Managing Food Safety Hazards: Shiga Toxin-producing Escherichia coli and Antibioticresistant Pathogens

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ABSTRACT

Emerging hazards in the United States and global food supply were discussed in a January 2011 conference focusing on antibiotic-resistant (ABR) and Shiga-toxin producing *Escherichia coli* (STEC) pathogens. Current scientific findings and policies, public health implications, and risk management approaches related to the control of these pathogens in the food supply were reviewed. Invited experts explained and assessed universal risk management tools for addressing food safety issues and described current approaches and research needs. Attendees deliberated on food safety matters related to ABR and STEC pathogens that require further scientific study and regulatory action. For both ABR and STEC pathogens, specific recommendations for risk management strategies, tools, policies, and research needs are given based on the comments from attendees. The conference did not attempt to arrive at consensus on the issues. Pathogens in the food supply linked to environmental contamination and food-animal husbandry practices have emerged as public health hazards requiring a comprehensive, collaborative, and multi-layered response. When problems are documented through surveillance systems, effective public health protection requires implementation of control measures at multiple points along the farm to fork continuum.

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INTRODUCTION

Emerging pathogens in the food supply are a growing concern for the public, the scientific community, and policymakers. In addition to well-known food safety hazards such as Escherichia coli O157:H7, Salmonella, and Listeria monocytogenes, consumers and the public health community must now grapple with the consequences of a host of new pathogens and strains. For example, in 2011, a foodborne outbreak occurred in Germany that was caused by a rare strain of multi-drug resistant E. coli O104:H4-a pathogen apparently resulting from a transfer of virulence determinants between a human and an animal pathogen (13). The outbreak resulted in over 4,000 illnesses worldwide, including more than 900 hemolytic uremic syndrome (HUS) cases and 50 deaths (58).

Also in 2011, a multistate outbreak of Salmonella Heidelberg infections associated with ground turkey sickened at least 129 people in the United States, with one death reported (8). The outbreak strain was resistant to tetracycline, streptomycin, ampicillin, and gentamycin (8)-drugs whose use in turkey production and resultant resistance of S. Heidelberg had been reported previously (31, 33). These recent outbreaks are evidence of the public health challenge of protecting the food supply from contamination by antibiotic-resistant (ABR) pathogens and Shiga toxinproducing E. coli (STECs). While each type of pathogen has a distinct natural history, controlling them will require the implementation of risk management improvements at multiple levels and enhanced surveillance to better protect public health.

STECs are a form of *E. coli* bacteria that can cause illnesses ranging from mild intestinal disease to severe kidney complications. Types of STECs include *E. coli* O157:H7 and more than 100 other, less studied, non-O157 strains. In October 2007, a U.S. Department of Agriculture (USDA) Federal Register Meeting Notice stated that there is growing awareness that STECs other than *E. coli* O157:H7 cause sporadic and outbreak-associated illnesses, with the number of non-O157:H7 STEC infections reported to the Centers for Disease Control and Prevention (CDC) nearly tripling over a five-year period (2000 to 2005) (42). CDC reported that non-O157 STECs are emerging pathogens that pose a significant health threat, with newly recognized strains reported every year (5). More recently, CDC analyzed FoodNet data (2005 to 2008) and estimated that non-O157 STEC illnesses may occur nearly twice as frequently as *E. coli* O157 illnesses (39).

Over 13 million kilograms (28 million pounds) of antibiotics sold or distributed in the United States in 2009 were for use in food-producing animals (48). Increases in ABR bacterial infections in the human population have led to public health concerns regarding the overuse and misuse of antibiotics in food-animals—particularly in light of research indicating that ABR bacteria are transferred from food-animals to humans through the food supply (51).

On January 25, 2011, The Pew Charitable Trusts and the Center for Science in the Public Interest (CSPI) convened a one-day conference in Washington, D.C., entitled Managing the Risk of Foodborne Hazards: STECs and Antibiotic-Resistant Pathogens. Participants included 130 government, academic, and industry experts who discussed the current science, knowledge gaps, public health implications, and practical solutions related to the growing problems of antibiotic-resistant pathogens and emerging strains of STECs in the food supply, but there was no attempt to produce consensus during the conference. The conference featured overviews of the topics, followed by short presentations by a panel of experts and an open dialogue. The following overview is based on Pew and CSPI's analyses of the panels, discussions, and presentations.

EMERGING FOODBORNE PATHOGENS: STECS

The STEC *E. coli* O157:H7 was first recognized as a pathogen in 1982 during an investigation of hemorrhagic colitis (*36*). Public awareness was heightened in 1993 after a multistate foodborne *E. coli* O157:H7 outbreak linked to undercooked ground beef sold by a fast-food restaurant chain caused over 700 illnesses and four deaths. Today, *E. coli* O157:H7 is broadly recognized as a foodborne pathogen of public health importance (36). CDC estimates that more than 175,900 people become ill from foodborne STECs (both O157 and non-O157 STECs) in the United States each year (39). HUS associated with *E. coli* infections is the most common cause of acute kidney failure in children (32), and affects one to nine percent of persons infected with an STEC (18).

