC serotyping was maintained at the same levels as baseline (5-day median), and the longest turnaround time decreased from a high of 42 days during Y1 to 7 days in Y2

FoodCORE centers use performance metrics to identify practices that improve outbreak response. Two model practices have been finalized and made publically available on the FoodCORE website:

- The interviewing model practice describes triage and routing of case-patient reporting and the process of attempting interviews with case-patients, recommends categories and essential elements to ascertain during an initial enteric disease interview, and provides a checklist to determine alignment of initial interview practice.
- The laboratory model practice describes practices for specimen receipt and subtyping and strategies for cluster detection and reporting results.

C. Improving cyclosporiasis surveillance

- ***Cyclosporiasis surveillance and outbreak investigation resources***

CDC's Division of Parasitic Diseases and Malaria staff created and deployed a cyclosporiasis national hypothesis-generating questionnaire for routine use by state and local health departments during the cyclosporiasis outbreak season of May–August 2014. This extended questionnaire captured relevant food exposure information before or at the start of an outbreak rather than after it was identified, which can be weeks or more later. CDC also deployed an online questionnaire for receiving and analyzing multistate outbreak data more quickly by eliminating paper forms from states.

DPDM developed a protocol enabling pilot sites at state public health laboratories to submit de-identified *Cyclospora*-positive specimens to CDC for AMD research. Currently, no molecular methods exist for linking *Cyclospora* cases to each other or to particular food vehicles or sources, making it difficult to characterize the extent of particular outbreaks or to distinguish between multiple concurrent outbreaks.

CDC produced several health communications for clinicians about cyclosporiasis and testing for *Cyclospora* in persons with prolonged diarrhea, particularly in those who traveled to tropical and subtropical regions during the 14 days before the illness. The publications were timed to coincide with the start of the period when most cyclosporiasis cases are reported (i.e., May to August).

Cyclosporiasis resources for state and federal partners

- Sample questionnaires for investigating outbreaks
- Fact sheets for health care providers and the general public
- Laboratory guidance for *Cyclospora* diagnosis

Health communications for clinicians

- Cyclosporiasis fact sheet (English and Spanish)
- CDC Health Partners Outreach on Facebook
- CDC Clinician Outreach and Communication (COCA) update
- American Academy of Family Physicians News in Brief
- Medscape Expert Commentary

D. Improving attribution of foodborne illness outbreaks to specific foods

- ***Interagency Food Safety Analytics Collaboration (IFSAC)***

Since its creation in 2011, IFSAC, a collaboration of CDC, FDA, and USDA/FSIS, has focused its analytic efforts to develop methods to estimate foodborne illness source attribution for four priority pathogens (*Salmonella*, *E. coli* O157, *Campylobacter,* and *Listeria)*. In 2014, IFSAC project teams, composed of members of each agency and coordinated by a steering committee, completed the following:

- Developed a shared method to estimate the percentages of foodborne illnesses caused by the four priority pathogens attributable to different food categories
- Completed webpages describing IFSAC and IFSAC activities

- Held a webinar in January 2014 to update over 300 participants from the food industry, consumer advocacy groups, academia, and public health on the results of a project exploring whether outbreak illnesses are representative of sporadic illnesses

- Reviewed agency priorities and determined subject areas for four new analytic projects to be developed and initiated in 2015

III. Collaborating and Sharing Information with External Stakeholders

A. Sharing surveillance information on a timelier basis with the food industry, academia, consumers, the public, and external partners

According to a survey by the publisher of *Food Processing*, food safety ranked as 2014's most important manufacturing issue. The public also showed a strong interest in food safety. CDC's second annual Twitter chat on holiday food safety reached 8.4 million readers—doubling the reach from the previous year's chat. In an ABC News Twitter chat hosted by Dr. Richard Besser, food safety tweets from CDC were the public's top source of information.

Examples of reaching a broader audience with important food safety information

- CDC's food safety website has had almost one million page views since January 2014—the highest number of page views of any cross-cutting CDC website about foodborne illness, not including individual foodborne pathogen pages.
- The cross-governmental project Whole Genome Sequencing: Future of Food Safety uses whole genome sequencing technology to detect and investigate foodborne illness.

Stakeholders—food producers, regulators, and consumers—depend on CDC for practical and understandable information about keeping the food supply safe. Historically, food safety communications included annual summaries with data from the surveillance networks, scientific publications and presentations, and outbreak alerts. Today, partners and the public want access to more information—more frequently, and through multiple channels.

