United States Government Accountability Office

GAO

Report to the Secretary of Agriculture

March 2012

FOOD SAFETY

Preslaughter Interventions Could Reduce *E. coli* in Cattle

GAO-12-257

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Highlights

Highlights of GAO-12-257, a report to the Secretary of Agriculture

Why GAO Did This Study

Since 2006, the U.S. beef industry has recalled over 23 million pounds of beef owing to contamination from pathogenic strains of Shiga toxin-producing *Escherichia coli* (STEC) bacteria. These strains do not harm cattle but may contaminate meat during slaughter. If humans eat contaminated meat without properly cooking it, STEC can cause illnesses, including bloody diarrhea and Hemolytic Uremic Syndrome, which is characterized by kidney failure and can be fatal. The Departments of Health and Human Services (HHS) and of Agriculture (USDA) play a role in reducing STEC. USDA stated that interventions to reduce STEC before slaughter offer a significant opportunity to improve food safety.

GAO reviewed (1) interventions before slaughter that may help reduce STEC in cattle; (2) USDA's role in approving STEC vaccines; (3) the extent to which STEC strains have been determined to be adulterants in beef and the status of tests to detect them; and (4) practices, if any, other countries have employed that could reduce STEC in cattle and may be relevant to U.S. efforts. GAO reviewed documents; visited cattle feedlots and a slaughter plant; and interviewed agency officials, researchers, and industry and consumer group representatives with expertise in STEC in cattle.

What GAO Recommends

GAO recommends, among other things, that USDA provide more specific public guidance on the license approval requirements of STEC vaccines. USDA neither agreed nor disagreed with this recommendation.

View GAO-12-257 or key components.
For more information, contact Lisa Shames at (202) 512-3841 or shamesl@gao.gov.

What GAO Found

U.S. Department of Agriculture (USDA) and university researchers identified several treatments administered before cattle are slaughtered, or preslaughter interventions, that could reduce Shiga toxin-producing *Escherichia coli* (STEC) in cattle. Such preslaughter interventions include bacteriophages (viruses that infect and kill bacteria), probiotics (live bacteria that can benefit the digestive system), vaccines (biological preparations that alter the immune system), and sodium chlorate (chemical that kills the STEC O157:H7 strain). However, few manufacturers have submitted applications for preslaughter intervention products to target STEC according to officials from USDA and the Food and Drug Administration. One exception is for vaccines to reduce STEC O157:H7.

For preslaughter interventions, USDA exercises responsibilities for licensing and regulating STEC vaccines. However, USDA's approval requirements for these vaccines are unclear, according to some industry representatives. Specifically, USDA's general guidance does not address some of the unique challenges faced by manufacturers of animal health products seeking STEC vaccine approval. For example, the guidance does not explain that, if studies conducted in the laboratory are insufficient to demonstrate efficacy, the manufacturer would also need to demonstrate that the vaccine is effective in a field setting such as a feedlot. In contrast, the Canadian Centre for Veterinary Biologics provides more specific guidance about when it requires the use of laboratory or field studies to demonstrate efficacy for vaccine license applications. Without guidance that gives manufacturers clear and more specific information they need to submit for an acceptable application, the approval process for STEC vaccines could face potential delays.

In addition to STEC O157:H7, which it stated in 1994 was an adulterant—a substance that renders food injurious to human health—in September 2011, USDA determined that six other STEC strains were adulterants in raw ground beef and beef trim (meat left after steaks and roasts are cut from beef). USDA has tests for these six strains and plans to use them in slaughter plants starting in June 2012. However, it may be difficult and time-consuming to confirm positive test results because certain test components are either not commercially available for all strains or do not always provide clear results. USDA is working to improve the tests and to find a commercial supplier for one key test component. Also, a few companies voluntarily test for these strains.

Some foreign governments have practices that could be relevant to U.S. efforts to reduce STEC in cattle such as the following:

- The European Parliament and the Council of the European Union require certain measures, such as verification of cleanliness by an inspector, to ensure that the cattle going to slaughter are clean. In contrast, USDA assesses the health of cattle but does not inspect for cleanliness.
- At least 12 European Union member countries collected and reported data on STEC in live cattle in 2009. USDA has conducted STEC testing in live cattle, but has not tested since 1999.
- When a person becomes ill from *E. coli* in Sweden, government officials try to determine the specific farm that sold the contaminated cattle so that other carcasses from the farm can be tested for STEC. USDA does not trace the STEC source back to the farm.

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Abbreviations

APHIS	Animal and Plant Health Inspection Service
ARS	Agriculture Research Service
CDC	Centers for Disease Control and Prevention
FDA	Food and Drug Administration
FSIS	Food Safety and Inspection Service
HACCP	Hazard Analysis and Critical Control Point
HHS	Department of Health and Human Services
NIFA	National Institute of Food and Agriculture
STEC	Shiga Toxin-Producing *Escherichia coli*
USDA	U.S. Department of Agriculture

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United States Government Accountability Office
Washington, DC 20548

March 9, 2012

The Honorable Thomas J. Vilsack
Secretary of Agriculture

Dear Mr. Secretary:

Since 2006, the U.S. beef industry has recalled over 23 million pounds of beef because of contamination from pathogenic strains of Shiga toxin-producing *Escherichia coli* (STEC). These bacterial STEC strains can live in the intestines or on the hide of cattle without harming them, but they may contaminate meat during the slaughter process. If humans then consume the contaminated meat without properly cooking it, STEC strains can cause illnesses, including bloody diarrhea and Hemolytic Uremic Syndrome, which is characterized by kidney failure and can be fatal. The Centers for Disease Control and Prevention (CDC) does not have estimates specific to beef, but it estimates that STEC contamination of food consumed domestically causes approximately 176,000 illnesses, 2,400 hospitalizations, and 20 deaths annually. Illnesses caused by STEC O157:H7, the most common STEC strain in the United States, cost those infected $489 million annually, in 2010 dollars, according to an estimate from the U.S. Department of Agriculture (USDA).

In addition to STEC O157:H7, over 150 other STEC strains can cause illness. In this report, we refer to these strains as STEC non-O157, and CDC has identified six common groups of such strains that cause approximately 113,000 illnesses in the United States each year. These strains are known as O26, O45, O103, O111, O121, and O145.

USDA's Food Safety and Inspection Service (FSIS) is responsible for examining and inspecting the carcasses and parts of cattle at slaughter plants and meat processing plants that will be used for human consumption. The Federal Meat Inspection Act prohibits the sale of adulterated meat or meat products—products bearing or containing a poisonous or deleterious substance that may render them injurious to human health, among other things—and provides FSIS with the authority to prescribe rules and regulations concerning the sanitation at slaughter plants and meat-processing plants. In 1994, FSIS stated that it considered STEC O157:H7 an adulterant in ground beef, which according to a USDA report, is the most frequently implicated source of STEC O157:H7 outbreaks in the United States. FSIS's inspection authority does not extend to the feedlot, where most cattle are fed grain for about 140

days prior to slaughter, but the agency encourages beef producers to use preslaughter interventions, such as vaccinating the animal against STEC, to control STEC O157:H7. FSIS has stated that such interventions offer a significant opportunity to improve food safety because they may reduce the level of STEC entering the slaughter plant. The beef industry generally supports researching and developing these interventions and has funded many intervention activities for possible future use.