Since the first nationwide surveillance effort for E. coli O157:H7 began in the mid-1990s, reported incidence of the pathogen has declined. The United States reached its Healthy People 2010 objective for E. coli O157:H7, with only one culture-confirmed case for every 100,000 people (46). Even as the United States has seen a reduction in human cases of E. coli O157:H7 infections, there has been an apparent increase in the incidence of non-O157 STEC infections. The top six non-O157 serogroups that cause infections in the United States (O103, O111, O121, O145, O26, and O45) have been associated with outbreaks and severe illnesses, including bloody diarrhea and HUS (16). Several studies have linked these lesser known STECs to the food chain. Ground beef was implicated in 76 percent of the E. coli O157:H7 cases and 58 percent of the non-O157 cases in a Minnesota study (19). In 2008, a private laboratory conducted a nationwide convenience sample survey of retail ground beef and found that non-O157 STECs was more commonly present than Salmonella in the samples; specifically, of the 5,070 tests, there were 96 confirmed positive results for non-O157 STECs and 86 confirmed results for Salmonella (27). A CDC review of six outbreaks occurring between 1990 and 2008 identified fruits/nuts, dairy products, leafy vegetables, and ground beef products as vehicles for STECs (18).

Government policy and riskmanagement options

USDA and FDA currently treat *E. coli* O157:H7 as an adulterant subject to zero tolerance in any food; when testing shows that the pathogen is present, the food is subject to a governmentannounced recall. As a result of a citizen petition (28), USDA announced in Sept-ember 2011 its intention to begin testing for the top six non-O157 STECs, affirming them as adulterants in some raw beef and prohibiting the sale of beef containing those bacteria. Enforcement is expected to begin mid-2012 (44).

The zero tolerance policy for *E. coli* O157:H7 has led to implementation of control systems that have resulted in significant reductions in the rates of positive samples in ground beef production, as demonstrated both by government and industry testing programs (2).

Surveillance and epidemiology

Improving foodborne illness surveillance and laboratory diagnosis to track STECs will provide a clearer picture of their true impact on the food supply and public health. E. coli foodborne outbreaks reported to CDC are most often linked to the O157:H7 strain (18). In the United States, non-O157 STECs are rarely identified in foodborne outbreaks or sporadic disease reports, though some improvements made in reporting, surveillance and laboratory testing has led to a slight increase in non-O157 outbreak detection and reporting since 2006. Surveillance for most STECs is nascent: while samples are routinely tested for E. coli O157:H7 in 70 percent of laboratories in FoodNet sites, only about four percent of these laboratories tested stool specimens for non-O157 strains in 2007 (18). In 2009, CDC recommended that all clinical laboratories routinely test for Shiga toxin production in human stool specimens of the top six serogroups (O26, 103, O111, O121, O45, and O145) that account for the majority of reported non-O157 STEC infections (6). In addition, improvements in the diagnosis of STECs would produce more robust data, but commercial diagnostic tests are not readily available for human diagnosis.

On-farm management strategies

On-farm controls are being evaluated for use in managing the risks from pathogenic *E. coli* strains. Some U.S. companies are testing feed management practices and the use of vaccinations in live animals to reduce the number of animals carrying *E. coli* O157:H7. It is unclear if these approaches would also be effective against other pathogenic strains of *E. coli* (22, 45).

Despite disease-causing pathogens originating in animals, many outbreaks have occurred in produce items, indicating the possibility of cross contamination on farms or in production facilities, retail establishments, or consumers' homes (22). The agriculture sector's involvement is needed to make food safety and awareness of STEC contamination and prevention a higher priority for farmers and consumers. FDA has the opportunity to establish science-based standards for the safe production of high-risk fruits and vegetables with the adoption of the FDA Food Safety Modernization Act. These standards will govern soil amendments, animals in the growing areas, and water use-each of which can play a role in cross contamination on the farm.

Processing management strategies

USDA recently announced its intention to require meat processing companies to "test-and-hold" product, a process in which USDA analyzes beef for pathogens and maintains control of the product until negative results are confirmed (43). In the wake of this announcement, at least one major processor announced the expansion of its own test-and-hold protocol to include testing for non-O157 STECs.

Driven in part by the government's zero tolerance policies, the meat industry has identified a number of control strategies used to manage E. coli O157:H7 that could also reduce the presence of other pathogenic E. coli strains, such as oxidizing treatments, thermal manipulations, and use of organic compounds in meat processing (2). Prevention and reduction of contamination and of cross contamination at the processing level is essential to reduce the impact of STECs in the food supply; however, government programs are still developing strategies for monitoring the industry control of these pathogens.

Further research priorities

To investigate risk factors and transmission of non-O157 STECs, descriptive studies of outbreaks and reviews of sporadic cases are needed. Case control studies that investigate the clinical features, patient outcomes, and potential reservoirs by serotype and virulence profile will enhance understanding of the risk factors and pathogenicity of STECs.

EMERGING FOODBORNE PATHOGENS: ANTIBIOTIC RESISTANCE

In 2003, a panel of international experts concluded that human health is threatened by adverse consequences from ABR pathogens resulting from the use of antibiotics in food-producing animals (56). These consequences include infections that would not have otherwise occurred, increased frequency of treatment failures (including death), and increased severity of infections (56).

Food-related outbreaks provide additional evidence that resistant pathogens have contaminated the U.S. food supply, resulting in adverse public health outcomes. Since 1973, approximately 20,000 people have been affected by 35 well-documented food-related outbreaks involving ABR pathogens (10). In addition, it appears that the incidence of multi-drug resistant pathogens is increasing, as is the total number of ABR foodborne outbreaks reported in the United States.

The 2003 expert panel further concluded:

"Evidence shows that the amount and pattern of non-human usage of antimicrobials impacts on the occurrence of resistant bacteria in animals and on food commodities and thereby human exposure to these resistant bacteria. The foodborne route is the major transmission pathway for resistant bacteria and resistance genes from food animals to humans, but other routes of transmission exist" (56).