Since the introduction of FSMA, CDC has integrated communication, science, and policy expertise to improve the exchange and dissemination of food safety information. This team-based approach supports FSMA's call-to-action to provide fast, accurate, and relevant information.

- ***Selected activities that support CDC's effort to collaborate and share information***

  - ***Vital Signs*: reaching a wider audience through multiple platforms, channels, and languages**

    Each year, CDC scientists and communicators create a *Vital Signs* campaign on food safety. This campaign includes a suite of communication materials with a call-to-action about an important public health topic based on current surveillance data.

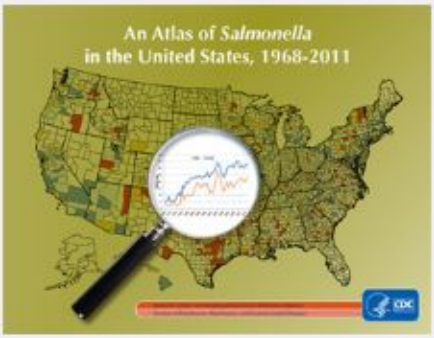
    The June 2014 Vital Signs presented the latest findings on norovirus outbreaks, which result in about 20 million illnesses each year, with 70% of reported outbreaks being caused by infected food workers.

The campaign translated the science to inform a wider audience by using multiple platforms and channels in English and Spanish, including a four-page infographic, a digital press kit, podcasts, a feature article, and social media posts. Although this Vital Signs provided recommendations for the food service industry, its content was relevant for the general public, health departments, and regulators. Using multiple platforms, channels, and languages made this important food safety information more accessible to a wider audience.

- ***Salmonella* Atlas: creating audience-centered information using plain language and the Clear Communication Index**

Salmonella infections are the leading cause of hospitalizations and deaths from foodborne illnesses in the United States and have contributed to many complex outbreaks, including those resistant to antibiotics.

CDC's *Salmonella* Atlas, published twice before in book and CD format, includes the most recent findings on *Salmonella* serotypes. In 2014, CDC put the Atlas online, giving instant access to *Salmonella* data. To add clarity and aid understanding of this complex topic, communicators used plain language and the CDC Clear Communication Index.



Accessing the 200-page Atlas could be intimidating until communicators divided it into 32 individual files based on serotypes, added context in story form, and an explanation about the importance of serotyping.

A CDC press release announced the Atlas, and media spread the word. The next day, the metrics had shifted to show that 90% of viewers were now from the general public rather than scientists and researchers. This shift is significant because it demonstrates a broader interest in the data than by public health departments and researchers. Under FSMA, CDC is tasked to make its data accessible, which is exemplified by the *Salmonella* Atlas and its supporting materials.

- **Interagency Food Safety Analytics Collaboration: working collectively to exchange information on preventing foodborne illness**

IFSAC, a tri-agency collaboration, is a novel approach to data sharing aimed at increasing food safety in the United States. A partnership between multiple food safety partners enables communication of surveillance data on a timelier basis with the food industry, academia, consumers, and the public.

Earlier this year, scientists from CDC, FDA, and USDA/FSIS worked with CDC communicators to create a website explaining IFSAC's strategic plan, projects on foodborne illness source attribution, past and future activities and events, and resources.

- **Epi-Ready: team-based training approach**

  CDC funded the National Environmental Health Association to conduct a 2-day Epi-Ready team training course combined with a special 1-day train-the-trainer course. The September 2014 course in Seattle drew 52 participants, including local and state public health officials. The primary purpose of both courses was to train three-member laboratory, epidemiology, and environmental teams from the five Integrated Food Safety Centers of Excellence so those teams would be able to conduct their own training courses in the coming year in non-CoE states. These courses will cover foodborne disease outbreak topics such as team formation, planning, detection, and investigation by epidemiologists, laboratorians, environmental health specialists, public health nurses, communication experts, and others.

- **Food allergy and anaphylaxis management: collaborating on a common goal**

  To meet FSMA requirements to establish guidelines for voluntary food allergy and anaphylaxis management for use in schools and early childhood education programs, CDC convened a panel of federal, medical, and school-affiliated experts.* This expert panel informed guidance priorities and content and summarized scientific and school health-related data and papers related to managing food allergies in schools. The HHS Secretary drafted and cleared guidelines for release on October 30, 2013.

  The National Association of School Nurses, the American Academy of Pediatrics, and Food Allergy Research and Education are supporting the release with communication materials and trainings. During FY 2014, CDC's school health programs created multiple food allergy publications for specific school audiences, including an allergy toolkit, tip sheets for school personnel, and downloadable PowerPoint presentations for specific school audiences. Future plans include producing a comprehensive list of resources, podcasts, and webinars.

