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Report to the Committee on Agriculture, House of Representatives

June 2011

ANTIBIOTIC RESISTANCE

Data Gaps Will Remain Despite HHS Taking Steps to Improve Monitoring

GAO-11-406

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Highlights

Highlights of GAO-11-406, a report to the Committee on Agriculture, House of Representatives

Why GAO Did This Study

Infections that were once treatable have become more difficult to treat because of antibiotic resistance. Resistance occurs naturally but is accelerated by inappropriate antibiotic use in people, among other things. Questions have been raised about whether agencies such as the Department of Health and Human Services (HHS) have adequately assessed the effects of antibiotic use and disposal on resistance in humans. GAO was asked to (1) describe federal efforts to quantify the amount of antibiotics produced, (2) evaluate HHS's monitoring of antibiotic use and efforts to promote appropriate use, (3) examine HHS's monitoring of antibiotic-resistant infections, and (4) describe federal efforts to monitor antibiotic disposal and antibiotics in the environment, and describe research on antibiotics in the development of resistance in the environment. GAO reviewed documents and interviewed officials, conducted a literature review, and analyzed antibiotic sales data.

What GAO Recommends

To better control the spread of resistance, GAO recommends that HHS's Centers for Disease Control and Prevention (CDC) develop and implement strategies to improve its monitoring of (1) antibiotic use and (2) antibiotic-resistant infections. HHS generally agreed with our recommendations. HHS, the Environmental Protection Agency (EPA) and the Department of the Interior (DOI) provided technical comments, which we incorporated as appropriate.

View GAO-11-406 or key components.
For more information, contact Marcia Crosse at (202) 512-7114 or crossem@gao.gov

What GAO Found

Federal agencies do not routinely quantify the amount of antibiotics that are produced in the United States for human use. However, sales data can be used as an estimate of production, and these show that over 7 million pounds of antibiotics were sold for human use in 2009. Most of the antibiotics that were sold have common characteristics, such as belonging to the same five antibiotic classes. The class of penicillins was the largest group of antibiotics sold for human use in 2009, representing about 45 percent of antibiotics sold.

HHS performs limited monitoring of antibiotic use in humans and has implemented efforts to promote their appropriate use, but gaps in data on use will remain despite efforts to improve monitoring. Although CDC monitors use in outpatient healthcare settings, there are gaps in data on inpatient antibiotic use and geographic patterns of use. CDC is taking steps to improve its monitoring, but gaps such as information about overall antibiotic use will remain. Because use contributes to resistance, more complete information could help policymakers determine what portion of antibiotic resistance is attributed to human antibiotic use, and set priorities for action to control the spread of resistance. CDC's Get Smart program promotes appropriate antibiotic use; CDC has observed declines in inappropriate prescribing, but it is unclear to what extent the declines were due to the program or to other factors. CDC's program has been complemented by efforts by the National Institutes of Health and the Food and Drug Administration, such as supporting studies to develop tests to quickly diagnose bacterial infections.

Gaps in CDC's monitoring of antibiotic-resistant infections limit the agency's ability to assess the overall problem of antibiotic resistance. There are data gaps in monitoring of such infections that occur in healthcare facilities; CDC does not collect data on all types of resistant infections to make facilitywide estimates and the agency's information is not nationally representative. CDC can provide accurate national estimates for certain resistant infections that develop in the community, including tuberculosis. Although CDC is taking steps to improve its monitoring, these efforts will not allow CDC to accurately assess the overall problem of antibiotic resistance because they do not fill gaps in information. Without more comprehensive data, CDC's ability to assess the overall scope of the public health problem and plan and implement preventive activities will be impeded.

Federal agencies do not monitor the disposal of most antibiotics intended for human use, but they have detected them, as well as antibiotics for animal use, in the environment, which results partly from their disposal. EPA and DOI's United States Geological Survey have examined the presence of certain antibiotics in environmental settings such as streams. Studies conducted by scientists have found that antibiotics present in the environment at certain concentrations can increase the population of resistant bacteria.