These conclusions are well supported by evidence spanning several decades linking the emergence and proliferation of ABR *Salmonella* and *Campylobacter* spp. in animal populations with antibiotic use in food-animal production (17, 26, 40). In studies comparing *Campylobacter jejuni* in organic and conventionally-raised poultry, the *Campylobacter* isolated from the organic birds was significantly more sensitive to antibiotics (25), while the *Campylobacter* found on conventionally-raised poultry exhibited significantly more resistance to the tested antibiotics. Researchers have identified fluoroquinolone-resistant *E. coli (12)*, third and fourth generation cephalosporin resistance in *Salmonella* spp. (1, 11), and zoonotic methicillinresistant *Staphylococcus aureus* (MRSA) (20) and *Clostridium difficile (37)* as emerging problems in the food supply.

Resistant bacteria can displace the sensitive bacteria in environments where antibiotics are in use, a phenomenon referred to as "second-hand selection of antibiotic resistance" (24, 30). When a single animal is treated, that animal is one potential reservoir of antibiotic resistance, but when multiple animals are administered even low levels of a drug, each animal becomes a potential reservoir of ABR bacteria. Antibiotics affect commensal organisms as well as pathogens, and nearly all bacteria have the potential to share resistance genes with other bacteria (29).

Government policy and riskmanagement options

Drug approval is the principal risk management strategy used to deal with the issue of antibiotic resistance. The U.S. Food and Drug Administration Center for Veterinary Medicine (FDA-CVM), which approves antibiotics for use in animals, has historically used antibiotic residues in meat from foodanimals as its primary criterion for approval, without examining the potential for ABR pathogens. In 2003, FDA published Guidance #152, which outlined a voluntary approach for assessing the safety of new antimicrobial animal drugs and the effects of these medicines on bacteria of human health concern (47). The agency's position is that this approach should be applied to all drugs, including those approved before the implementation of the guidance, but FDA has given no timeline for doing this (52).

Periodic review and revision of FDA-CVM policies on extralabel use of drugs in veterinary medicine for foodproducing animals are also needed. In 2008, FDA proposed a rule to prohibit extralabel use of cephalosporins. That rule was not implemented, pending investigation of concerns raised by the agricultural industry. In 2011, consumer, medical, and animal health advocacy groups requested that FDA issue the rule, following an outbreak of cephalosporin-resistant *Salmonella* Hadar in frozen turkey patties that caused 12 cases of human illness (7).

In June 2010, FDA issued Draft Guidance on the Judicious Use of Medically Important Antimicrobial Drugs in Food-Producing Animals, Guidance #209 (49). These voluntary guidelines propose limiting the use of medically important antibiotics in food-animals to instances necessary for assuring animal health, as well as increasing veterinary oversight or consultation. The draft guidelines declare that antibiotics used for growth promotion are not considered judicious. While the guidance signals that FDA's policy position on risk management is consistent with many in the public health community, the time frame for implementation should be made explicit.

The World Health Organization (WHO) and World Organization for Animal Health (OIE) also have recommended the implementation of "thresholds of resistance" and strict use requirements for classes of antibiotics identified as critically important for human health. Following the European Union's (EU) ban on the use of antibiotics as growth promoters in 2006, a number of countries have put in place restricted use requirements (55). Harmonized data collection and protective policies on antibiotic usage in food-animals between the United States and the EU was also recommended in the June 2011 Transatlantic Consumer Dialogue (TACD) meeting (41).

To summarize, important risk management strategies and policy considerations that could reduce antibiotic resistance include the following:

- eliminating over-the-counter availability;
- requiring a veterinarian's prescription for antibiotics used in food-animals if the drugs are also used in human medicine or if they cross react with other antibiotics used in human medicine;
- developing drugs that do not promote antibiotic resistance;
- reducing the levels of human pathogens in the food-animal population;
- implementing improvements in animal genetics, husbandry, and hygiene practices; and

• enhancing farmer education on ABR pathogens (3).

Surveillance and epidemiology

An integrated monitoring system, with coordinated inputs from the medical, veterinary, and food sectors, is necessary to identify appropriate risk management strategies. WHO specifies that such a system would include ongoing testing of foodborne bacteria recovered from humans, food-animals, and meat (57).

The National Antimicrobial Resistance Monitoring System (NARMS), a joint project of FDA, CDC, and USDA, was established in 1996 to monitor antimicrobial susceptibility among some types of enteric bacteria from humans, retail meats, and food animals. Those currently under surveillance are Salmonella, Campylobacter, E. coli, and Enterococcus. Each agency that participates in NARMS publishes its own annual report, reflecting results from the portion of the program for which it is responsible. In addition, FDA-CVM compiles an executive report summarizing NARMS data in an integrated format (50). However, sampling, collection, analysis, and reporting from the three agencies vary widely and are not integrated to provide an early warning system or to determine the risks from ABR pathogens and the strategies necessary to combat them (52). Conference participants agreed that NARMS has been chronically underfunded and that adequate resources are needed to develop coordinated collection and laboratory methods as well as to allow researchers improved access to comparable data for further analyses.

In the United States, drug companies are required to report antibiotics sold for food-animal use by class under the Animal Drug User Fee Amendments (48) of the Federal Food, Drug, and Cosmetic Act (14). However, the information collected and reported lacks details that would help target risk management strategies. Tracking antibiotics used in food-animals would be more useful for ABR monitoring if it included the species, method of administration, and intended purpose of their use. WHO and OIE recommend this more robust approach be used to analyze antibiotic use and determine what targeted steps could be taken to reduce it (57).