- **VoluntaryNet: encouraging data sharing among food safety partners**

  VoluntaryNet, a collaboration between CDC's PulseNet and the University of Georgia Center for Food Safety, provides food industry partners with indirect access to current PulseNet data. This new collaboration began in FY 2014. VoluntaryNet encourages industry to share their own data (without compromising themselves) and data from PulseNet (without violating data-sharing agreements or compromising state or federal patient privacy laws).

- **Integrated Food Safety Centers of Excellence: sharing best practices for foodborne disease surveillance and outbreak investigation**

  The five Integrated Food Safety CoEs serve as resources for local, state, and federal public health professionals who respond to foodborne illness and outbreaks. Each Center leads a workgroup

*Panel members were from the following agencies and organizations: CDC; U.S. Department of Education; USDA; FDA; NIH/National Heart, Lung, and Blood Institute; Food Allergy and Anaphylaxis Network; Food Allergy Institute; American Academy of Allergy, Asthma, and Immunology; National School Boards Association; National Education Association; National Association of School Administrators; National Association of School Nurses; and American School Health Association.

(Colorado—training, Florida—academic coordination, Minnesota—metrics, Oregon—informatics, and Tennessee—communications/website).

Selected projects of the Centers include the following:

Integrated Food Safety Centers of Excellence

CDC named Colorado, Florida, Minnesota, Oregon, and Tennessee state health departments and their partner academic institutions as Centers in 2012 under the authority of FSMA.

Colorado

– Created the Food Source Information wiki, with input from other Centers, providing needed information for epidemiologists to understand how various agricultural products are grown, processed, stored, and distributed

– Created the online QuickTrain environmental health module and helped Wyoming conduct a self-assessment of their outbreak systems and processes by using the CIFOR metrics

Florida

– Conducted Epi Info training to all Florida counties

– Used the CIFOR metrics and target ranges to conduct an evaluation of the state's outbreak performance

– Provided information to the Colorado Center for the Food Source Information wiki

Minnesota

– Provided outbreak investigation guidance to several states and local health departments

– Created a database of food exposure data using past case interviews

– Developed brief model practice guides and a case study based on their investigation experience

Oregon

– Created a video for public use that clearly explains stool collection processes

– Developed case exposure information in collaboration with Minnesota

– Helped teach a distance-based graduate-level foodborne illness course with Minnesota Center staff

– Trained Washington and California staff to use the highly regarded Oregon "shotgun" questionnaire

Tennessee

- Created a final version of an online outbreak training course that targets laboratory, epidemiology, and environmental health staff at the local and state levels

- Conducted training for students at University of Tennessee who will provide surge capacity for outbreak interviews

- Conducted a self-evaluation of outbreak processes using the CIFOR metrics

- **Council to Improve Foodborne Outbreak Response: developing and sharing guidelines, processes, and products that will facilitate good foodborne outbreak response**

  CIFOR is a diverse, multidisciplinary collaboration of national associations and federal agencies that seeks to improve methods at the local, state, and federal levels to detect, investigate, control, and prevent foodborne disease outbreaks. CIFOR, which held its first meeting in 2006 and is primarily funded by CDC, includes member organizations that represent epidemiology, environmental health, public health laboratories, and regulatory agencies involved in foodborne disease surveillance and outbreak response. The food industry is represented on the CIFOR Industry Workgroup.

  CIFOR held two face-to-face meetings, began development of new products, and released several products in FY 2014, including the following:

  - *Guidelines for Foodborne Disease Outbreak Response* (2nd Edition), which includes FSMA information; model practices in outbreak investigation and response; updated statistics, references, and examples; and enhanced alignment between the Guidelines and the Toolkit (*Guidelines for Foodborne Disease Outbreak Response* was developed to aid government agencies responsible for investigating, managing, and preventing foodborne disease).

  - Development of Target Ranges for Selected Performance Measures, which includes specific metrics and target ranges for 16 performance indicators selected from among many performance indicators.

    This key subset of 16 metrics and target ranges is intended to help agencies self-assess their public health performance and effectiveness in foodborne disease surveillance and outbreak control activities and to compare their performance with the target ranges developed from existing data. Metrics documents include both an abridged version of the 16 metrics and target ranges and the full project report, which describes the detailed methodologies used to develop the 16 metrics and target ranges.

  - CIFOR Lab-Epi Integrated Reporting Software, an open source application, analyzes patient laboratory (serotype, subtype, or other) results to identify patterns or clusters that would suggest a possible foodborne outbreak or situation of interest.