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Abbreviations

ABCs	Active Bacterial Core Surveillance
ANDA	Abbreviated New Drug Application
CCL	Contaminant Candidate List
CDC	Centers for Disease Control and Prevention
CMS	Centers for Medicare & Medicaid Services
DOI	Department of the Interior
EIP	Emerging Infections Programs
EPA	Environmental Protection Agency
FDA	Food and Drug Administration
GISP	Gonococcal Isolate Surveillance Project
HAI	healthcare-associated infection
HHS	Department of Health and Human Services
MDRO	multidrug-resistant organism
MIC	minimum inhibitory concentration
MRSA	Methicillin-resistant *Staphylococcus aureus*
NAMCS	National Ambulatory Medical Care Survey
NARMS: EB	National Antimicrobial Resistance Monitoring System: Enteric Bacteria
NCQA	National Committee for Quality Assurance
NDA	New Drug Application
NHAMCS	National Hospital Ambulatory Medical Care Survey
NHSN	National Healthcare Safety Network
NIH	National Institutes of Health
NNDSS	National Notifiable Diseases Surveillance System
NTSS	National Tuberculosis Surveillance System
PhRMA	Pharmaceutical Research and Manufacturers of America
RCRA	Resource Conservation and Recovery Act
SDWA	Safe Drinking Water Act
TB	tuberculosis
UCMR	Unregulated Contaminant Monitoring Rule
USGS	United States Geological Survey
USITC	United States International Trade Commission

GAO
Accountability * Integrity * Reliability

United States Government Accountability Office
Washington, DC 20548

June 1, 2011

The Honorable Frank D. Lucas
Chairman
The Honorable Collin Peterson
Ranking Member
Committee on Agriculture
House of Representatives

Over 60 years ago penicillin was the first antibiotic introduced to treat bacterial infections, leading to a dramatic drop in deaths from bacterial infections that were previously untreatable, as well as significant gains in life expectancy. The eventual emergence and spread of bacterial infections that are resistant to antibiotics, however, has jeopardized these gains because infections that were once easy to cure with antibiotics are becoming difficult, if not impossible, to treat. Some bacterial infections, such as certain types of pneumonia and gonorrhea that are acquired in the community, have developed resistance to almost all currently available antibiotics. Furthermore, the bacterial infections that contribute most to human disease are also those in which antibiotic resistance is most common, such as respiratory tract infections and infections acquired in hospitals. Although not all infections acquired in hospitals are resistant to antibiotics, individuals with resistant infections are more likely to have a poor prognosis and to remain in the hospital for a longer time, resulting in greater medical costs.[1]

While the development of antibiotic resistance is not new, as resistance is a natural biological phenomenon and can occur when any antibiotic is present, it is accelerated by a variety of factors including the inappropriate use of antibiotics in the absence of a bacterial infection and the prolonged use of antibiotics to treat patients who are critically ill. Antibiotic-resistant bacteria that are present in the human body can be spread to others. In addition, antibiotic-resistant bacteria that occur in the environment, either

[1]For example, the medical costs attributable to the treatment of an antibiotic-resistant infection ranged from about $19,000 to $29,000 per patient in a study of one hospital. In addition, the excess duration of a hospital stay was about 6 to 13 days and the death rate was twofold higher among those patients who were treated for such infections. See R.R. Roberts et al., "Hospital and Societal Costs of Antimicrobial-Resistant Infections in a Chicago Teaching Hospital: Implications for Antibiotic Stewardship, *Clinical Infectious Diseases*, vol. 49 (2009), pp. 1175-1184.

from natural causes or their discharge into soil or bodies of water, may spread their resistance to other bacteria.