On-farm management strategies

The participation of persons representing agricultural interests was sparse at the conference. Several panel members discussed potential on-farm strategies that may be used for future discussions or symposia, but much of the focus was on lessons to be learned from European countries that have implemented stronger measures to decrease/ban non-therapeutic antibiotic use in food-producing animals.

Educating farmers on best husbandry practices is a critical component of any system, since it could be expected to reduce the need for animal drugs. Furthermore, providing farmers and veterinarians with feedback in the form of surveillance and drug use data could be important change management tools.

One existing method that couples analysis of surveillance data with specific farm action is the use of a "yellow card" system. This method was implemented in Denmark in 2010 to alert farmers when they are at risk of overusing antibiotics, based on deviations from average antimicrobial use (55). The success of the yellow card system demonstrates that, to have an impact on farms, the social norms and operating practices of the agriculture industry, agricultural workers, and veterinarians all need to change (21). The yellow card initiative, in combination with several other initiatives (including strict limitations on the use of medicines deemed critical for treating human illness; renewal of veterinary advisory service contract agreement requirements; revised treatment guidelines) targeting the swine industry, were put into action in 2010. Thus far, results show a reduction in the total antimicrobials consumed by pigs in Denmark (9). Among the countries where data is collected, Denmark has one of the lowest levels of veterinary antibiotic use.

However, the current dominant belief in U.S. agriculture is that nontherapeutic antibiotic use is an acceptable husbandry practice even when there is no medical indication that it is necessary for the health of the animal. This attitude would have to change before actions similar to those in Denmark would be effective in the United States (3).

The continued success of the food animal production industry in several

European countries, where the use of antibiotics as growth-promoters has been disallowed, provides evidence regarding the effectiveness of regulations limiting drug use in food-animals as a method of reducing ABR pathogens. However, increasing the number of veterinarians directly involved in U.S. food-animal production was described by conference participants as a potential obstacle to requiring prescription-only antibiotic use on the farm.

Processing management strategies

The transportation and housing of food-animals provides opportunities for pathogens to transfer from one animal or group to other groups of uninfected animals. Cross contamination of carcasses is also possible in slaughter and processing facilities (35, 54).

To encourage best practices in slaughter and processing, CSPI has petitioned USDA to declare four ABR strains of *Salmonella* as adulterants within the meaning of the Federal Meat Inspection Act (FMIA) (4, 15). The adoption of this type of legal action level or tolerance may promote further preventive steps at the processing level by improved monitoring of the meat supply that may decrease consumer exposure to ABR pathogens. USDA has yet to act on the petition.

Further research priorities

Additional suggested research priorities on ABR pathogens include developing effective alternatives to antibiotics to combat bacterial disease; evaluating the effectiveness of non-antibiotic alternatives that already exist; developing better diagnostic tests to enable earlier detection and targeted treatment; quantifying the effects of antibiotics on modern food-animal production; and developing methods to reduce or eliminate established ABR pathogens (23).

LEGAL RESPONSES

In 2011, CSPI filed a petition seeking expansion of the definition of adulteration to include particular strains of ABR *Salmonella* spp. (*Salmonella* Heidelberg, *Salmonella* Newport, *Salmonella* Hadar, and *Salmonella* Typhimurium) that are known to cause disease or have appeared frequently in NARMS samples. Such a declaration would require industry and the government to expand its testing for these pathogens and to withhold products from commerce when positive isolates are found. USDA was urged to expand the definition of adulteration through the use of its interpretive rule authority.

In 1999, the Natural Resources Defense Council (NRDC), CSPI, and several other organizations petitioned FDA to rescind its approval for subtherapeutic uses of certain medically important antibiotics in animal feed (34). The petition alleged that such uses are unsafe under the Federal Food, Drug, and Cosmetic Act because their use in food animal production leads to antibiotic resistance and, ultimately, constitutes a public health danger for consumers. In 2011, those same organizations filed a lawsuit against FDA for its failure to act on the petition. Citing the 2003 National Academy of Sciences' report warning that the presence of untreatable infections is growing, the plaintiffs asked the court to declare FDA's failure to withdraw approval for the listed drugs as unlawful, to compel FDA to withdraw approval, and to compel a final response to the 1999 petitions (and a similar petition filed in 2005) (34). In March 2012, the United States District Court in the Southern District of New York ordered FDA to initiate withdrawl proceedings, as requested in the petition. This order will redirect FDA from its previous response to petitioners, stated in November 2011, to work with the animal pharmaceutical industry, veterinarians, and public health communities on a voluntary strategy to implement the principles of judicious use of antibiotics in food-producing animals.

Legislation

The Preservation of Antibiotics for Medical Treatment Act (PAMTA) was re-introduced in the 112th Congress. PAMTA would require FDA to phase out the non-therapeutic use in livestock of medically important antibiotics and require public health standards to be applied to new approvals of animal antibiotics. The bill would continue to allow the use of the drugs to treat sick animals. PAMTA does not restrict the use of antibiotics in food-animals unless those antibiotics are classified as important in human medicine (53).

DISCUSSION

Both STEC and ABR pathogens have emerged as public health hazards requiring a comprehensive and collaborative response utilizing multi-layered risk management approaches and activities. When problems are documented through surveillance, effective consumer protection entails control measures implemented at multiple points along the farm-tofork continuum. Post-production risk management by consumers alone is not sufficient to protect either public health or business; risk management strategies must be implemented at every step of the food system, beginning with raising animals and progressing to final food preparation and consumption.