This free software is intended as a tool for epidemiologists or public health personnel conducting disease surveillance for foodborne pathogens to more quickly identify potential clusters of enteric illness within their own jurisdiction.

- **Cooperative agreements**

The CDC Food Safety Office manages several cooperative agreements with national associations. Many, but not all, of the activities funded through these associations involve CIFOR workgroups, projects, and products. The overall goal of the work with the associations is to improve foodborne disease surveillance and outbreak response at the local and state levels, which directly affects federal disease control efforts. By funding these associations, CDC gains direct access to front-line experts at the local and state levels who provide guidance and extensive effort on workgroups and in meetings to develop solutions to current barriers to prompt outbreak detection and response.

- **Association of Public Health Laboratories (APHL)**
  APHL assists with several CIFOR projects, including the CIFOR *Guidelines*, the CIFOR Lab-Epi Integrated Reporting software (freeware to help states and large cities more quickly identify clusters of enteric illness), the CIFOR Economic evaluation of PulseNet, and the APHL Food Safety Workgroup, which is actively addressing many issues, including WGS and culture-independent diagnostic testing.

- **Association of State and Territorial Health Officials (ASTHO)**
  ASTHO members and staff participate in development of all CIFOR products, such as the CIFOR *Guidelines* and the *Guidelines* Toolkit, CIFOR deliberations at all in-person meetings, and development of a wide range of foodborne illness fact sheets and background materials for new and longtime state health officials.

- **Council of State and Territorial Epidemiologists (CSTE)**
  CSTE is heavily engaged in the development of the *Second Edition of the CIFOR Guidelines for Foodborne Disease Outbreak Response*, development of the *Second Edition CIFOR Guidelines* Toolkit, convening the CIFOR Council and Governance Committee meetings twice a year, managing the CSTE Food Safety Fellowship (fellows are placed in state health departments for 2 years), and other activities.

- **National Association of County and City Health Officials (NACCHO)**
  NACCHO actively maintains the CIFOR website, including the CIFOR Clearinghouse, and manages the CIFOR Industry Workgroup and the CIFOR Marketing Workgroup. ACCHO members assisted with the drafting of the *Second Edition of the CIFOR Guidelines* and the development of the revised *Guidelines* Toolkit. NACCHO also has a very active Food Safety Workgroup, which is involved in a wide range of local issues related to foodborne illness reporting and investigation.

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Appendix 3: Additional Background on Surveillance for Antimicrobial Resistance in Foodborne Pathogens

Antimicrobials have been critical for treating bacterial infections in humans and animals since the 1940s, with resistance soon noted. In veterinary medicine, antimicrobials have been used to prevent and control disease and to promote growth and improve fee efficiency in food production animals. However, the use of antimicrobials for growth promotion and for preventive and therapeutic purposes in food production animals has been documented to select for bacteria that are resistant to antibiotics, including those that are of medical importance in treating human infections. Resistance has been shown to spread from one bacterial strain to another, and the use of one antibiotic can co-select for resistance to several antibiotics when resistant genes are linked.[1]

Recent trends in the resistance of foodborne pathogens to antibiotics used currently and in the recent past to treat serious foodborne infections, have raised serious questions and concerns of public health importance. In in its recent report, *Antibiotic Resistance Threats in the United States, 2013 (*http://www.cdc.gov/drugresistance/threat-report-2013/), the Centers for Disease Control and Prevention (CDC) estimated that each year, approximately 441,000 antibiotic-resistant illnesses and 66-70 deaths occur in people ill from infections caused by the pathogens *Campylobacter*, non-typhoidal *Salmonella*, *Salmonella* Typhi, and *Shigella* (Table 3.1).

Table 3.1. Estimates of Illnesses and Deaths from Resistant Enteric Infections in the U.S. Per Year*

Pathogen	Antibiotic	Percent Resistant	Resistant Infections	Deaths from Resistant Infections
Campylobacter	Ciprofloxacin or azithromycin	24%	310,000	28
Nontyphoidal Salmonella	Ceftrioxone or ciprofloxacin† or ≥ 5 classes	8%	100,000	38
Salmonella Typhi	Ciprofloxacin†	67%	3,800	<5
Shigella	Ciprofloxacin or azithromycin	6%	27,000	<5
Total			**440,800**	**66-70**

*CDC. Antibiotic Resistance Threats in the United States, 2013; http://www.cdc.gov/drugresistance/threat-report-2013/;
†Resistance or decreased susceptibility

The CDC report confirmed that the maintenance and protection of an arsenal of antibiotics that are effective in treating human foodborne illness can now be considered under threat and that conducting surveillance for antimicrobial resistance of foodborne pathogens is essential for formulating evidence-based policies that assure protection of existing medically important antibiotics, implementing practices that ensure best use of existing antibiotics, and identifying needs in the development of new ones.

