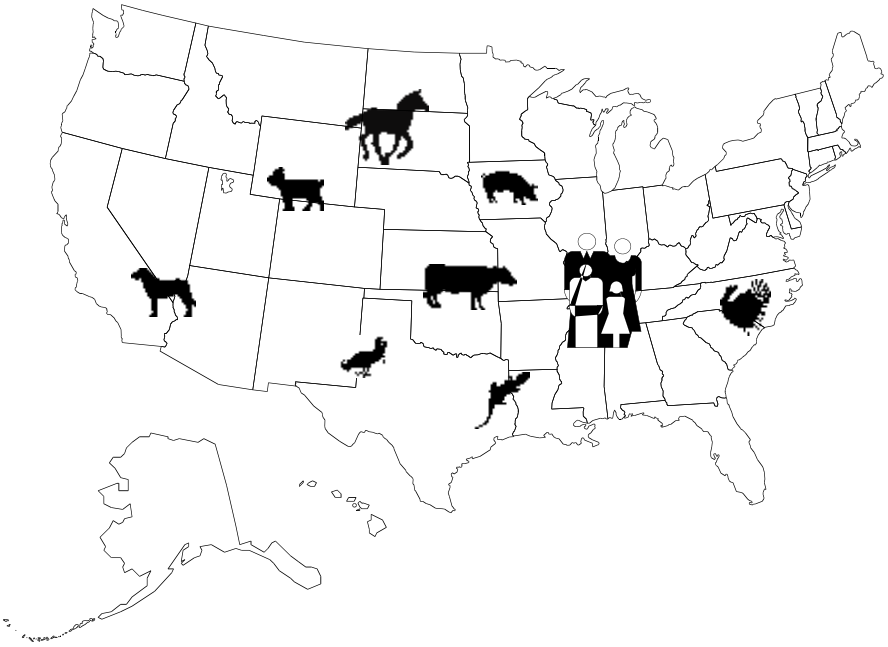
National Antimicrobial Resistance Monitoring System - Enteric Bacteria



A program to monitor antimicrobial resistance in humans and animals

Antimicrobial resistance in foodborne pathogens is an important health issue. Levels of resistance are increasing and there is much we do not know about this problem. We need more information to help us understand this problem and the very real threat it presents to public health. There is a program in place to monitor changes in resistance of bacteria to the antimicrobial drugs used to treat animals and humans. That program is the National Antimicrobial Resistance Monitoring System (NARMS).

What is an antimicrobial?

Antibiotics and other antimicrobial drugs enable doctors to treat bacterial illnesses such as ear infections and strep throat in humans. Antimicrobial drugs are also used to treat or prevent illness caused by bacteria in humans or animals. They work by killing or inhibiting the growth of bacteria.

What are antimicrobial-resistant bacteria?

The use of antibiotics may eliminate susceptible bacteria, leaving resistant bacteria behind. If those resistant bacteria spread, they can cause an infection that may not respond to the usual antibiotics, or may require an increased dose or a longer treatment time. As a result, people or animals infected with resistant bacteria may be sick for a longer time than if they had an infection caused by bacteria that were easily treatable with antibiotics.

How does resistance develop?

The increase in bacterial resistance to antimicrobial drugs is a natural phenomenon -- an outcome of evolution. Any population of organisms, including bacteria, naturally includes variants with unusual traits. In this case, some bacteria have the ability to fend off the action of an antimicrobial. The use of antimicrobial drugs in humans and animals over the past 50 years has inadvertently accelerated the development of resistance because resistant bacteria are more likely to survive treatment with antimicrobial drugs. Once it has been introduced into an environment, resistance may be spread to other microbes.

Food animals can carry organisms that can make people sick, but may not necessarily make the animals sick. For example, *Salmonella*, *Campylobacter,* and *E. coli* O157 are common bacteria found in the intestines of various food animals. These bacteria might not cause disease in the animal, but, all three bacteria can cause foodborne illness in humans. These bacteria might develop resistance when exposed to antibiotics given to the animal. These resistant bacteria can contaminate meat at slaughter and then infect humans who eat the meat, particularly if it is undercooked or cross-contaminated after cooking.

Evidence of increasing resistance to antimicrobial drug treatment in bacteria that infect humans has raised questions about the role that antimicrobial drug use in food animals plays in the emergence of antimicrobial drug resistant bacteria. The link between antimicrobial resistance in

foodborne bacteria that cause disease (which are considered human pathogenic bacteria) and use of antimicrobials in food animals has been reported in a number of studies. For foodborne pathogens, particularly *Salmonella* that are rarely transferred from person to person in the United States, food (such as meat or eggs) from animals is considered the most likely source of human exposure to resistant bacteria.

