

## THE NATIONAL ANTIMICROBIAL RESISTANCE MONITORING SYSTEM (NARMS)

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Bacterial antimicrobial resistance in both the medical and agricultural fields has become a serious problem worldwide. Antibiotic resistant strains of bacteria are an increasing threat to animal and human health, with resistance mechanisms having been described for all known antimicrobials currently available for clinical use. Although much scientific information is available on this subject, many ecological aspects of the development and dissemination of antimicrobial resistance remain uncertain. What is known is that the emergence and dissemination of bacterial antimicrobial resistance is the result of numerous complex interactions among antimicrobials, microorganisms, and the surrounding environments.

The emergence of antimicrobial resistance is neither an unexpected nor a new phenomenon. It is, however, an increasingly problematic situation due to the frequency with which new emerging resistance phenotypes are occurring among many bacterial pathogens. Over the past 6 decades, the introduction of new classes or modifications of older classes of antimicrobials has been matched slowly but surely by the development of new bacterial resistance mechanisms. Infections caused by resistant bacteria have been shown to be more frequently associated with increased morbidity and mortality than those caused by susceptible pathogens (Helms et al., 2002; Travers and Barza, 2002; Varma et al., 2005). In areas of concentrated use, such as hospitals, this had led to lengthened hospital stays, increased health care costs and in extreme cases, to untreatable infections. The modern predicament of widespread antimicrobial resistance has led the WHO to warn that these drugs may be lost, unless there is comprehensive and concerted action to combat the present problem and reverse anticipated trends.

Numerous retrospective and prospective studies have demonstrated that increases in antimicrobial resistance occur among both pathogenic and commensal bacteria after introduction of an antimicrobial (McDermott et al., 2003; Molbak et al., 1999; Murphy et al., 2001). The common observation of a relationship between increasing use of broad spectrum antimicrobials and escalating resistance to these agents suggests a continuous cycle of antibiotic use, bacterial resistance development, reduced efficacy of antibiotics, and the constant need for newer antimicrobial agents.

In food animals, antimicrobials are used for the control, prevention and treatment of infectious bacterial diseases, as well as for feed efficiency purposes. An undesired consequence of antimicrobial use in animals is the potential development of antimicrobial-resistant zoonotic foodborne pathogens, and their subsequent transmission to humans via foods. The emergence of antimicrobial resistance is increasing the overall mortality, morbidity and economic costs associated with treating bacterial infections caused by resistant organisms. Thus, addressing the

issue of antimicrobial resistance is one of the most urgent priorities in the field of infectious disease today

The increased international concern regarding the transfer of bacterial foodborne pathogens, including resistant variants, between animals and humans has helped spur the development of numerous surveillance systems and networks around the world (Aarestrup, 2004; Centers for Disease Control and Prevention, 5 A.D.; CIPARS, 2004; DANMAP, 2003; Esaki et al., 2004; Fisher and Threlfall, 2005; Swaminathan et al., 2001; Tollefson et al., 1999; Wray and Gnanou, 2000). In the United States, three programs are in place that combine active and passive surveillance with epidemiologic studies to help public health officials better understand the dynamics of foodborne diseases: these are FoodNet, PulseNet, and the National Antimicrobial Resistance Monitoring System (NARMS) (Botteldoorn et al., 2004; Centers for Disease Control and Prevention, 5 A.D.; Gerner-Smidt et al., 2005; Swaminathan et al., 2001; Tollefson et al., 1999). As part of the overall FDA-CVM strategy to assess relationships between antimicrobial use in agriculture and subsequent human health consequences, the National Antimicrobial Resistance Monitoring System (NARMS) program was developed to monitor changes in susceptibility of select bacteria to antimicrobial agents of human and veterinary importance (Tollefson et al., 1999). NARMS is a multi-faceted monitoring system that takes advantage of the expertise and resources of a number of federal agencies and state public health laboratories. NARMS was established in 1996 as a collaborative effort among the Food and Drug Administration's Center for Veterinary Medicine (FDA CVM), U.S. Department of Agriculture (USDA), and the Centers for Disease Control and Prevention (CDC). The NARMS program is sentinel surveillance system designed to detect changes in susceptibilities among foodborne pathogens recovered from food animals, retail meats and humans. On an annual basis, isolates *E. coli*, *Salmonella*, *Enterococcus*, and *Campylobacter* from human clinical specimens, samples at slaughter, and raw meat and poultry product from food animals are tested to monitor changes in resistance/susceptibility to select antimicrobial drugs. The antimicrobial drugs tested are selected based on their importance in human and animal medicine. As a public health surveillance system, the primary objectives of NARMS include:

- To provide descriptive data on the extent and temporal trends of antimicrobial drug susceptibility in *Salmonella* and other enteric bacteria from humans, food animals and retail foods of animal origin;
- To respond to unusual or high levels of bacterial drug resistance in humans, animals, and retail meats in order to contain or mitigate resistance dissemination;
- To design follow-up epidemiology and research studies to better understand the emergence and transfer of antimicrobial drug resistance.