History of and needs for surveillance of antimicrobial resistance in foodborne pathogens

Public health officials, as early as 1948, began to test for resistance to tetracycline of *Salmonella* Typhimurium cultured from human and poultry specimens to tetracycline, but none was detected. By 1956-1957, resistance was detected in 5% and 9% of human and poultry isolates, respectively, and, by 1959-1960, resistance had increased to 14% of human isolates (also found resistant to chloramphenicol), and 29% of poultry isolates. In addition, strains from four *Salmonella* Typhimurium foodborne outbreaks were also tested, with two found to be pan-susceptible, and two tetracycline-resistant.[2] CDC continued monitoring antimicrobial resistance of human salmonellosis infections through nationwide surveys in 1967 and 1975, followed by periodic sentinel county surveys that tested for resistance among isolates of *Salmonella* (1985, 1990, 1995), *Shigella* (1979, 1986), and *Campylobacter* (1990), with accompanying data obtained through patient interviews.[3]

Questions remain on the nature of the relationship between nontherapeutic uses of antibiotics in food production animals, the emergence of antibiotic resistance, and the health of people on farms and more distant consumers.[4] Accordingly, federal agencies have identified several needs for antimicrobial resistance surveillance data that include:

- Identifying and tracking temporal and spatial patterns and trends in resistance
- Describing emergence and spread of resistant bacterial strains and resistance genes
- Studying associations between antibiotic use practices and antimicrobial resistance
- Generating hypotheses about sources and reservoirs of resistant bacteria
- Providing data for risk analysis studies of foodborne antimicrobial resistance hazards
- Identifying risk factors and clinical outcomes of infections caused by resistant bacteria
- Identifying potential interventions and evaluating their effectiveness
- Informing outbreak investigations and food source attribution
- Guiding the design of research studies
- Providing data for evidence-based policy formulation that addresses medical and veterinary uses of antibiotics

Launching the National Antimicrobial Resistance Monitoring System (NARMS)

To meet these and other needs, the federal agencies of HHS/CDC, HHS/Food and Drug Administration (FDA), and U.S. Department of Agriculture (USDA) in 1996, joined forces to conduct surveillance of foodborne antimicrobial resistance of selected enteric bacteria isolated from samples collected from clinically ill humans (CDC) and food production animals at slaughter (USDA/Agricultural Research Service [ARS] and /Food Safety and Inspection Service [FSIS]). In 2002, FDA added a third component of sampling and testing isolates collected from retail meats. This innovative and comprehensive approach to antimicrobial resistance surveillance was named the National Antimicrobial Resistance Monitoring System (NARMS) for Enteric Bacteria. NARMS was incorporated as part of an overall, multi-faceted strategy to assess the potential impact of antimicrobial use in animal agriculture on the evolution of antimicrobial resistance and to preserve the effectiveness of medically important antimicrobial drugs.

Today, NARMS is the only nationwide U.S. surveillance system for tracking antimicrobial susceptibility and resistance patterns among enteric bacteria isolated from clinically ill humans, retail meats, and food production animals at slaughter. FDA coordinates the overall program, which is based on the use of common test platforms,

standardized test methods and interpretations, standardized agent panels, and sharing of test results. NARMS activities are complemented by epidemiologic and microbiologic research studies on risk factors and clinical outcomes of resistant enteric infections, on understanding the genetic mechanisms of antimicrobial resistance in enteric bacteria and the mechanisms that permit the transfer of resistance between bacteria, on improving methods for isolation and typing, and on developing new methods for antimicrobial susceptibility testing. NARMS has examined *Salmonella* and *Campylobacter* strains for genetic relatedness using pulsed-field gel electrophoresis (PFGE). PFGE patterns are entered into CDC's PulseNet database or USDA's VetNet database. PulseNet (http://www.cdc.gov/pulsenet/) and VetNet (http://www.aphl.org/conferences/proceedings/Documents/2010/2010_APHL_PulseNet_Meeting/011-Cray.pdf) are national molecular subtyping networks for foodborne and zoonotic disease surveillance, which are critical links to the NARMs database.