In this context, we reviewed USDA's and others' efforts to reduce STEC contamination in beef. Our objectives were to identify (1) preslaughter interventions—that is, treatments administered before cattle are slaughtered that can target STEC—that may help reduce STEC in cattle; (2) USDA's role in approving STEC vaccines; (3) the extent to which STEC strains have been determined to be adulterants in beef and the status of tests to detect them; and (4) practices, if any, other countries have employed that could reduce STEC in cattle and may be relevant to U.S. efforts.

For all four objectives, we visited several cattle feedlots and a cattle slaughter plant in Colorado, which we selected because it is one of the largest beef producing states, and interviewed USDA officials, beef industry representatives, and university researchers in Colorado. In addition, using a nonprobability sample, we conducted a total of 71 interviews with USDA, CDC, and Food and Drug Administration (FDA) officials; foreign government officials; beef industry representatives; manufacturers of animal health products; federal and university researchers; and consumer group representatives with expertise in STEC in cattle. Because this was a nonprobability sample, the results cannot be generalized to the entire United States, but can provide examples of research conducted on preslaughter interventions. To determine the preslaughter interventions that may help reduce STEC in cattle, we reviewed USDA and academic studies on preslaughter interventions, reviewed USDA documents on funding for STEC research, and met with USDA and university researchers and beef and pharmaceutical industry representatives. To determine USDA's role in approving STEC vaccines, we reviewed USDA guidance and interviewed USDA officials, manufacturers of animal health products, and university researchers. To determine the extent to which STEC strains have been determined to be adulterants in beef and the status of tests to detect them, we reviewed USDA documents on STEC detection tests and interviewed FDA and USDA officials, beef industry representatives, and detection test manufacturers. To determine practices, if any, other countries have employed that could reduce STEC in cattle and may be relevant to U.S.

efforts, we asked CDC, FDA, and USDA officials; beef industry representatives; university researchers; and consumer group representatives if they were aware of any such practices. We also reviewed international studies, guidance, and requirements for food safety in beef and interviewed international food safety officials. Appendix I contains an expanded explanation of our objectives, scope, and methodology.

We conducted this performance audit from January 2011 to March 2012 in accordance with generally accepted government auditing standards. Those standards require that we plan and perform the audit to obtain sufficient, appropriate evidence to provide a reasonable basis for our findings and conclusions based on our audit objectives. We believe that the evidence obtained provides a reasonable basis for our findings and conclusions based on our audit objectives.

Background

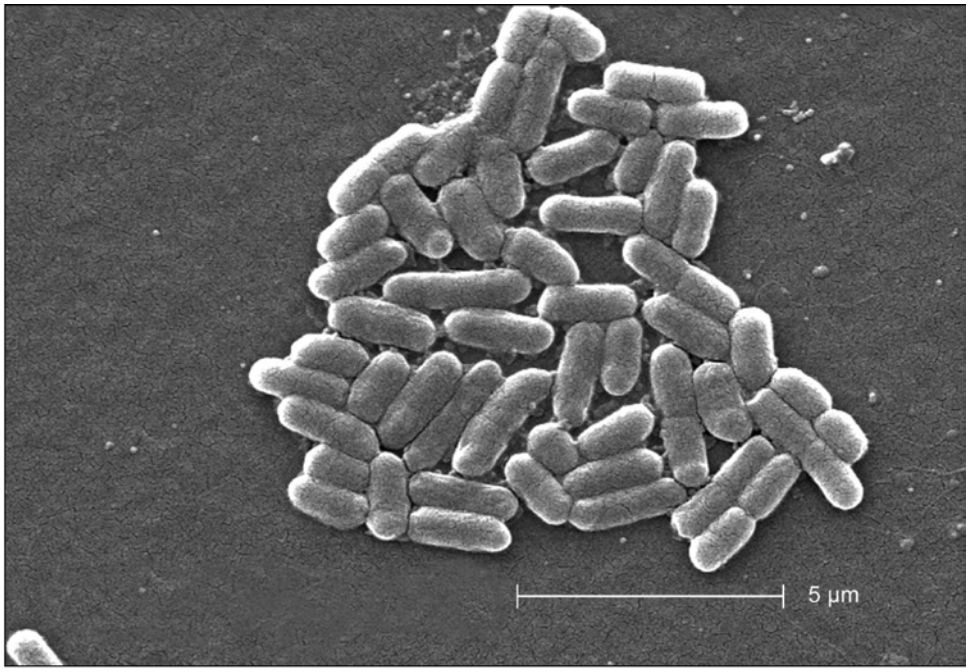
This section discusses STEC and agencies that play a role in reducing STEC contamination.

Shiga Toxin-Producing *E. coli*

E. coli bacteria live in the intestines of healthy cattle and have a symbiotic relationship with the cattle, an association in which the *E. coli* derives the benefit, and cattle are not harmed. The organism has been found in young beef calves and older cows, as well as in dairy calves and dairy cows. *E. coli* tends to colonize at the end of a cow's intestinal system, in an area known as the anorectal junction. A cow with *E. coli* in its intestinal system typically "sheds" the organism through its feces. As cattle shed *E. coli*, the bacteria can contaminate the hides and then the meat as the cattle are slaughtered. Several strains of *E. coli* have evolved to being highly pathogenic and capable of causing death when they infect humans.

STEC O157:H7, pictured in figure 1, is the strain of STEC bacteria of primary interest to USDA and researchers. STEC O157:H7 was first recognized as a disease-causing organism in 1982 and became a research priority in 1993, when over 700 people were affected after eating undercooked hamburgers at a fast-food restaurant chain. This outbreak was the largest reported outbreak in North America, and 55 patients, including 4 children who died, developed Hemolytic Uremic Syndrome. Symptoms of STEC O157:H7 can also include severe bloody diarrhea, profuse bleeding, seizures, kidney failure, coma, and death.

Figure 1: STEC O157:H7 Bacteria



Source: CDC.

In 1994, USDA's FSIS made public that it considered STEC O157:H7 as an adulterant in raw ground beef; it established a zero-tolerance policy for this pathogen in this food product and began a sampling program to test for the pathogen in federally inspected establishments and retail stores. FSIS also made public that it would use available enforcement tools, such as requesting a recall from beef producers if the product had entered commerce. Any raw ground beef found to contain STEC O157:H7 must be disposed of or sent for further processing that involves a "lethality step," such as cooking the meat before selling it.[1]

Under current law, thousands of FSIS regulatory inspectors maintain continuous inspection at slaughter facilities and examine all slaughtered meat carcasses. Inspectors also visit other meat-processing facilities at least once each operating day. In 1996, FSIS established Hazard

[1]According to FSIS, thorough cooking of ground beef to an internal temperature of 160° F throughout kills STEC O157:H7.

Analysis and Critical Control Point (HACCP) system requirements for all processing plants. The HACCP system requires that plants identify biological, chemical, and physical food safety hazards that are reasonably likely to occur and develop and implement plans to prevent and control those hazards.

In addition to STEC O157:H7, CDC has identified six groups of STEC strains—O26, O45, O103, O111, O121, and O145—that are also pathogenic. These STEC non-O157 strains have been found in ground beef and on cattle hides and feces at levels comparable to those for STEC O157:H7, and they have been found to cause the same human illnesses. In 2010, for the first time, the number of laboratory-confirmed STEC infections from strains other than STEC O157:H7 was greater than the number of STEC O157:H7 infections.

Agencies that Play a Role in Reducing STEC Contamination

Two federal departments are primarily responsible for ensuring the safety of the U.S. food supply, including the prevention of STEC contamination—USDA and the Department of Health and Human Services (HHS). Each department contains agencies that contribute to the national effort to assess, measure, and track STEC contamination (see table 1).