The NARMS program consists of three components or arms:

*Animal Arm* -- *Salmonella* isolates are collected from both on-farm studies (e.g. NAHMS) and federally-inspected slaughter and processing facilities across the U.S. and sent to the Bacterial Epidemiology and Antimicrobial Resistance Research Unit of the USDA in Athens, GA for antimicrobial susceptibility testing. The USDA Bacterial Epidemiology and Antimicrobial

Resistance Research laboratory also receives *Salmonella* isolates from ill animals from veterinary diagnostic laboratories and NVSL. *Campylobacter*, *Enterococcus*, and *E. coli* isolates are recovered from chicken carcass rinsates from the Athens, GA Food Safety Inspection Service Laboratory.

Human Arm -- The human-origin isolates are sent to the CDC Foodborne and Diarrheal Diseases Laboratory in Atlanta, GA, by state and local health departments in all 50 states. 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 also forwarded to CDC. Additionally, the state public health laboratory in each of the participating 10 FoodNet surveillance sites makes arrangements for submission of a representative sample of *Campylobacter* isolates to CDC.

Retail Arm -- CVM's role in NARMS involves isolating and identifying specific foodborne bacterial pathogens and commensal organisms from ground beef, ground turkey, pork chops, and chicken breasts) on a monthly basis from 10 participating FoodNet sites throughout the U.S. (California, Colorado, Connecticut, Georgia, Maryland, Minnesota, New Mexico, New York, Tennessee, and Oregon). Bacteria under surveillance include *Salmonella*, *Campylobacter*, *Enterococcus* and *E. coli* and are initially identified by the FoodNet laboratories and sent to CVM's office of research where their identity is confirmed, and subsequent analyses are performed, including antimicrobial susceptibility testing following CLSI/NCCLS standards.

The NARMS program is designed so that comparable testing methods are used in the human, animal, and retail programs. Participating NARMS laboratories adhere to the appropriate published CLSI/NCCLS guidelines and standards for antimicrobial susceptibility testing and quality control monitoring to ensure accuracy and comparability of the data. Recently, the Office of Research at CVM developed a new standardized broth microdilution antimicrobial susceptibility testing method for *Campylobacter* that will be instituted at all 3 NARMS laboratories this year.

NARMS is a very strong program that has made some excellent progress in meeting the above stated objectives. Several years of antimicrobial susceptibility/resistance monitoring data have now been collected on important human foodborne pathogens (e.g., *Campylobacter*, *Salmonella*, *Shigella*) and commensal bacteria (e.g. enterococci and *E. coli*) from across the United States. This is a very valuable resource that is revealing important trends in antimicrobial susceptibility profiles to a wide variety of antimicrobial agents of importance to human and veterinary medicine. This information is valuable in identifying the source and magnitude of antimicrobial resistance and is important for the development of public health recommendations for the use of antimicrobial drugs in humans and food animals. All three agencies involved in NARMS are capable characterizing isolates at the molecular level, and have been helpful with past foodborne disease outbreak investigations. Additional information on NARMS, as well as links to CDC and USDA NARMS data can be obtained from the CVM website ([http://www.fda.gov/cvm/narms\\_pg.html](http://www.fda.gov/cvm/narms_pg.html)).

In summary, there are many gaps in our knowledge of the development and dissemination of bacterial antimicrobial resistance related to the animal production environment. Understanding the complex ecological, biochemical, and molecular aspects of antimicrobial resistance is needed, both to develop new antimicrobial agents and to protect the potency of the currently available agents. There will also be a continuing need for high-quality, population-based antimicrobial susceptibility/resistance data to support regulatory and other science-based efforts to mitigate antimicrobial resistance both here in the United States and abroad. Additionally, the integration of susceptibility data with molecular fingerprinting methods (e.g. pulsed field gel electrophoresis) between NARMS and PulseNet is currently underway in the U.S. and will help lead to an increased understanding how antimicrobial resistant bacteria develop and disseminate in the animal production environment, retail foods, and human illness. Further insights into these areas should lead to better strategies for managing antimicrobial resistance development and limiting resistance dissemination among animal and human environments. The factors responsible for the emergence and dissemination of antimicrobial resistance and the potential strategies for addressing the dilemma are complex and encompass an expansive range of scientific disciplines. Solving the problems associated with antimicrobial resistance will demand a concerted effort by veterinarians, physicians, drug manufacturers, researchers, and regulatory agencies. A comprehensive research and surveillance effort will help ensure that any actions taken to control resistance will be based on sound scientific data and guidance.

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