NARMS structure, approach, and sampling schemes

The human component of NARMS was launched in 1996 within the framework of CDC's Emerging Infections Program and Foodborne Diseases Active Surveillance Network (FoodNet; http://www.cdc.gov/foodnet/) sites. The program began by testing isolates for non-Typhi *Salmonella* and *Escherichia coli* (*E. coli*) O157 isolates. By 1999, surveillance was expanded to include additional bacteria and testing sites, as well as testing of *Salmonella* serotype Typhi and *Shigella*. By 2003, the human arm of NARMS was conducting nationwide surveillance for *Salmonella, Shigella, and E. coli* O157. Testing of *Campylobacter* from human infections began in five FoodNet sites in 1997 and expanded to all 10 FoodNet sites by 2003. In 2009, NARMS began testing *Vibrio* species other than *V. cholerae* from all 50 states. Today, participating public health laboratories submit every 20th non-typhoidal *Salmonella, Shigella*, *E. coli* O157 isolate, and all *Salmonella* serotypes Typhi, serotype Paratyphi A and Paratyphi C, and *Vibrio* (other than *V. cholerae)* isolates received at their laboratories to CDC's NARMS laboratory for antibiotic susceptibility testing.

The Food Producing Animal Component began in 1997 with the testing of *Salmonella* isolates from chicken carcass rinsates; carcass swabs from turkey, cattle and swine; and ground meat products (chicken, turkey, and beef). In 1998, NARMS began to receive chicken carcass rinsates and cultured them for *Campylobacter*, followed by *E. coli* (2000), and *Enterococcus* (2003). Antimicrobial susceptibility testing in the past was conducted by USDA/ARS laboratories at the Russell Research Center, Athens, Georgia. Beginning in 2013, USDA/FSIS began sampling cecal contents collected from animals processed at slaughter. Samples are cultured for the presence of *Salmonella*, generic *E. coli*, *Campylobacter*, *and Enterococcus* spp. at the USDA/FSIS laboratory in Athens GA. Recovered isolates are characterized for antibiotic susceptibility, serotype, and subjected to PFGE.

The Retail Meat Component was launched in 2002, and is an ongoing collaboration among the FDA/Center for Veterinary Medicine (CVM), CDC, and the FoodNet State public health laboratories of California, Colorado, Connecticut, Georgia, Maryland, Minnesota, New Mexico, New York, Oregon, Tennessee; as well as public health laboratories in Washington, Louisiana, Missouri, and Pennsylvania. Each site purchases approximately 40 food samples per month—comprising 10 samples each from chicken, ground turkey, ground beef, and pork chops—at retail stores that are selected randomly. Each laboratory at those sites cultures the meat and poultry samples

for *Salmonella*; and poultry samples are cultured for *Campylobacter*. In addition, each year, 3-4 of the 11 participating laboratories (in 2010, it was Georgia, Oregon, Maryland, and Tennessee) culture meat and poultry samples for *E. coli* and *Enterococcus*. The USDA/FSIS laboratory in Athens Georgia confirms species and serotype for *Salmonella* isolates, and conducts antimicrobial susceptibility testing, and genetic analysis.

Information Collected and Reported by NARMS

NARMS reports on trends in the resistance to antimicrobials of enteric pathogens, including *Salmonella, Campylobacter, generic E. coli*, and *Enterococcus* cultured from isolates obtained from clinically ill humans, retail meats, and food-producing animals at slaughter. NARMS also reports on antimicrobial susceptibility testing results of human isolates for *Shigella, Salmonella* Typhi*, and Vibrio* (other than *V. cholerae*). The antimicrobial agents, for which resistance is tested, are listed at right, by agent class and agent. Agents tested vary by pathogen, year, and for some, testing is done only when a certain resistance is present (i.e., cephalosporin or quinolone).

Box 3.1. List of Agents tested for Resistance in NARMS, by Agent Class

Aminoglycosides	Amikacin, Gentamicin, Kanamycin, Streptomycin
B-Lactam/B-Lactamase Inhibitor Combinations	Amoxicillin-Clavulanic Acid
Cephems	Piperacillin-tazobactam, Cefoxitin, Ceftiofur, Ceftrioxone, Cephalothin, Cefepime, Ceftazidime
Folate Pathway Inhibitors	Sulfonamides, Trimethoprim-sulfamethoxazole, Sulfamethoxazole, Sulfisoxazole
Glycopeptide	Vancomycin
Glycocycline	Tigecycline
Ketolides	Telithromycin
Lincosamides	Clindamycin, Lincomycin
Lipopeptides	Daptomycin
Macrolides	Azithromycin, Erythromycin, Tylosin
Monobactam	Aztreonam
Oxazolidinome	Linezolid
Nitrofurans	Nitrofurantoin
Penems	Imipenem
Penicillin	Penicillin, Ampicillin
Phenicols	Chloramphenicol, Florfenicol
Quinolones	Ciprofloxacin, Nalidixic acid
Streptogramin	Quinupristin/Dalfopristin
Tetracyclines	Tetracycline