Table 1: Agencies with Responsibilities Related to STEC Contamination in Beef

Department and agency	Responsibilities related to STEC contamination in beef
USDA	
Food Safety and Inspection Service	Regulates the safety, wholesomeness, and proper labeling of domestic and imported meat under authority of the Federal Meat Inspection Act.[a] Inspects slaughter plants, processing plants, and import establishments in the United States and can keep some products from entering the food supply via meat inspections at the plant level. May not mandate recalls of contaminated meat but does provide assistance and monitors voluntary recalls by the beef industry. Provides guidance to the beef industry regarding best practices for reducing STEC contamination.
Animal and Plant Health Inspection Service (APHIS)	Protects U.S. livestock and poultry from domestic and foreign diseases and pests under the Animal Health Protection Act.[b] Reviews and approves applications for biological product licenses, such as vaccines, that could be used as part of a STEC preslaughter intervention. Manages the National Animal Health Monitoring System—a periodic, national survey of producers that focuses on management practices and animal health in feedlots.
Agricultural Research Service (ARS)	Conducts research on a variety of STEC-related issues, such as prevention of STEC colonization in cattle, interventions to reduce STEC in beef, and STEC strain detection methods.
National Institute of Food and Agriculture (NIFA)	Funds research on the prevention, detection, and colonization of STEC in cattle through grants to universities and other organizations.
HHS	
FDA	Regulates the manufacture and distribution of food, food additives, and drugs for humans and animals under the Federal Food, Drug and Cosmetic Act.[c] Ensures the safety and effectiveness of animal drugs, including those intended to reduce STEC prevalence in cattle, such as sodium chlorate.
CDC	Routinely gathers information from local and state health departments and laboratories and reports information about human STEC infections and the foods with which they are associated.

Source: GAO.

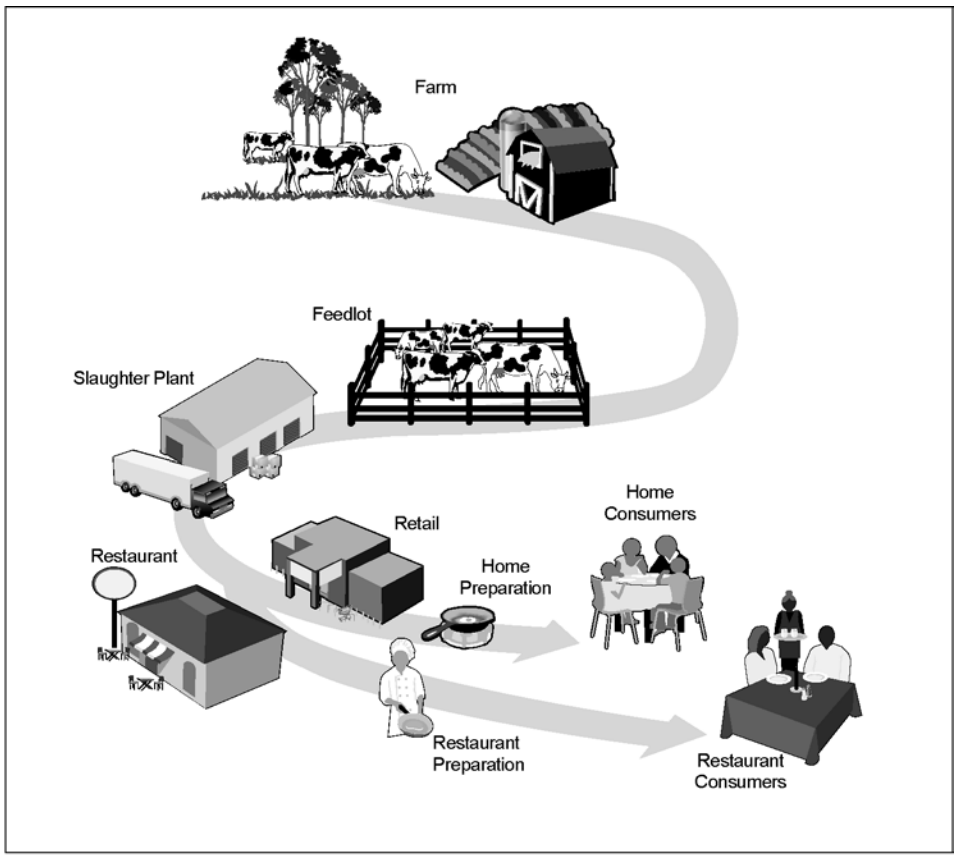
[a]21 U.S.C. §§ 601-683.

[b]7 U.S.C. §§ 8301-8322.

[c]21 U.S.C. §§ 301-399d.

Several steps are involved in getting cattle from the farm to the consumer. Often, USDA and FDA provide regulatory oversight after the cattle leave the farm or feedlot and arrive at slaughter plants and food handling and manufacturing facilities. Figure 2 illustrates the beef production process from the farm to the consumer.

Figure 2: Beef Production Process



Sources: CDC and GAO.

In 2007, GAO designated federal oversight of food safety as a high-risk area because of risks to the economy and to public health and safety. As GAO has reported, the current fragmented system has caused inconsistent oversight, ineffective coordination, and inefficient use of resources.[2]

[2]See most recently in GAO, *Federal Food Safety Oversight: Food Safety Working Group Is a Positive First Step but Governmentwide Planning Is Needed to Address Fragmentation*, GAO-11-289 (Washington, D.C.: Mar. 18, 2011).

Several Interventions Could Reduce STEC in Cattle

USDA and university researchers identified several potential preslaughter interventions—including probiotics, sodium chlorate, and vaccines—that could reduce STEC O157:H7 in cattle and, in some cases, may have potential for reducing other strains of STEC. USDA conducts and funds research relevant to these interventions, including research on the prevalence of STEC and on the interventions themselves.

Researchers Identified Preslaughter Interventions That Could Reduce STEC in Cattle

Preslaughter interventions are treatments administered before cattle are slaughtered that can target STEC, usually the O157:H7 strain. Some interventions, such as sodium chlorate and vaccines, may also reduce other pathogenic strains, but researchers have not conducted testing for the effects of interventions on other strains. According to representatives for a beef industry group, most research on preslaughter interventions has focused on those administered at the feedlots, although they may also be administered in the holding pen of a slaughter plant. Preslaughter interventions are not likely to eliminate STEC O157:H7 in cattle; instead, the goal is to reduce the pathogen to levels that the HACCP systems at slaughter plants are able to control effectively, according to beef industry representatives and researchers. They also said that multiple interventions are needed to accomplish this. Some studies suggest that a few interventions are effective in reducing STEC O157:H7 in the digestive systems or on the hides of cattle, but it may be difficult to demonstrate that they reduce the levels of STEC O157:H7 in beef, according to manufacturers of animal health products and researchers.