How we monitor

We need to carefully watch for evidence of changes in levels of resistance to antibiotics because increases in resistance can make it more difficult to treat diseases caused by these bacteria. The NARMS program allows the Food and Drug Administration (FDA) to monitor resistance to antimicrobial drugs used in humans and food animals. NARMS combines the activities of FDA, the Centers for Disease Control and Prevention (CDC), and the U.S. Department of Agriculture (USDA) to create a nationwide monitoring system. As a part of NARMS, isolates of foodborne bacteria including *E. coli*, *Salmonella*, Enterococci, and *Campylobacter* from humans, animals, and retail meats are collected and tested to determine changes in susceptibility to antimicrobial drugs. Each year, samples are taken and tested to determine if there have been changes over time in the resistance of certain enteric (gut) bacteria to selected antimicrobial drugs. The antimicrobial drugs tested are selected based on their importance in human and animal medicine. The human samples are collected from sick people. The animal samples are gathered from healthy farm animals, animal clinical specimens, carcasses of food animals at slaughter, ground products at processing plants. The retail meat samples are collected from grocery stores and shops that sell meat to the public.

Where are the samples tested?

The human-origin isolates are sent to the CDC in Atlanta, GA, by state and local health departments in all 50 states.

Animal-origin isolates are collected from sites across the U.S. and sent to the Antimicrobial Resistance Research Unit (ARRU) of USDA in Athens, GA, for susceptibility testing. Animal isolates come from federally inspected slaughter and processing facilities, USDA's animal health monitoring studies on farms, and veterinary diagnostic laboratories.

The NARMS program also includes a retail program (the Iowa Retail Meat Pilot Survey) that conducts susceptibility testing of enteric bacteria isolated from retail meat samples collected from grocery stores in states participating in the CDC FoodNet program (a program that shares information electronically with researchers and public health officials across the country) on resistant bacteria isolated from people who got sick from the food they ate). The FDA Center for Veterinary Medicine (CVM) Office of Research Laboratory in Laurel, MD, conducts the susceptibility testing of these samples.

CDC, USDA, and FDA test *Salmonella, E. coli, Campylobacter,* Entercocci, and other bacteria for susceptibility to the same group of antimicrobial drugs. The results of these tests are compared with results from previous years to look for changes in resistance patterns of the bacteria to these drugs. NARMS reports are published annually. NARMS data can be

accessed through links on the CVM home page:
(**www.fda.gov/cvm/index/narms/narms_pg.html**). Human data is located on the CDC web site: (**www.cdc.gov/narms**). Animal data is on the USDA web site:
(**www.arru.saa.ars.usda.gov/narms.html**)

Public health officials, animal producers, drug manufacturers, physicians, and veterinarians can use the information from NARMS to control and prevent harm from the use of antimicrobial drugs in food animals.

NARMS Methods

Human data: State public health laboratories systematically select every 20th non-Typhi *Salmonella* isolate, *Shigella*, and *E. coli* O157:H7 submitted to their laboratory and send the isolates to CDC. All *Salmonella Typhi*, *Listeria monocytogenes*, and non-cholerae *Vibrio* isolates are forwarded to CDC.

Additionally, health departments that participate in the FoodNet Program submit one *Campylobacter* isolate each week to the CDC Foodborne and Diarrheal Diseases Laboratory for susceptibility testing. The number of states that participate in this program continues to increase as more health departments join the FoodNet Program. The FoodNet Web Site at: http://www.cdc.gov/foodnet/ contains a listing of current participants.

The antimicrobial susceptibility testing results are sent from the CDC laboratory to NARMS epidemiologists at CDC, where data are analyzed.

Animal data: The USDA ARRU laboratory receives *Salmonella*, *Campylobacter*, *E. coli* and Enterococci isolates from animals for antimicrobial susceptibility testing. The Athens laboratory receives isolates from the sources described in ***"How We Monitor."*** Samples of water used to rinse poultry carcasses at slaughter plants are sent to ARRU from the Food Safety Inspection Service laboratories for culture, isolation, and susceptibility testing of *Campylobacter*, *E. coli*, and Enterococci organisms. *Salmonella* isolates are received from USDA programs and veterinary diagnostic laboratories. *E. coli* and Enterococci also come from samples collected on farms.