Scientists, public health officials, and clinicians agree that antibiotic resistance has become a national and global health challenge. While there are various causes of antibiotic resistance—including the use of antibiotics in humans and animals—the actual scope of the overall problem is not clear and there is uncertainty about the relative contributions of each cause.[2] Recommendations for government action to address antibiotic resistance have been made by various organizations and scientific experts, including a task force made up of federal agencies, and there is agreement that, among other things, improved surveillance of antibiotic use and antibiotic-resistant infections is needed to adequately understand antibiotic resistance and implement effective strategies to help control this complex problem.[3] Further, a congressional committee[4] and others have made recommendations to increase the geographic coverage of existing federal agency surveillance to address concerns such as gaps in the ability to track and monitor certain antibiotic-resistant infections, such as methicillin-resistant *Staphylococcus aureus* (MRSA).

Questions have been raised as to whether federal agencies, including the Department of Health and Human Services (HHS), have adequately assessed the relationship among the volume of antibiotics produced for human use, the human use of antibiotics, the presence of antibiotics in the environment, and the problem of antibiotic resistance. The House Committee on Agriculture asked us to evaluate how federal agencies track the occurrence of antibiotic resistance and the use and disposal of antibiotics into the environment. In this report, we (1) describe efforts by federal agencies to quantify the amount of antibiotics produced for human use, (2) describe and evaluate HHS efforts to monitor antibiotic use and promote the appropriate use of antibiotics by humans, (3) examine HHS

[2]GAO has ongoing work examining antibiotic use in food animals.

[3]For example, a recent report from the American Academy of Microbiology outlined several recommendations to help control the development and spread of antibiotic resistance, including improved surveillance to better assess the actual scope of the problem. See American Academy of Microbiology, *Antibiotic Resistance: An Ecological Perspective on an Old Problem* (Washington, D.C.: 2009).

[4]See House of Representatives, *Departments of Labor, Health, and Human Services, and Education, and Related Agencies Appropriations Bill, 2010: Report of the Committee on Appropriations together with Minority Views*, Report 111-220 (Washington, D.C.: July 22, 2009).

efforts to monitor cases of antibiotic-resistant infections in humans in the United States, and (4) describe federal efforts to monitor the disposal of antibiotics intended for human use, federal efforts to monitor the presence of antibiotics in the environment, and the scientific evidence regarding the role of antibiotics in the development of antibiotic-resistant bacteria in the environment.

To describe efforts to quantify the amount of antibiotics produced for human use by federal agencies, we interviewed HHS officials to determine whether HHS collects information about, and quantifies, the amount of antibiotics that are produced for human use. We also reviewed documents from HHS and the U.S. International Trade Commission (USITC)—a federal agency that collects and analyzes trade data to inform U.S. trade policy—to learn about federal efforts to quantify antibiotic production in the United States. We purchased 2009 national sales data for antibiotics from IMS Health to estimate the volume of antibiotics produced in the United States for human use.[5] IMS Health provided us the total volume of antibiotics, in kilograms, that were sold, based on all antibiotic drugs that were included in the Red Book Advanced database, as of April 2010.[6] We converted the total volume from kilograms to pounds. To further describe the antibiotics that were sold in 2009, we classified the total volume of antibiotics by antibiotic class, the route of administration (e.g., oral), and the types of pharmacies that purchased antibiotics (e.g., chain store pharmacy). To assess the reliability of IMS Health data, we reviewed existing information about the data and interviewed officials knowledgeable about the data to assess their completeness.[7] We determined that the data were sufficiently reliable for their use in this report.

To describe HHS efforts to monitor the use of antibiotics in humans, we reviewed HHS documents and interviewed HHS officials. We reviewed HHS documents describing the various surveys that HHS uses to routinely

[5]The company IMS Health, on a monthly basis, collects data on drugs—including antibiotics—purchased by retail pharmacies from about 100 drug manufacturers and about 500 distribution centers. These manufacturers and distribution centers provide data to IMS Health on the number of units sold.

[6]The Red Book Advanced database includes a comprehensive list of drug products approved for use by the Food and Drug Administration.