USDA and university researchers we spoke with identified several potential preslaughter interventions for reducing STEC O157:H7 and, in some cases, these interventions may have potential for reducing other strains of STEC. Some of these interventions are in use for other purposes, but few manufacturers have submitted applications for preslaughter intervention products to target STEC—with the exception of bacteriophages (viruses that infect and kill bacteria) and vaccines—according to officials from USDA and FDA. The following are the interventions that researchers identified, along with challenges for bringing these interventions to market:

- *Antimicrobials.* These are drugs used to treat infections by microorganisms, such as bacteria and viruses, and include synthetic and natural antibiotics. Antibiotics are currently used in cattle to treat or prevent diseases and increase growth. According to some researchers, it may not be feasible for industry to use antibiotics as a preslaughter intervention to reduce STEC because of concerns that

such use will lead to greater prevalence of bacteria that are resistant to antibiotics. If resistant bacteria were to reach humans and cause illness, this illness might be more difficult to treat. Researchers also said that, for the same reason, it is unlikely that the veterinary pharmaceutical industry would pursue requesting approval for antibiotics as a preslaughter intervention. In April 1999, we reported that according to scientists, resistant strains of *E. coli* found in humans acquired resistance to antibiotics while in food animals.[3] Resistant strains of *E. coli* may be transferred to humans through food or through contact with animals or animal waste.

- *Bacteriophages.* These naturally occurring viruses infect bacteria and are highly specific—each type typically can kill a single strain or species of pathogenic bacteria. USDA, in consultation with FDA, licensed a mixture of bacteriophages that may be applied to cattle hides in holding pens at slaughter plants. Other bacteriophages, which could be administered orally, are at the experimental stage. According to researchers, it is possible for STEC O157:H7 to become resistant to some bacteriophages.

- *Colicins.* These antimicrobial proteins are produced by certain STEC strains and can kill other strains. According to researchers, studies to date on the use of colicins to reduce STEC in cattle are few, and colicins are difficult to produce and expensive to use in studies.

- *Natural product extracts.* These are compounds that are generally extracted from spices, aromatic herbs, fruits, and flowers, but can also be obtained from other natural products, such as marine plants. In particular, essential oils—a type of natural product extract—demonstrate antimicrobial activity that may reduce STEC O157:H7, according to researchers. Studies on the effect of essential oils on STEC O157:H7 in cattle are limited to the laboratory, but USDA and university researchers are developing field trials of citrus by-products, such as orange peel, which contain essential oils. Some compounds, or the products from which they are extracted, such as orange peel and brown seaweed extract, are currently used in cattle feed in some

[3]GAO, *Food Safety: The Agricultural Use of Antibiotics and Its Implications for Human Health*, GAO/RCED-99-74 (Washington, D.C.: Apr. 28, 1999). For more information about the use of antibiotics in animals, see GAO, *Antibiotic Resistance: Agencies Have Made Limited Progress Addressing Antibiotic Use in Animals,* GAO-11-801 (Washington, D.C.: Sept. 7, 2011).

feedlots. Research is unclear on how much of the compounds or the products from which they are extracted, such as citrus and thyme oils, will pass through the cattle's stomach, and it may be challenging to obtain a large quantity of these compounds to feed to cattle on a commercial basis, according to researchers.

- *Prebiotics.* These nondigestible organic compounds can promote the growth and activity of beneficial bacteria in the digestive system of cattle, which in turn can reduce the prevalence of bacterial pathogens. According to USDA researchers, little work has been conducted on the effects of these compounds on STEC O157:H7 in cattle. Furthermore, the compounds may be expensive to use in cattle and may not pass through the cattle's stomach.

- *Probiotics.* These are live bacteria that can benefit the digestive system of cattle. According to USDA researchers, probiotics can prevent harmful colonization by bacteria by producing antibacterial compounds or by promoting healthy immune function. Researchers have conducted field trials to test whether varying amounts of certain probiotic strains reduce STEC O157:H7. Probiotics are widely used to increase weight gain. According to a few researchers, in order for probiotics to reduce STEC O157:H7, cattle may need to be fed large quantities, which may be costly to producers.

- *Sodium chlorate.* This chemical kills STEC O157:H7 when it transforms to toxic chlorite inside the bacterial cell. This transformation occurs in both the stomach and the intestinal tract of cattle. According to representatives for a veterinary pharmaceutical manufacturer, the manufacturer is discussing with FDA applying for approval of sodium chlorate as an animal drug. According to a few researchers, it is likely that sodium chlorate would also reduce STEC non-O157.

- *Vaccines.* These are biological preparations that alter the immune system to better fight specific pathogens. At least two manufacturers of animal health products have developed vaccines to target STEC O157:H7 in cattle and are seeking approval from APHIS to market them. One of these manufacturers received a conditional license for a vaccine in 2009 and, according to representatives from these manufacturers, applications for full licenses for two vaccines are

pending.[4] According to a few researchers and representatives for a veterinary pharmaceutical manufacturer, administering higher doses of a vaccine would increase its efficacy but may be costly. For example, handling the cattle to specifically administer a STEC vaccine may increase labor costs. USDA officials also said that cattle producers may not directly benefit from administering these vaccines. Additionally, according to one university researcher and one animal health product manufacturing official, vaccines have the potential to reduce STEC non-O157, but a vaccine study of STEC non-O157 has not been conducted on animals. APHIS officials told us that they have not received information that could support this theory.

Table 2 provides a summary of preslaughter interventions, their approval status, the agency responsible for their approval, and challenges for the use of intervention.

[4]Conditional licenses are effective for a finite period, usually 1 year and may be renewed at the discretion of APHIS. The data required for conditional licensure are reduced from that needed for full licensure in that there needs only to be a "reasonable expectation" of efficacy as defined by APHIS. Conditional licenses are not required prior to receiving a full license but can be used to bring a product to market. For example, the conditional license for the STEC O157:H7 vaccine allows cattle producers to use the vaccine under the supervision of a veterinarian.

Table 2: Approval Status and Challenges for Preslaughter Interventions

Preslaughter intervention	Approved for use to reduce STEC O157:H7 in cattle	Agency responsible for approval	Challenges for use of intervention
Antimicrobials	No	FDA	STEC O157:H7 may become resistant.
Bacteriophages	Yes[a]	USDA FDA	STEC O157:H7 may become resistant.
Colicins	No	FDA	Expensive and difficult to produce.
Natural product extracts	No	FDA	May not pass the cattle's stomach and may be difficult to obtain in large quantities.
Prebiotics	No	FDA	May be costly and may not pass the cattle's stomach.
Probiotics	No	FDA	Cattle may need to be fed large amounts to reduce STEC.
Sodium chlorate	No	FDA	None[c]
Vaccines	Yes[b]	USDA	Cost associated with specifically administering a STEC vaccine.

Source: GAO analysis of interviews with USDA officials, FDA officials, and university researchers.

[a]USDA, in consultation with FDA, licensed a bacteriophage hide wash to be applied at the slaughterhouse prior to slaughter. Bacteriophages could also be administered orally, but FDA has not licensed any such product.

[b]USDA granted conditional approval to one vaccine manufacturer.

[c]Researchers we spoke with did not identify challenges when we asked them to discuss the challenges or roadblocks for each intervention. This does not mean that the intervention is without challenges, because there may be challenges that researchers are not aware of.

USDA, the beef industry, and several researchers also identified preslaughter management practices that may affect STEC prevalence in cattle but that are not targeted to STEC. For example, basic sanitation practices—such as providing clean feed and water and keeping feedlots drained—have been identified by the beef industry and USDA as important steps in reducing the risk of STEC contamination in beef products. These practices are believed to be beneficial for the cattle's health and welfare, although they have not been shown to be effective in reducing the pathogen, according to the beef industry and a USDA study. Researchers from one university noted interest in testing the effects of this and other preslaughter practices on STEC in cattle.

Another preslaughter management practice researchers identified is diet modification, which includes modifying feed type, from feed grain to grasses, or the reverse; the frequency of feeding; and the quality of the grasses. Researchers have examined diet modification's effect on the prevalence of STEC O157:H7 but have not reached a consensus about it.