Managing the risks of STEC and ABR pathogens in the food supply provides both unique and complementary challenges. Although both pose significant risks to consumers, the approaches employed to combat them may not be identical. Current risk management strategies for STECs are focused at the processing and consumer level, with little emphasis on the animal production level, whereas those used for managing ABR pathogens occur at both the drug approval stage and with improved application on the farm. Controlling antimicrobial use in food-animals would be most effective to reduce the occurrence of ABR pathogens in the food supply (38).

Currently, several federal agencies are responsible for specific aspects of regulation and oversight. While USDA regulates the meat and poultry supply and some egg products, FDA has oversight over all other food categories and approval authority for all drugs used for humans or animals. The involvement of multiple agencies with differing regulatory approaches has resulted in inconsistent policies as well as confusion in the industries and among the public. For example, USDA has announced an expansion of its test-and-hold program to keep E. coli O157:H7 adulterated products out of commerce. However, no FDA-regulated product is managed under a test-and-hold program, and non-meat products containing STEC

pathogens can reach consumers without consistent testing or control systems. Coordination is needed to ensure that protection from these hazards is robust and streamlined across industries and across products, regardless of which agency has oversight. The streamlining of interagency coordination, communication, and transparency would allow for better management of foodborne hazards and would decrease industry and consumer confusion.

In addition, on-farm oversight is not utilized by the federal government in the food safety arena, which leaves consistent federal tools confined to drug approval and at processing plants. As STEC and ABR pathogens evolve, production agriculture must examine the practices that may exacerbate food safety risks, such as the crowded, unhygienic conditions that can give rise to the spread of pathogens and the overuse of antibiotics. Collaborative discussions with industry, government, academia, and public health advocates are most likely to lead to substantive and sustainable change.

USDA and FDA have held such discussions, including a joint public meeting in November 2011 with FSIS, the Animal and Plant Health Inspection Service (APHIS) and the Agricultural Research Service (ARS), to discuss on-farm issues and their relationship to food safety. The Pre-harvest Food Safety for Cattle Public Meeting focused on pathogen control strategies at pre-harvest for reducing the prevalence of STECs and Salmonella in and on live cattle. Discussion centered on interventions and strategies that can control pathogens to reduce the likelihood of end-product contamination (and thus human foodborne illnesses). Pre-harvest technologies, such as probiotics, sodium chlorate and bacteriophage, were a focus of many presentations and workshop discussions. Participants also reviewed scientific studies on food-producing animal vaccines, considered by many to be one of the more promising pre-harvest technologies (45).

Vaccinating food-producing animals at the pre-harvest level for STECs, primarily targeting *E. coli* O157:H7 in cattle, is gaining attention from industry and academia. Vaccines can decrease fecal shedding of pathogenic bacterium, which decreases their prevalence in the environment, on carcasses, and in the final food product (45). Both Iowa State University and Texas Tech University have conducted research (field trails and whole-herd vaccination approaches) to demonstrate the efficacy and potential impact of a particular vaccine for *E. coli* O157:H7 in beef cattle (*45*). Currently, the vaccine has a conditional license, but use of the vaccine by the cattle industry has been low. Stakeholders should explore ways to remove barriers to adoption of such interventions where they are shown to be effective.

Federal databases, such as NARMS, PulseNet and VetNet, use different nomenclature and are often incompatible with one another. Communication between agencies is scanty, leading to duplication of data collection and wasted resources. Better management of emerging pathogens requires a more responsive surveillance system and better screening tools so that information can be gathered and analyzed rapidly. The surveillance system requires cooperation between the federal agencies as well as with the state and local agencies that often collect the data. Great variability exists among state and local health departments in discovering, investigating, and reporting foodborne illness, often because of a lack of adequate funding for even core public health services.

The prioritization of research needs to be clearly delineated by government agencies to forge a coherent plan for risk management, but identifying research gaps and finding effective control measures and interventions are a shared responsibility of industry and government. Developing a mechanism for collecting and sharing industry data outside a regulatory framework may be appropriate to discover and implement solutions to these challenging problems.

Utilizing industry data to support best practices will advance successful methods and interventions most rapidly. Creating a feedback loop for data sharing with industry, along with government incentives, can help mobilize the industry to improve practices more rapidly. Combining positive rewards with disincentives, such as fines for non-compliance, may motivate companies to engineer new and retool existing technologies to manage food safety hazards related to ABR and STEC pathogens.

CONCLUSIONS

The vulnerability of food systems in the United States and across the world

to outbreaks of ABR pathogens and STECs are due to a combination of factors: the evolution and mutation of bacteria in response to their environment, the shared global food supply, outdated or inadequate risk management procedures and policies, and the overuse and misuse of antibiotics. Although there is strong evidence of the threats facing the public from both STEC and ABR pathogens in the environment and in the food supply, the existing surveillance system has not captured the impact of emerging pathogens on the food supply and human health in a systematic and proactive way. When problems are documented through integrated surveillance systems, effective public health protection will require implementation of control measures at multiple points along the farm-to-fork continuum. All stakeholders must be willing to entertain new approaches to protect human and animal health and ensure the safety of the food supply.

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REFERENCES

- Alcaine, S. D., S. S. Sukhnanand, L. D. Warnick, W. L. Su, P. McGann, P. McDonough, and M. Wiedmann. 2005. Ceftiofur-resistant Salmonella strains isolated from dairy farms represent multiple widely distributed subtypes that evolved by independent horizontal gene transfer. Antimicrob. Agents Chemother. 49:4061–4067.
- Bernard, D. 2011. Strategies for Managing Risk of STEC. Available at: http://www.saveantibiotics.org/ resources/Bernard%20PEW%20 CSPI%20Jan%2025%202011%20 conference.pdf. Accessed 6 March 2012.
- 3. Brown, S. A. 2011. Approaches to Risk Mitigation: a Research and Development Perspective. Available at: http://www.saveantibiotics. org/resources/Brown%20PEVV%20 CSPI%20Jan%2025%202011%20 conference.pdf. Accessed 6 March 2012.