CDC, FDA, and USDA each publish annual reports online (CDC reports available at http://www.cdc.gov/narms/reports/; FDA reports and interagency executive reports available at http://www.fda.gov/AnimalVeterinary/SafetyHealth/AntimicrobialResistance/NationalAntimicrobialResistanceMonitoringSystem/ucm059103.htm), which are available to NARM's multiple stakeholders. In general, these reports are highly technical, and for the year of report, present the following information:

- Descriptions of the population, sampling methods used, demographic information accompanying resistance data
- Overviews of findings, with a focus on what's new and highlights for the year of report
- Test results for all pathogens including resistance to individual agents and to multiple antimicrobials (i.e., no resistance detected, ≥ to 1, 2, 3, 4, or 5 CSLI classes, at least ACSSuT, ACT/S, ACSSuTAuCx, at least ceftriazone and nalidixic acid resistant[5])
- Changes in resistance patterns observed since last report
- Detailed results tables and graphs, presenting the antimicrobial agents used for susceptibility testing, by pathogen, and serotype, and year(s)
- Annual resistance percentages for 10 years
- Minimum inhibitory concentration distributions for isolates from the current year, accompanying numbers of isolates tested, and numbers and percent resistant to antimicrobial agents

- A summary of antimicrobial resistance trend analyses comparing the year of report surveillance to 5-year baseline
- For retail meat reports, results on resistance patterns (including PFGE profiles) are reported by meat type, pathogen and subtype, and antimicrobial agent
- For food producing animal reports, resistance data are presented by species, pathogen and subtype, and antimicrobial agent

An integrated database project was undertaken to improve access to data from all three arms of NARMS with the following goals: 1) consolidate antimicrobial susceptibility data from the NARMS program's three arms– human, food-producing animal, and retail meat; 2) enable efficient production of consolidated data tables and graphs for reporting; 3) enable NARMS epidemiologists to more easily identify baselines, search for trends, test hypotheses, etc.; and 4) enable FDA regulators to use NARMS data to support risk assessments and other evaluations. In response, and beginning with 2003 data, HHS/CDC, HHS/FDA, and USDA/FSIS have jointly published a NARMS Annual Executive Report, which presents NARMS data from each of the three agencies in an integrated format, allowing readers to more easily compare data from all three component NARMS programs. The 2009 Executive Report is the first report to include a summary in addition to a full report. NARMS Executive Reports are available on the FDA NARMS reports website http://www.fda.gov/AnimalVeterinary/SafetyHealth/AntimicrobialResistance/NationalAntimicrobialResistanceMonitoringSystem/ucm059103.htm). In addition, all three Federal agency partners recently have enhanced their reports to include on-line interactive data displays that allow users to visualize resistance trends by pathogen and antimicrobial agent.

Additional Examples of How NARMS Data Have Been Used to Improve Food Safety

In addition to examples provided in the text, below are other examples of how NARMS data have been used to improve food safety.

Food safety officials at USDA/FSIS have used NARMS data to provide ongoing baseline data on the prevalence of specific pathogens in their regulated food products such as food-producing animals presented for slaughter. NARMS data have been used as the evidence-base supporting USDA/FSIS microbial food safety activities in slaughter facilities.

As mentioned in the main report, NARMS data have also been used to investigate[6,7] and respond to foodborne outbreaks. Comparisons of enteric pathogen subtypes, strains, and susceptibility information from human outbreak cases ("outbreak strain") may provide clues regarding likely sources. Along with other information (i.e., epidemiologic, laboratory, environmental information, food tracebacks, product investigations), these data have helped investigators form hypotheses on possible food sources of the outbreak. Taken together, this information has guided additional investigations and, in turn, helped identify and implement effective public health measures (e.g., advice to consumers on safe handling of raw poultry; several voluntary and or regulatory actions) more quickly.

NARMS collaborators also have linked the NARMS database to other systems (e.g., the National Outbreak Reporting System (NORS), FoodNet, and PulseNet) to categorize outbreaks by antimicrobial susceptibility, leading to a better understanding of the sources of enteric infections (i.e., attribution analyses), and to characterize the resistance profiles associated with PFGE patterns. These data have been used to track changes

in resistance/susceptibility of a single serotype, and provided improved discrimination of pathogen strains. Providing susceptibility data from multiple points in the food-chain has provided opportunities to assess attribution over the farm-fork continuum.