For example, some researchers have found that a diet with distillers grains—a co-product of the production of ethanol from corn—increases STEC O157:H7 prevalence in cattle, but others have found that it has no effect. Furthermore, according to several USDA and university researchers, diet modification may not be practical for reducing STEC O157:H7 in cattle, partly because of the potentially high cost.

USDA Has Funded and Conducted Relevant Research

USDA has funded and conducted research on STEC prevalence in cattle, as well as research specific to preslaughter interventions. In fiscal years 2009 and 2010, USDA's NIFA, through its Agriculture and Food Research Initiative, approved approximately $35 million in research grants related to understanding and reducing STEC prevalence in cattle. NIFA provided a total of about $28 million in five grants for research on how preslaughter interventions may reduce STEC in cattle, a total of about $5 million in three grants for research on how STEC behaves in the digestive system of cattle, and about $2.5 million for one grant for research on both preslaughter interventions and the behavior of STEC in the digestive system of cattle.

In addition, USDA's ARS has worked closely with other USDA agencies, university researchers, and pharmaceutical manufacturers to research the prevalence of STEC in cattle's digestive systems and potential preslaughter interventions, according to ARS officials. For example, these officials said that ARS has conducted research on "super-shedders," which are cattle that appear to shed more STEC than other cattle in the same herd. Regarding preslaughter interventions, ARS researchers have investigated the effect of sodium chlorate on STEC in the digestive system and, according to agency officials, ARS has collaborated with companies to develop preslaughter interventions such as prebiotics, bacteriophages, and sodium chlorate.

USDA Exercises Responsibility for Approving STEC Vaccines, but Its Approval Requirements Are Unclear

USDA's APHIS exercises responsibility for licensing and regulating animal biologic products that diagnose, prevent, manage, cure, or otherwise treat diseases of animals, including vaccines that can be used as a preslaughter intervention. Industry representatives have identified at least two manufacturers of animal health products that have each submitted an application to APHIS for approval of a STEC vaccine to treat the O157:H7 strain in cattle, and USDA announced the approval of a conditional license for one of these manufacturers.

According to representatives from two manufacturers of animal health products that sought a license for STEC O157:H7 vaccines, it was unclear whether FDA or USDA was responsible for reviewing and approving their applications when they wanted to apply in 2001 and 2003. It took more than a year before APHIS accepted their applications for review, in part because of lack of clarity over whether FDA or APHIS should be responsible for approving such vaccines, according to these representatives. Specifically, APHIS is responsible for regulating vaccines that diagnose, prevent, manage, cure, or otherwise treat diseases of animals, but APHIS officials told us that because STEC O157:H7 does not harm cattle, the agency had found prior to 2005 that regulatory jurisdiction for STEC O157:H7 vaccines resided with FDA as a food safety issue. According to these officials, the manufacturers of animal health products told them that the licensing process would be clearer under APHIS because it had more experience regulating conventional veterinary vaccines than FDA.

In 2005, APHIS stated its policy on animal vaccines in a directive explaining that it was responsible for regulating biological products such as the STEC O157:H7 vaccine.[5] Specifically, the directive stated that APHIS had the authority to approve products that claim to reduce colonization or shedding of organisms that may not cause significant clinical disease in animals but have the potential to cause the animal to be a disease carrier. According to an FDA official, if a manufacturer contacts FDA's Office of New Animal Drug Evaluation seeking a license for a STEC O157:H7 vaccine product, this office assists APHIS by immediately directing the manufacturer to APHIS. The APHIS directive expired as guidance in 2006, but because APHIS has not issued any

[5]Animal and Plant Health Inspection Service, USDA, Center for Veterinary Biologics Notice No. 05-07 (Mar. 4, 2005).

subsequent statements on this policy, an APHIS official said that the policy in the directive remains in effect. This 2005 directive clarified APHIS's approval authority and role concerning vaccine approvals, but APHIS's approval requirements for STEC vaccines are not clear, according to industry representatives.

APHIS officials said that they direct potential applicants for STEC vaccine licensing to both the agency's general guidance on demonstrating the safety and efficacy of biological products and to its 2005 directive.[6] According to an APHIS official, the STEC vaccine is one of the most difficult vaccines for which to show definitive, consistent, and reproducible efficacy results. However, APHIS's general guidance does not address this and other unique challenges faced by manufacturers of animal health products seeking STEC vaccine approval. For example, APHIS officials said that a STEC vaccine manufacturer may need to demonstrate that its vaccine is effective in a field setting—such as a feedlot in which cattle can be naturally exposed to pathogens—if studies conducted in the laboratory in which cattle are intentionally exposed to pathogens are insufficient to demonstrate efficacy. With other vaccines, a laboratory study is often sufficient because it can demonstrate consistent efficacy. However, information on when laboratory and field studies are required to demonstrate efficacy is not documented in the general guidance or 2005 directive. In contrast, the Canadian Centre for Veterinary Biologics provides more specific guidance about when it requires the use of laboratory or field studies to demonstrate efficacy for vaccine license applications. In addition, neither the 2005 directive nor APHIS's general guidance provides clear, specific instruction to manufacturers on the application process for STEC vaccines. For example, the 2005 directive states that the vaccine products will be required to show "clinically relevant efficacy as defined by APHIS" but does not explain what such efficacy means. According to an APHIS official, "clinically relevant efficacy" is the expectation that the vaccine's efficacy is measurable, reproducible, consistent, and shows a long-term effect in reducing the disease in the animal, but this clarification is not specified in written guidance. Guidance that does not give manufacturers the information they need to submit an acceptable application could delay the approval

[6]APHIS's general guidance includes Veterinary Services Memorandum No. 800.202 and No. 800.204.

process even with the clarification on APHIS's role concerning vaccine approvals.

More specific guidance on the vaccine approval requirements may be especially important to manufacturers of animal health products working on STEC because of the challenges they face in demonstrating the efficacy of targeted preslaughter interventions. This difficulty is due to several biological factors specific to STEC, according to USDA officials, industry representatives, and university researchers. First, the prevalence of STEC is highly variable. For example, researchers said that STEC can be absent from cattle—or present only at low levels—during a field trial at a feedlot. That is, both treated and untreated cattle can have little or no detectable STEC, and thus it can be difficult for researchers to demonstrate that treated cattle have significantly lower levels of the pathogen. Second, many factors—such as weather, the time of year, and the cleanliness of the cattle's hide—may affect the level of pathogenic STEC in cattle, making it difficult to isolate the effects of an intervention. Third, unlike other pathogens, STEC causes no visible symptoms in animals, so detection requires testing for the presence of the pathogen rather than just observation of the cattle.

APHIS officials said that APHIS does not have specific guidance on STEC vaccines because it typically does not release such guidance for a particular biological product until it has reviewed and approved three applications, which gives the agency sufficient information to provide specific guidance. They said that the agency's general vaccine guidance offers it flexibility during the application review process by not being too prescriptive on requirements. During the course of our study, APHIS addressed some of the concerns we raised by releasing a one-page summary on licensing of preslaughter vaccines for a public meeting on food safety, but it still does not have documented guidance on the application process, including requirements specifically for these vaccines.

USDA Determined That Six Additional STEC Strains Were Adulterants and Has Tests to Detect Them

USDA determined that six additional STEC non-O157 strains were adulterants in beef in September 2011, has developed a method to test for them in beef, and plans to use this method starting in June 2012. Commercial tests are also available, and a few companies are voluntarily testing for these strains.