- 4. Center for Science in the Public Interest. 2011. Citizen petition to USDA Food Safety and Inspection Service for an interpretive rule declaring specific strains of antibiotic-resistant Salmonella in ground meat and poultry to be adulterants within the meaning of 21 U.S.C. § 601(m)(1) and (2)(A) and 21 U.S.C. §453(g)(1) and (g)(2). Available at: http://www.fsis.usda.gov/PDF/Petition_CSPI_052511.pdf. Accessed 2 August 2011.
- 5. Centers for Disease Control and Prevention. 2007. Bacterial foodborne and diarrheal disease national case surveillance annual report, 2005. Available at: http:// www.cdc.gov/nationalsurveillance/PDFs/fbsurvsumm2005.pdf. Accessed 3 August 2011.
- Centers for Disease Control and Prevention. 2009. Recommendations for diagnosis of shiga toxinproducing Escherichia coli infections by clinical laboratories. MMWR 58(No. RR-12). Available at: http:// www.cdc.gov/mmwr/pdf/rr/rr5812. pdf.Accessed 10 August 2011.
- 7. Centers for Disease Control and Prevention. 2011. Investigation announcement: Multistate outbreak of Salmonella Hadar infections associated with turkey burgers. Available at: http://www.cdc.gov/salmonella/ hadar0411/040411/index.html. Accessed 15 July 2011.
- Centers for Disease Control and Prevention. 2011. Investigation update: multistate outbreak of human Salmonella Heidelberg infections linked to turkey. Available at: http:// www.cdc.gov/salmonella/heidelberg/092911/index.html. Accessed 1 October 2011.
- 9. Danish Agriculture and Food Council. 2011. Denmark to take the lead in limiting the spread of antimicrobial resistance. Available at: http://www.agricultureandfood. co.uk/Current_issues/Danish_ Matters/2011/July/Denmark_to_ take_the_lead_in_limiting_the_ spread_of_antimicrobial_resistance.aspx#.TtfUFLJwjJN. Accessed 15 November 2011.
- DeWaal, C. S., C. Roberts, and C. Catella. 2011. Antibiotic resistance in foodborne pathogens: evidence of the need for a risk management strategy. Center for Science in the Public Interest, 25

January. Available at: http://cspinet. org/new/pdf/abrfoodbornepathogenswhitepaper.pdf. Accessed 15 July 2011.

- Dutil, L., R. Irwin, R. Finley, L. K. Ng, B. Avery, P. Boerlin, A. M. Bourgault, L. Cole, D. Daignault, A. Desruisseau, W. Demczuk, L. Hoang, G. B. Horsman, J. Ismail, F. Jamieson, A. Maki, A. Pacagnella, and D. R. Pillai. 2010. Ceftiofur resistance in Salmonella enterica serovar Heidelberg from chicken meat and humans, Canada. Emerg. Infect. Dis. 16(1):48–54.
- Endtz, H. P., G. J. Ruijs, B. van Klingeren, W. H. Jansen, T. van der Reyden, and R. P. Mouton. 1991. Quinolone resistance in *Campy-lobacter* isolated from man and poultry following the introduction of fluoroquinolones in veterinary medicine. *J. Antimicrob. Chemother*. 27(2):199–208.
- European Food Safety Authority. 2011. Urgent advice on the public health risk of Shiga-toxin producing *Escherichia coli* in fresh vegetables. *EFSA J.* 9(6):2274; doi:10.2903/j. efsa.2011.2274. Available at: www.efsa.europa.eu/efsajournal/ doc/2274.pdf. Accessed 2 August 2011.
- 14. Federal Food, Drug, and Cosmetic Act. 1938. Public Law 75–717.
- Federal Meat Inspection Act. 1906. Available at: http://www.fsis.usda. gov/regulations_&_Policies/Federal_Meat_Inspection_Act/index. asp.Accessed 2 August 2011.
- 16. Gerner-Smidt, P. 2011. The Public Health Impact of STECs in Food. Available at: http://www.save antibiotics.org/resources/Gerner % 2 0 S m i d t % 2 0 P E W % 2 0 C S P I % 2 0 J a n % 2 0 2 5 % 2 0 2011 % 2 0 c onference.pdf. Accessed 6 March 2012.
- Glynn, M. K., C. Bopp, W. DeWitt, et al. 1998. Emergence of multidrug-resistant Salmonella enterica serotype Typhimurium DT104 infections in the United States. New Engl. J. Med. 338:1333–1338.
- 18. Griffin, P. 2011. State of the Science Knowledge and Gaps about Shiga Toxin-producing *E. coli* (STEC) Infections in the United States. Available at: http://www.saveantibiotics.org/resources/Griffin%20 PEW%20CSPI%20Jan%2025%20 2011%20conference.pdf. Accessed 6 March 2012.