In 2005, NARMS data were used to support FDA's withdrawal of approval for the use of enrofloxacin in chickens and turkeys. Enrofloxacin, a fluoroquinolone, marketed under the trade name Baytril, had been approved for use in poultry production. In September 2005, FDA withdrew its approval because of concerns about the spread of fluoroquinolone-resistant *Campylobacter* from poultry to humans. NARMS data from 1996-2006 were also used to identify mechanisms of resistance to cephalosporins among specific types of *Salmonella*.[8]

Previous Reviews and Documented Strengths of and Challenges to NARMS

Given the importance of NARMS, previous reviews have been conducted to identify its considerable strengths and enhancements for improvement. With respect to strengths, NARMS has been noted to be the most extensive program for integrated laboratory-based surveillance of antimicrobial resistance in enteric bacteria in the world. The system has a strong base of stakeholder support, and has provided critical, comprehensive susceptibility data for managing risks associated with food animal antibiotic use, including pre-approval review of new animal antibiotic drugs and post-approval safety monitoring. NARMS has provided data invaluable to hypothesis-driven food hazard analyses, and has served well as a platform for robust intramural and extramural research. Moreover, it has demonstrated its value as a rich source of reference data that are finding greater use in outbreak investigation and response and attribution analyses. Operation of the system has led to the development of an exceptional cadre of well-trained and dedicated microbiologists and epidemiologists with expertise in antimicrobial resistance, and has become a recognized model for international capacity building and technical standards. And, it has shown, by example to be an excellent model for federal-state partnerships (i.e., CDC-FoodNet, CDC-PulseNet, USDA-FSIS, USDA-ARS, USDA-APHIS, ORA, CFSAN, universities, and others).

Previous review groups have also identified improvements made to date,[9] which have led to improved sampling schemes, representativeness of samples, and integrated reporting of results for easier access to and use of data. Lastly, prior reviews also identified a number of future improvements that would enhance the provision and use of NARMS data going forward (Table 3.2).

Table 3.2. Summary of Challenges and Recommendations for Improving NARMS Documented in Previous Reviews[10–14]

Sampling Human	• Need greater number of isolates from clinically ill people (> current every 20th sample from those submitted to public health laboratories) • Need to test pathogens outside of those targeted in NARMS, without compromising core monitoring functions (e.g., methicillin-resistant *Staphylococcus aureus* (MRSA); Extended Spectrum Beta-Lactamases (ESBL)
Food Producing Animals and Retail meats	• Need on-farm samples complemented by antibiotic use information • Need greater numbers of isolates (3 additional retail meat testing sites [WA, LA, MO]) were added in 2013) • Need to test different commodities, as needed, without compromising core monitoring functions (e.g., seafood, animal feeds)
Environmental	• Need for environmental samples/isolates along potential routes of dissemination
Combined	• Need sound sampling scheme along the food chain
Linking relevant databases	• Food safety (FoodNET, NORS, PulseNet, etc.) • Connecting and strengthening a network of hospitals and clinics to exploit other human isolate AR data sources • Incorporating FDA/Office of Regulatory Affairs food and facility inspection data into NARMS
Database development	• Continued and improved integrated database development • Gathering and integrating information is expensive and laborious • Burden of illness and food consumption data needed for design and prioritization of pathogens and commodities • Cooperation of, and good communication between, agriculture and public health sectors needed • Collaboration and information sharing between laboratory scientists, epidemiologists and public health officials within and across sectors and disciplines • Need for greater political/financial support in recognition of the importance of public health issues and need for ongoing risk assessments • Need for continued flexibility to stay current • Establish a regular process for review and enhancement
Data generation, analysis, reporting, interpretation, and use	• Provide timelier data generation, analysis and reporting to immediate stakeholders (agencies participating in NARMS) • Obtain detailed drug/antibiotic use information in food production animals on the farm • Publish findings to different audiences in a timely manner
Identify new opportunities to leverage the NARMS platform	• Promote awareness on and understanding of the implications of the data and the need for research • Professional development and training on emerging technologies • Secure additional resources for research • Research tool and early detection system when sampling on-farm with antibiotic use information in some cases (ARS) • Strengthen international harmonization and cooperation

Promoting use of NARMS surveillance data	• Promote and facilitate use of data for formulating sound public health policy • Measure the impact of policies, such as FDA issued GFI #209 • Increase use of information for improved outbreak investigation and response

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