USDA Determined That Six Additional Strains Were Adulterants and Has Tests to Detect Them, but It Can Be Difficult to Confirm Positive Results

In September 2011, USDA's FSIS announced that it determined that six pathogenic strains of STEC—O26, O45, O103, O111, O121, and O145—were adulterants in raw ground beef and beef trim (the meat left over after steaks and roasts are carved from a side of beef), in addition to STEC O157:H7. According to CDC, at least 150 STEC non-O157 strains have been associated with illness, but the majority of those illnesses have been traced to these six STEC non-O157 strains. There are several consequences to these strains being adulterants, including the following:

- Sale of beef contaminated with these strains is prohibited.
- Beef slaughter and processing plants must have a HACCP plan in place to identify and control the strains and to verify that the methods used to control the strains are working properly. Verification could include testing, but testing is not mandatory.
- FSIS has more reason to routinely test a subset of products for these strains and to request a recall for products deemed to be adulterated.

According to a September 20, 2011, notice in the *Federal Register*,[7] FSIS intended to begin testing for these six strains in samples of raw ground beef and beef trim at slaughter and processing plants in March 2012, after it has reviewed comments from the public. Subsequent to this notice, FSIS moved its test date to June 4, 2012. In conducting these tests, FSIS plans to use a method developed by USDA's ARS that was first published in October 2010 and revised in November 2011. This method has two key phases: (1) preliminary testing, which may take up to 2 days, and (2) isolation and confirmation, which may take an additional 2 to 4 days. These two phases are also used for STEC O157:H7 testing.

Preliminary testing involves two main steps. First, beef samples are tested for two genes—known as *stx* and *eae*—that are known to make *E. coli* pathogenic. Second, the samples are tested for other genes that are specific to each of the six STEC non-O157 strains. Positive results in both steps are considered a "potential positive," which means the pathogen may be present. According to an ARS official, if used as planned, preliminary tests for the six strains are reliable. However, it is possible that these genes are present in a beef sample but come from

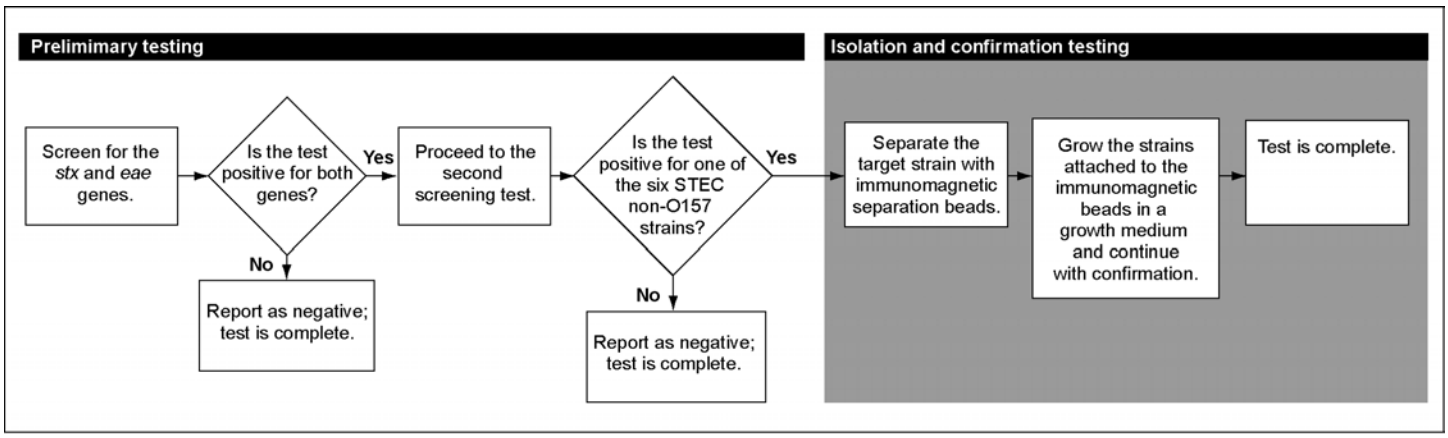
[7]76 Fed. Reg. 58,157 (Sept. 20, 2011).

different strains of bacteria. It is, therefore, necessary to isolate the suspect strain and confirm that it is the source of the two genes that make *E. coli* pathogenic.

Several steps are involved in the isolation and confirmation phase; two of these steps may be difficult and time-consuming, according to ARS officials. The first involves separating the suspected strain of pathogenic *E. coli* from other bacteria using immunomagnetic separation beads that contain antibodies (components of the human immune system) that adhere to a specific strain of *E. coli*. According to an ARS official, it would be very difficult to isolate the target strain without the use of these beads. However, the official also said that the beads are not commercially available for two of the six strains—O45 and O121. ARS currently buys beads from a commercial supplier for the other four strains but has to make them for O45 and O121, which is a time-consuming and costly process, according to an ARS official. FSIS is currently searching for companies willing to produce beads for the two strains and make them commercially available and, according to an FSIS official, expects to have test manufacturers in place by June 2012.

The second step involves growing the target strain by placing the immunomagnetic beads onto a solid growth medium containing a mix of nutrients that is specific to this strain and suppresses the growth of other bacteria. According to an ARS official, scientists allow the bacteria sticking to the beads to grow and multiply on the medium, using methods that ensure the bacteria form colonies that are all from the same strain. This makes it easier to identify the target strain and confirm that it has the two disease-causing genes—*stx* and *eae*. However, according to the ARS official, some of the six STEC non-O157 strains may not always grow well on the medium that FSIS is currently using. If the strains do not grow well, it will be difficult to confirm potentially positive results and, consequently, beef samples that contain one of the six pathogenic strains could incorrectly test negative. According to the ARS official, a revised November 2011 testing method includes an improved growth medium for the six strains. This official added that ARS has conducted various tests to find the optimal growth medium for the six strains, and the medium FSIS is using is the best currently available. Research is ongoing by ARS and in the broader scientific community to develop a better growth medium, according to this ARS official, and ARS will evaluate other mediums as they become commercially available. See figure 3 for a summary of the testing process.

Figure 3: Preliminary and Isolation and Confirmation Testing Phases for the Six STEC Non-O157 Strains



Source: GAO summary of USDA information.

Note: This figure shows the two main phases *for E. coli* detection testing. For a comprehensive description of all of the detection testing steps, see USDA's *Microbiology Laboratory Guidebook MLG 5B.01*.

Commercial Tests Are Available and Some Companies Are Testing

Preliminary tests to detect the six strains are commercially available, and at least one test manufacturer sells these tests for all six strains. ARS collaborated with this manufacturer to develop the tests and is now collaborating with other manufacturers, many of which became interested in developing tests after USDA's announcement that it had determined to consider the six strains as adulterants, according to an ARS official. A representative from one test manufacturer told us he was confident that his company could produce enough tests to meet the demand of the U.S. beef industry. Similarly, a representative from a second manufacturer told us that it is preparing to meet the demand.

Starting on June 4, 2012, FSIS will expect slaughter and processing plants to have a plan in place to identify and control the six STEC non-O157 strains. Such a plan may include information on how the plant will use testing to verify that food safety systems are working properly. FSIS officials estimate that about 20 percent of U.S. slaughter plants are currently testing for STEC non-O157 strains, although FSIS did not know for which specific strains these plants are testing. Representatives from two beef processing plants—one of which is also a retailer—told us that they are testing for all six strains. The plant that is also a retailer will also require its beef suppliers to test for these strains before it accepts the beef. The retailer will also test for STEC O104, an additional STEC non-O157 strain, as soon as a test is commercially available for beef. The

representative from this retailer did not report challenges with using the commercially available preliminary test for the six strains. However, commercial preliminary tests for the six strains are new, and according to representatives from a test manufacturer, the manufacturer recently started conducting field trials on the tests.