Retail data: The **Iowa Retail Meat Pilot Survey** included collection and antimicrobial susceptibility testing of bacterial isolates from retail meats purchased from Iowa retail grocery stores. This study was conducted to figure out the best way to collect and test samples from retail stores. Samples of ground beef, ground turkey, pork chops, and chicken breasts were tested for *Salmonella, Campylobacter, E. coli*, and Enterococci. The bacteria were then tested for resistance to antimicrobials. The **FoodNet Retail Meat Surveillance** was set up using the Iowa study as a model. Samples of ground beef, ground turkey, pork chops and chicken breasts are being collected from grocery stores in participating FoodNet States. Enteric bacterial isolates from these samples are being sent from the FoodNet laboratories to CVM Office of Research for antimicrobial drug susceptibility testing of *Salmonella, Campylobacter, E. coli,* and Enterococci.

The NARMS program is designed so that the same testing methods are used in the human, animal, and retail programs. For all isolates, testing bacteria for susceptibility to antimicrobials currently involves the determination of the minimum inhibitory concentration (MIC) for a panel of selected antimicrobial agents. The MIC is the lowest concentration of a drug that will slow or stop the growth of the bacteria being tested. The higher the MIC number, the greater resistance the bacteria have. These antimicrobial drugs are evaluated each year by FDA, CDC, and USDA for their continued importance in human and animal medicine. Based on these evaluations, some drugs may be removed and others added in their place. Standardized national guidelines for conducting laboratory studies are followed, when possible, throughout the testing procedure.

What Can NARMS Tell Us?

Data collected by NARMS can provide useful information about patterns of emerging resistance, which in turn can help guide treatment decisions in human and veterinary medicine. NARMS data are an asset to outbreak investigations. Antimicrobial resistance patterns are useful in identifying the source and magnitude of resistance. Antimicrobial resistance data from humans and animals are important for the development of public health recommendations for the use of drugs in humans and food animals.

What Else is Being Done?

FDA's goal is to protect the public health by ensuring that significant human antimicrobial therapies are not lost due to use of antimicrobial drugs in food-producing animals, while providing for the safe use of antimicrobial drugs in food-producing animals.

FDA's Center for Veterinary Medicine is working to develop a comprehensive approach to combat the complex problem of antimicrobial resistance. Draft Guidance for Industry #152, titled "Evaluating the Safety of Antimicrobial New Animal Drugs with Regard to Their Microbiological Effects on Bacteria of Human Health Concern," represents the Agency's current thinking and discusses a suggested approach for assessing the safety of antimicrobial new animal drugs with regard to their microbiological effects on bacteria of human health concern. (See www.fda.gov/cvm/guidance/published.htm#published_3)

This guidance document is an evolution of several previous documents including the concept paper titled "Proposed Framework for Evaluating and Assuring the Human Safety of the Microbial Effects of Antimicrobial New Animal Drugs Intended for Use in Food-Producing Animals" (Framework Document). The Framework Document was published by the Agency in January 1999 and discussed possible strategies for managing the potential risks associated with the use of antimicrobial drugs in food-producing animals. Please refer to the FDA CVM web site for the latest information on publications to implement the Framework Document (www.fda.gov/cvm).

In addition to the work being done by CVM, the American Veterinary Medical Association (AVMA), veterinary practitioner groups, and producer groups have developed prudent and judicious antimicrobial drug use programs to help veterinarians and producers make safe and sound decisions about the use of these products in animal production. Brochures and

videotapes on the appropriate use of antimicrobial drugs were developed by CVM in collaboration with the AVMA and other groups. They are posted on the CVM website and copies are available from CVM upon request. The CDC, in collaboration with the American Medical Association (AMA) and medical specialty groups, has developed prudent use guidelines for physicians. Medical and veterinary school curricula are also the focus of educational efforts to promote the appropriate use of antimicrobial drugs. NARMS isolates are also used in research on the molecular determinants of resistance.

Using NARMS as a template, CVM and Mexico are working together on a cooperative project known as ***"ResistVet"*** to conduct monitoring for trends in antimicrobial resistance in humans, animals, and retail foods at four sites in Mexico. To further support antimicrobial resistance monitoring in Mexico, CVM collaborated with the World Health Organization to conduct a training course in 2001 on the surveillance of *Salmonella* and antimicrobial resistance in foodborne pathogens. The training took place at a participating ***ResistVet*** site in Mexico.

For additional information on the NARMS program, contact Dr. Marcia Headrick, FDA CVM NARMS Coordinator, at mheadric@cvm.fda.gov or (706)546-3689.

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