- Hedberg, C.W. 2011. Personal communication [hedbe005@umn. edu].
- Huijsdens, X. W., B. J. van Dijke, E. Spalburg, M. G. van Santen-Verheuvel, M. E. Heck, G. N. Pluister, A. Voss, W. J. B. Wannet, and A. J. de Neeling. 2006. Community-acquired MRSA and pig-farming. Ann. Clin. Microb. Antimicrob. 5(26).
- Jan, J. S., W. A. McIntosh, and H. M. Scott. 2010. The effects of moral obligations to others and others' influence on veterinarians' attitudes toward and recommendations to utilize antibiotics in feedlot cattle. *J. Rural Soc. Sci.* 25(2):122–148.
- LeJeune, J. 2011. Risk Analysis Framework for STEC. Available at: http://www.saveantibiotics.org/ resources/LeJeune%20PEW%20 CSPI%20Jan%2025%202011%20 conference.pdf. Accessed 6 March 2012.
- Levy, S. B. 2011. Environmental and Societal Impacts of Antibiotics. Available at: http://www.saveantibiotics.org/resources/Levy%20 PEW%20CSPI%20Jan%2025%20 2011%20conference.pdf. Accessed 6 March 2012.
- 24. Levy, S. B., and B. Marshall. 2004. Antibacterial resistance worldwide: Causes, challenges and responses. *Nature Med.* 10: 5122–5129.
- Luangtongkum, T., T. Y. Morishita, A. J. Ison, S. Huang, P. F. McDermott, and Q. Zhang. 2006. Effect of conventional and organic production practices on the prevalence and antimicrobial resistance of *Campylobacter* spp. in poultry. *Appl. Environ. Microb.* 72(5):3600–3607.
- Lyons, R. W., C. L. Samples, H. N. DeSilva, et al. 1980. An epidemic of resistant Salmonella in a nursery. J. Am. Med. Assoc.; DOI: 10.1001/ jama.1980.03300320038021. Accessed 2 August 2011.
- Marler, B. 2010. Press Advisory

 Non-E. coli O157:H7 EHEC should be "adulterants." Food Poisson Journal. 28 August. Available at: http://www.foodpoisonjournal. com/food-policy-regulation/pressadvisory-none-coli-0157h7-ehec-should-be-adulterants/. Accessed 2 August 2011.
- Marler Clark LLP PS, Outbreak Inc., the family of June Dunning, M. Richards, and S. Johnson. 2009. Citizen petition

to USDA Food Safety and Inspection Service for an interpretive rule declaring all enterohemorrhagic shiga toxin-producing serotypes of *Escherichia coli* (*E. coli*), including non-O157 Serotypes, to be adulterants within the meaning of 21 U.S.C. § 601(m)(1). Available at: http://www.fsis.usda.gov/PDF/ Petition_Marler_100509.pdf. Accessed 2 August 2011.

- Marshall, B. M., D. J. Ochieng, and S. B. Levy. 2009. Commensals: Underappreciated reservoirs of resistance. *Microbe Mag.* 4(5):231–8.
- Miller, Y. W., E. A. Eady, R. W. Lacey, J. H. Cove, D. N. Joanes, and W. J. Cunliffe. 1996. Sequential antibiotic therapy for acne promotes the carriage of resistant staphylococci on the skin of contacts. J. Antimicrob. Chem. 38:829–837. Available at: http://jac.oxfordjournals.org/content/38/5/829.full.pdf. Accessed 3 August 2011.
- 31. National Antimicrobial Resistance Monitoring System. 2008. Animal Arm Annual Report. Available at: https://www.ars.usda.gov/ SP2UserFiles/Place/66120508/ NARMS/NARMS2008/NARMS-AnimalArm2008.pdf. Accessed 5 August 2011.
- 32. National Center for Biotechnology Information. 2010. PubMed Health. Available at: http://www. ncbi.nlm.nih.gov/pubmedhealth/ PMH0001539/. Accessed 1 August 2011.
- Nayak, R., and P. B. Kennedy. 2002. Screening of Salmonella isolates from a turkey production facility for antibiotic resistance. *Poult. Sci.* 81:1496–1500.
- 34. Natural Resources Defense Council INC, Center for Science in the Public Interest, Food Animal Concerns Trust, Public Citizen INC, Union of Concerned Scientists INC v. United States Food and Drug Administration, Margaret Hamburg, Center for Veterinary Medicine, Bernadette Dunham, United States Department of Health and Human Services, Kathleen Sebelius, 2011. Civil Action No. 11 CV 3562. U.S. District Court for the southern District of New York, 25 May 2011. Available at: http://cspinet.org/new/ pdf/nrdc_complaint.pdf. Accessed I August 2011.

- Nde, C. W., J. M. McEvoy, J. S. Sherwood, and C. M. Logue. 2007. Cross contamination of turkey carcasses by *Salmonella* species during defeathering. *Poult. Sci.* 86(1):162– 167.
- Rangel, J. M., P. H. Sparling, C. Crowe, P. M. Griffin, and D. L. Swerdlow.
 2005. Epidemiology of *Escherichia coli* O157:H7 outbreaks, United States, 1982–2002. *Emerg Infect Dis*. Available at: http://www.cdc.gov/ ncidod/EID/voll1no04/04-0739. htm. Accessed 2 August 2011.
- Rupnik, M. 2007. Is Clostridium difficile-associated infection a potentially zoonotic and foodborne disease? Clin. Microbiol. Infect. 13:457–459.
- SafeFood. 2010. The problem of antimicrobial resistance in the food chain. ISBN: 878–1–905767–10–6. Available at: http://www.safefood. eu/Global/Publications/Research%20reports/The_Problem_ of_antimicrobial_resistance_in_the_ food_chain.pdf?epslanguage=en. Accessed 18 August 2011.
- Scallan, E., R. M. Hoekstra, F.J. Angulo, R.V. Tauxe, M. A. Widdowson, S. L. Roy, J. L. Jones, and P.M. Griffin. 2011. Foodborne Illness Acquired in the United States—Major Pathogens. *Emerg. Infect. Dis.* Available at: http:// www.nc.cdc.gov/eid/article/17/1/ p1-1101_article.htm. Accessed 6 March 2012.
- Smith, K. E., J. M. Besser, and C. W. Hedberg, et al. 1999. Quinoloneresistant *Campylobacter jejuni* infections in Minnesota, 1992–1998. *New Engl. J. Med.* 340:1525–1532.
- Transatlantic Consumer Dialogue. 2011. Resolution on antimicrobials in animal and food production. Available at:http://cspinet.org/new/ pdf/tacd_amr_resolution_-_final. pdf.Accessed 15 July 2011.
- 42. U.S. Department of Agriculture. 2007.Non-Escherichia coli O157:H7 shiga toxin-producing E. coli. Docket No. FSIS-2007-0041. Available at: http://www.fsis.usda.gov/OP-PDE/rdad/FRPubs/2007-0041.pdf. Accessed 3 August 2011.
- 43. U.S. Department of Agriculture. 2011. USDA announces proposed test-and-hold requirement for meat and poultry products. News Transcript No. 0151.11. Available at:http://www.usda.gov/wps/portal/