Both beef processing plants said they also carry out confirmation tests for potential positive results through a third-party laboratory. An official from one of these plants told us that he has not observed any difficulty in growing the six strains after separation using the commercially available growth mediums, but he noted confirmation of potentially positive results for the six pathogenic strains can be a time-consuming process. According to a test manufacturer representative, confirmation of potentially positive results will likely be difficult for the beef industry, for the same reasons it is proving difficult for FSIS.

If a plant detects one of the six strains in ground beef or beef trim, its response is generally dictated by FSIS requirements. Possible responses to a positive test include disposing of the beef or cooking it to kill bacteria.

Some Countries Have Practices That Could Be Relevant to U.S. Efforts to Reduce STEC in Cattle

Several researchers, U.S. agency officials, and a foreign government official said that the United States is the leader in researching and employing preslaughter interventions. USDA officials, however, commented that they would consider preslaughter practices other countries have conducted if they are relevant to U.S. efforts to reduce STEC in cattle. The following are some practices other countries have employed that may help reduce STEC in cattle and that are not currently used in the United States:

Cattle cleanliness inspections. Several foreign governments conduct cleanliness inspections that may reduce STEC in beef. For example, European Parliament and the Council of the European Union regulations, referenced by European Commission officials, require that (1) farmers take adequate measures to ensure the cleanliness of cattle going to slaughter, (2) operators of slaughter plants ensure cattle are clean before accepting them, and (3) meat inspectors verify that the cattle about to be slaughtered are clean. In the United Kingdom, meat inspectors use a five-category rating system for cattle cleanliness that ranges from “clean and dry” to “filthy and wet,” according to a 2002 guidance document from the Food Standards Agency. Only cattle rated in the two highest categories for cleanliness may proceed to slaughter. In Australia, according to its standard for the hygienic production and transportation of meat and meat

products for human consumption, an inspector must determine that cattle are clean prior to slaughter. If they are not, they can be passed for slaughter subject to conditions that ensure that they do not contaminate other animals, carcasses, and carcass parts. According to New Zealand government officials, their inspectors check for hide cleanliness to help prevent meat contamination. In contrast, in the United States, FSIS assesses the health of cattle prior to slaughter but does not inspect for cleanliness.

Testing for STEC. At least 12 European Union member countries collected and reported data on STEC in live cattle in 2009, according to a 2011 European Food Safety Authority and European Centre for Disease Prevention and Control report.[8] Such data are important to identify the main sources of infections. In countries such as Sweden and Denmark, this testing is conducted regularly. For example, in Sweden, government officials collect about 2,000 fecal samples every 3 years, according to an official from Sweden's National Veterinary Institute. These samples are collected at geographically distributed slaughterhouses throughout Sweden. Sweden tests for STEC O157:H7 and started to test 1,000 fecal samples for STEC O26 in its 2011 study. In Denmark, the National Food Institute collects fecal samples from approximately 200 bulls per year to test for STEC O157:H7, according to an institute official. In the United States, APHIS has conducted feedlot studies that involved testing for STEC in live cattle, but this testing was voluntary and last conducted in 1999.

Testing cattle from specific farms in Sweden. When a person becomes ill from *E. coli* in Sweden, Swedish government officials try to determine its source by interviewing this person, according to an official from Sweden's National Food Administration. If this person is suspected of having been in contact with cattle from a specific farm, cattle from this farm will be sampled. If there is an *E. coli* strain match with that of the ill person, this official said that Sweden's Board of Agriculture would then recommend that the cattle from this farm be slaughtered at a slower rate so that the carcasses can be tested for STEC and heat-treated if found positive. Although this is a recommendation, this official stated that its

[8]European Food Safety Authority, European Centre for Disease Prevention and Control; *The European Union Summary Report on Trends and Sources of Zoonoses, Zoonotic Agents and Food-borne Outbreaks in 2009*; EFSA Journal 2011 (Parma, Italy: Mar. 22, 2011).

slaughterhouses follow the board's recommendations. According to this official, since 1996, Sweden has had 52 cases of human illnesses from STEC—46 from the O157:H7 strain, 2 from O26, 2 from O121, 1 from O8, and 1 from O103. In the United States, STEC O157:H7 in beef can be traced back to the beef supplier, but USDA officials said that they do not trace the source of the pathogen back to the farm and thus cannot make recommendations for special testing from specific farms.

Conclusions

Preslaughter interventions for cattle have the potential to help reduce STEC-related illnesses, although they are unlikely to be able to eliminate all pathogenic strains in cattle. USDA, the beef industry, and university researchers have been working to develop these interventions. Few manufacturers have submitted applications for preslaughter intervention products to target STEC, but at least two have submitted applications for STEC vaccines. However, the approval requirements are unclear. In 2005, USDA's APHIS clarified its responsibility for vaccines, but it still has not provided specific guidance on the information it needs to approve a vaccine for STEC. Without guidance that gives manufacturers clear and more specific information they need to submit an acceptable application, the approval requirements for STEC vaccines could face delays and thereby increase the risk to public health. In addition, some countries have employed practices not currently used in the United States that potentially can inform U.S. efforts for reducing STEC in cattle.

Recommendations for Executive Action

GAO recommends that the Secretary of Agriculture take the following two actions:

- Direct the Administrator of APHIS to provide more specific public guidance on the license approval requirements for STEC vaccines in order to help improve clarity and reduce potential delays in the application process for these vaccines.
- Explore practices employed by other countries that are not currently used in the United States for reducing STEC in cattle and consider whether the identified practices can inform U.S. efforts.

Agency Comments and Our Evaluation

We provided a copy of our draft report to the Departments of Agriculture and of Health and Human Services. In its written response, USDA generally agreed with the information in the draft report. USDA neither agreed nor disagreed with our recommendation that it provide more

specific public guidance on the license approval requirements for STEC vaccines. USDA's APHIS acknowledged that additional public guidance may be beneficial to applicants and stated that it is committed to providing as much specific public guidance as possible. However, APHIS stated that more specific requirements may discourage product development efforts, and APHIS does not release specific guidance about a new product until it has reviewed and approved at least three applications. Further, according to industry representatives, APHIS's approval requirements for STEC vaccines are not clear. Our recommendation is intended to help improve clarity and reduce potential delays in the application process for STEC vaccines. As stated in our report, we found that guidance that does not give manufacturers the information they need to submit an acceptable application could delay the approval process. We also provided examples of areas in which more specific guidance, such as clarifying the term "clinically relevant efficacy," could reduce confusion. APHIS addressed some of the concerns we raised by releasing a one-page summary on licensing of preslaughter vaccines for a public meeting, but this is not documented as guidance. We encourage APHIS to provide more specific guidance that can reduce confusion without discouraging product development of STEC vaccines. USDA agreed with our recommendation to explore practices that are currently not used in the United States for reducing STEC in cattle and consider whether the identified practices can inform U.S. efforts. USDA's letter is presented in appendix II. The Department of Health and Human Services did not comment on the draft report but provided technical comments. As appropriate, we incorporated these technical comments and those provided by USDA.

This report is intended for use by USDA management. We are sending copies of this report to the appropriate congressional committees and members, the Secretary of Health and Human Services, and other interested parties. In addition, this report is available at no charge on the GAO website at http://www.gao.gov.