[7]IMS Health conducts detailed data reliability assessments, which include comparing monthly data from drug manufacturers and distribution centers to data from the prior month and the prior year in order to ensure consistency.

collect data about antibiotic use, including information about the survey samples, the types of data that are gathered, and how antibiotic use is measured. We also reviewed agency documents that summarize trends in antibiotic use, based on the surveys. We interviewed HHS officials with responsibility for the surveys about the strengths and limitations of each survey and how the agency uses the collected data to monitor antibiotic use. To evaluate HHS's efforts to monitor antibiotic use, we compared HHS's data collection and monitoring activities with broad guidelines for monitoring antibiotic use, which we identified by reviewing relevant HHS documents and expert organization (e.g., World Health Organization) guidelines. To describe HHS efforts to promote the appropriate use of antibiotics, we reviewed documents from HHS about programs and activities focused specifically on decreasing inappropriate antibiotic use. We also interviewed officials from HHS about the objectives and implementation of these programs and activities. To evaluate HHS's efforts to promote the appropriate use of antibiotics, we reviewed relevant HHS documents and research articles in peer-reviewed journals about the effectiveness of intervention programs to reduce inappropriate antibiotic use and we interviewed HHS officials about the strengths and limitations of its program to promote appropriate antibiotic use and how the agency has evaluated its program.

To examine HHS efforts to monitor cases of antibiotic-resistant infections in humans, we reviewed agency documents from HHS and interviewed HHS officials and representatives from an HHS advisory committee on healthcare infection control. We reviewed HHS documents describing each of the agency's surveillance systems that are used to monitor antibiotic resistance. The documents described the purpose and objectives of each system, and what surveillance data are collected and how the data are collected; the documents also provided annual summary information about monitored infections. We interviewed HHS officials with responsibility for each of the surveillance systems about the strengths and limitations of each system and how the data gathered by each system are used by the agency. We also interviewed four members of a federal advisory committee that provides guidance to HHS regarding infection control, surveillance, and prevention, as well as officials from three

organizations that serve as liaisons to the committee, to obtain their opinions of the strengths and limitations of HHS's surveillance systems.[8]

To describe federal efforts to monitor the disposal of antibiotics intended for human use, we interviewed officials from the Environmental Protection Agency (EPA), HHS, and the Department of the Interior's (DOI) United States Geological Survey (USGS) to determine if these agencies collect data about the disposal of antibiotics and, if applicable, how they use such data for monitoring. We also reviewed relevant federal laws under which EPA may have responsibility to regulate disposal of certain antibiotics and to monitor certain antibiotics in drinking water, as well as a Food and Drug Administration (FDA) consumer guidance document describing recommended disposal practices for unused drugs. We interviewed officials from the Pharmaceutical Research and Manufacturers of America (PhRMA) to learn about the drug disposal practices that are commonly used by pharmaceutical manufacturers.[9] To describe federal efforts to monitor the presence of antibiotics found in the environment, we reviewed documents describing relevant studies conducted by EPA and USGS, including methods for selecting study sample sites and the study findings. We focused on the extent to which antibiotics were present in environmental settings, including soil, sediment, and bodies of water, and in certain pathways to the environment, such as waste water in treatment plants. We interviewed EPA and USGS officials to obtain background information and context about the studies as well as EPA's use of the study findings. We also interviewed EPA and USGS officials about their plans for further related studies.

[8]The Healthcare Infection Control Practices Advisory Committee is comprised of public infection control experts, as well as nonvoting federal agency representatives and nonvoting liaison representatives of several national organizations. The committee is charged with providing advice and guidance to the Secretary of HHS and the Centers for Disease Control and Prevention, among others, regarding the practice of healthcare infection control, strategies for surveillance, and prevention and control of healthcare-associated infections in U.S. healthcare facilities. The officials we interviewed from the three liaison organizations represented the Association of Professionals of Infection Control and Epidemiology, Inc., the Infectious Diseases Society of America, and the Society for Healthcare Epidemiology of America.

[9]PhRMA officials provided us information on how pharmaceutical manufacturers dispose of unused drugs, such as those that are expired or were recalled, and active ingredients that do not get used in the manufacturing process.