usda/usdahome?contentidonly=tr ue&contentid=2011/04/0151.xml. Accessed 5 August 2011.

- 44. U.S. Department of Agriculture. 2011. USDA takes new steps to fight *E. coli*, protect the food supply. Available at: http://www. usda.gov/wps/portal/usda/ usdahome?contentid=2011/09/0400. xml&contentidonly=true. Accessed 13 September 2011.
- U.S. Department of Agriculture. 2011. Pre-harvest for cattle public meeting. Available at: http://www. fsis.usda.gov/PDF/Cattle_Public_Mtg_110911.pdf. Accessed 21 February 2012.
- 46. U.S. Department of Health and Human Services. 2011. Healthy-People.gov 2020 topics & objectives: food safety. Available at: http://healthypeople.gov/2020/ topicsobjectives2020/objectives list.aspx?topicld=14. Accessed 16 August 2011.
- 47. U.S. Food and Drug Administration. 2003. #152 Guidance for industry, evaluating the safety of antimicrobial new animal drugs with regard to their microbiological effects on bacteria of human health concern. Available at: http://www.fda. gov/downloads/AnimalVeterinary/ GuidanceComplianceEnforcement/ GuidanceforIndustry/ucm052519. pdf.Accessed 2 August 2011.
- 48. U.S. Food and Drug Administration. 2009. Summary report on antimicrobials sold or distributed for use in food-producing animals. Available at: http://www.fda.gov/ downloads/ForIndustry/UserFees/

AnimalDrugUserFeeActADU-FA/UCM231851.pdf. Accessed 2 August 2011.

- 49. U.S. Food and Drug Administration. 2010. FDA issues draft guidance on the judicious use of medically important antimicrobials in foodproducing animals. Available at: http://www.fda.gov/newsevents/ newsroom/pressannouncements/ ucm217464.htm. Accessed 20 July 2011.
- 50. U.S. Food and Drug Administration. 2011. National antimicrobial resistance monitoring system. Available at: http://www.fda.gov/ AnimalVeterinary/SafetyHealth/ AntimicrobialResistance/National-AntimicrobialResistanceMonitoringSystem/default.htm. Accessed 15 July 2011.
- 51. U.S. General Accounting Office. 2004. Antibiotic resistance federal agencies need to better focus efforts to address risk to humans from antibiotic use in animals. GAO-04-490. Available at: http:// www.gao.gov/new.items/d04490. pdf.Accessed I August 2011.
- 52. U.S. General Accounting Office. 2011. Antibiotic resistance agencies have made limited progress addressing antibiotic use in animals. GAO-11-801. Available at: http:// www.gao.gov/new.items/d11801. pdf.Accessed 27 September 2011.
- 53. U.S. House of Representatives, Congresswoman Louise M. Slaughter. 2011. PAMTA. Available at: http://www.louise.house.gov/index. php?option=com_content&view =article&id=1315<emid=138. Accessed 2 August 2011.

- Warriner, K., T. G. Aldsworth, S.Kaur, and C.E.Dodd. 2002. Crosscontamination of carcasses and equipment during pork processing. *J. Appl. Microbiol.* 93(1):169–177.
- 55. Wegener, H.C. 2011. The Public Health Impact of Antibiotic Resistant Pathogens in Food. Available at: http://www.saveantibiotics.org/ resources/Wegener1PEW%20 CSP1%20Jan%2025%202011%20 conference.pdf. Accessed 6 March 2012.
- 56. World Health Organization. 2004. Joint FAO/OIE/WHO expert workshop on non-human antimicrobial usage and antimicrobial resistance: scientific assessment. Available at: http://www.who.int/foodsafety/ publications/micro/en/amr.pdf. Accessed 3 August 2011.
- 57. World Health Organization. 2009. Report of the 1st meeting of the WHO advisory group on integrated surveillance of antimicrobial resistance (AGISAR). ISBN: 9789241501446.Available at: http:// www.who.int/foodsafety/foodborne_disease/AGISAR_2009_report_final.pdf. Accessed 15 July 2011.
- 58. World Health Organization Regional Office for Europe. 2011. Outbreaks of *E. coli* O104:H4 infection: update 30. Available at: http://www.euro.who.int/en/whatwe-do/health-topics/emergencies/ international-health-regulations/ news/news/2011/07/outbreaks-ofe.-coli-o104h4-infection-update-30. Accessed 3 October 2011.