We acknowledge and appreciate the cooperation and assistance provided by USDA management and staff during our audit. If you have questions about this report, please contact me at (202) 512-3841 or shamesl@gao.gov. Contact points for our Offices of Congressional Relations and Public Affairs may be found on the last page of this report. GAO staff who made key contributions to this report are listed in appendix III.

Sincerely yours,

Lisa Shames
Director, Natural Resources and Environment

Appendix I: Objectives, Scope, and Methodology

Our objectives were to determine (1) preslaughter interventions that may help reduce Shiga toxin-producing *Escherichia coli* (STEC) in cattle; (2) the U.S. Department of Agriculture's (USDA) role in approving STEC vaccines; (3) the extent to which STEC strains have been determined to be adulterants in beef and the status of tests to detect them; and (4) practices, if any, other countries have employed that could reduce STEC in cattle and may be relevant to U.S. efforts.

For all four objectives, we visited several cattle feedlots and a cattle slaughter plant in Colorado, which we selected because it is one of the largest beef-producing states. While in Colorado, we also interviewed USDA officials, beef industry representatives, and university researchers. In addition, in a nonprobability sample, we conducted a total of 71 interviews with USDA, Centers for Disease Control and Prevention (CDC), and Food and Drug Administration (FDA) officials; foreign government officials; beef industry representatives; manufacturers of animal health products; federal and university researchers; and consumer group representatives with expertise in STEC in cattle. Our questions included descriptions of preslaughter interventions, roles of federal government in preslaughter interventions, and practices other countries have employed to reduce STEC in cattle that may be relevant to U.S. efforts. Because this was a nonprobability sample, the results cannot be generalized to the entire United States, but they can provide examples of research conducted on preslaughter interventions.

To determine the preslaughter interventions that may help reduce STEC in cattle, we reviewed USDA and academic studies on preslaughter interventions, reviewed USDA documents on funding for STEC research, and met with USDA and university researchers and beef and pharmaceutical industry representatives. We identified these studies through interviews with USDA and university researchers.

To determine USDA's role in approving STEC vaccines, we reviewed USDA guidance, and interviewed USDA officials, manufacturers of animal health products, and university researchers.

To determine the extent to which STEC strains have been determined to be adulterants in beef and the status of tests to detect them, we reviewed USDA documents on STEC detection tests and interviewed FDA and USDA officials, beef industry representatives, and detection test manufacturers.

To determine practices, if any, other countries have employed that could reduce STEC in cattle and may be relevant to U.S. efforts, we interviewed CDC, FDA, and USDA officials; beef industry representatives; university researchers; and consumer group representatives to determine if they were aware of any such practices. We also reviewed international studies, guidance, and requirements for food safety in beef and interviewed international food safety officials. We did not independently verify statements of foreign law.

We conducted this performance audit from January 2011 to March 2012 in accordance with generally accepted government auditing standards. Those standards require that we plan and perform the audit to obtain sufficient, appropriate evidence to provide a reasonable basis for our findings and conclusions based on our audit objectives. We believe that the evidence obtained provides a reasonable basis for our findings and conclusions based on our audit objectives.

Appendix II: Comments from the U. S. Department of Agriculture

United States Department of Agriculture

Office of the Secretary
Washington, D.C. 20250

FEB 23 2012

Ms. Lisa Shames
Director
Natural Resources and Environment
United States Government Accountability Office
441 G Street, NW.
Washington, D.C. 20548

Dear Ms. Shames:

The United States Department of Agriculture (USDA) has reviewed the U.S. Government Accountability Office's (GAO) draft report, "Food Safety: Pre-Slaughter Interventions Could Reduce *E. coli* in Cattle" (12-257). USDA generally agrees with the information provided in the GAO draft report.

While reducing *E. coli* contamination cuts across several USDA agencies, the Animal and Plant Health Inspection Service's (APHIS) Center for Veterinary Biologics has the lead responsibility for vaccine approval. As stated in the report, APHIS does not release guidance specific about a new product until it has reviewed and approved at least 3 applications. This provides for flexibility in how each new product is evaluated and takes into account the "state of the science" in determining the proper regulatory standards to apply. Product-specific issues, most notably identifying a path to licensure, and determining what type of data is most suitable for demonstrating the purity, safety, potency, and efficacy of a product have historically been handled through official correspondence between the agency and the applicant. Most—if not all—of this information is proprietary and highly confidential, thus, APHIS' guidance, in this regard, is confidential as well.

While APHIS does not disagree that additional public guidance related to these products may be beneficial to both the current applicants (one of which has a license for their product) and future applicants who have not yet brought new interventions forward, how best to provide that guidance will need to be carefully considered. Unlike many regulatory agencies (such as the Food and Drug Administration (FDA), the European Medicines Agency, etc.), APHIS manages licensing applications through an iterative process. APHIS does not generally attempt to review applications in total, rejecting them if a specific part is found lacking. Rather, APHIS works with manufacturers to identify licensing issues and provides specific guidance to address the specific issue that they have encountered to ensure that pure, safe, potent, and effective products are brought to market consistent with our mandate under the Virus-Serum-Toxin Act. Regardless, APHIS is committed to providing as much specific public guidance as possible in order to better inform industry.

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In response to Recommendation #1, in APHIS' experience, the general guidance that is currently in the public domain provides the basic framework for the licensing of most of the products that are currently on the market. More specific requirements that attempt to address some of the challenges noted with *E. coli* O157:H7 may in fact discourage product development efforts unless the standards are appropriately established. Of course, standards that are set too low support neither animal health nor public health by extension.

APHIS will continue to use a variety of forums to provide licensing information and guidance for these types of products to a broad group of stakeholders. The Agency remains an active member of the '*E. coli* Coalition' led by the National Cattlemen's Beef Association (NCBA), by providing information and updates at NCBA meetings; continuing to engage the biologics industry associations in forums designed to clarify any questions around licensing pathways; providing detailed and specific guidance to manufacturers, licensees, and permittees on individual submissions and studies presented to APHIS to support licensing requirements; working with other USDA agencies, such as the Food Safety and Inspection Service; and lastly, working with Federal counterparts, like the FDA, on specific and broader intervention possibilities.

In response to Recommendation #2, USDA agrees with this Recommendation. USDA, specifically APHIS, will explore practices employed by other countries that are not currently used in the United States for reducing pathogenic *E. coli* in cattle, and will consider whether those practices can inform U.S. efforts. USDA will also continue its other efforts to explore and enhance pre-slaughter interventions, such as the 2011 public meeting, jointly held by APHIS, FSIS, and the Agricultural Research Service, to discuss how pre-harvest pathogen control strategies for animals presented for slaughter can reduce the likelihood that beef could become contaminated with Shiga toxin-producing *E. coli*, *Salmonella*, and other pathogens.

Thank you for the opportunity to comment on this draft report.

Sincerely,

Thomas J. Vilsack
Secretary

Appendix III: GAO Contact and Staff Acknowledgments

GAO Contact

Lisa Shames, (202) 512-3841, or shamesl@gao.gov

Staff Acknowledgments

In addition to the individual named above, Thomas Cook, Assistant Director; Kevin Bray; Mark Braza; Christina E. Bruff; Allen T. Chan; Barbara El Osta; Brenda Muñoz; Katherine M. Raheb; Sushil Sharma; Benjamin Shouse; Carol Herrnstadt Shulman; and Kiki Theodoropolous made key contributions to this report.