To describe the scientific evidence regarding the role of antibiotics in the development of antibiotic-resistant bacteria in the environment, we conducted a literature review and interviewed agency officials. Our literature review included 105 articles that met defined search criteria on antibiotic resistance in the environment, published on or between January 1, 2007, and July 8, 2010. The articles included those published in peer-reviewed journals. In our review, we analyzed the scientific findings reported about antibiotic concentrations that induce environmental bacteria to become resistant and the ability of environmental bacteria to spread resistance through the transfer of resistance genes. We also interviewed EPA and USGS agency officials to obtain context for the scientific evidence presented in the articles. For a detailed description of our literature review, see appendix I.

We conducted our performance audit from March 2010 to June 2011 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

Antibiotics and the Development and Spread of Antibiotic-resistant Bacteria

Antibiotics are drugs that are used to treat bacterial infections.[10] Antibiotics work by killing or slowing the growth of bacteria and they are not effective against nonbacterial infections, such as those caused by viruses. Antibiotic resistance is the result of bacteria changing in ways that reduce or eliminate the effectiveness of antibiotics to cure infection. Antibiotic use forces bacteria to either adapt or die in a process known as "selective pressure." Selective pressure means that when an antibiotic is used, some bacteria will be killed by the antibiotic while other bacteria will survive. Bacteria are able to survive, in part, because they have certain genetic material that allows them to avoid the effects of the antibiotic. The surviving bacteria will multiply and pass on to future generations their genetic material that is coded for resistance to antibiotics. Any use of

[10]Antibiotics are a type of antimicrobial. Antimicrobials are drugs or other chemicals that kill or slow the growth of organisms such as bacteria, viruses, and fungi.

antibiotics—appropriate and inappropriate—creates selective pressure among bacteria. (For more information on resistant bacteria, see app. II).

The inappropriate use of antibiotics, or the additional use of antibiotics that could have been avoided, can occur when healthcare providers prescribe antibiotics when they are not beneficial, such as to treat a viral infection, or when antibiotic treatments are not targeted to the specific bacteria causing the infection.[11] Inappropriate antibiotic use also occurs when healthcare providers do not prescribe the correct antibiotic dose and duration of treatment. Further, inappropriate use includes when patients do not complete a full course of prescribed antibiotics.

Antibiotic Disposal and Pathways for Antibiotics to Enter the Environment

Individual consumers, health care facilities, pharmacies, and pharmaceutical manufacturers dispose of unused antibiotics using various methods. For the purposes of this report, the disposal of antibiotics refers to the discard of unused antibiotics by consumers, companies, and others. Common disposal methods for individual consumers include throwing unused antibiotics in the trash, flushing them down the toilet, and pouring them down the drain.[12] According to EPA officials, healthcare facilities and pharmacies often return unused or expired drugs to contracted companies, known as reverse distributors, for manufacturer credit. The reverse distributor is then instructed by the manufacturer to return the unused drug to the manufacturer, or in most cases, the reverse distributor is instructed to dispose of the drugs. The unused drugs are then most likely incinerated as solid waste, subject to state and local environmental regulations. The federal guidelines on how consumers should properly dispose of their unused drugs, including antibiotics, recommend that consumers dispose of their unused drugs either by returning them through

[11]Diagnostic tests are used to determine the types of bacteria that cause infection and this information can be used by healthcare providers to choose an appropriate antibiotic. Different antibiotics target different types of bacteria.

[12]In addition, some communities conduct pharmaceutical take-back programs that allow the public to bring unused or expired drugs to a central location for disposal.

a drug take-back program, where available, or by mixing them with coffee grounds or kitty litter and throwing them in the household trash.[13]

Unused antibiotics intended for human use may enter the environment through various pathways such as sewage systems and landfills, depending upon the method of disposal and other factors. Unused antibiotics enter sewage systems after they are flushed down the toilet or poured down the drain. Unused antibiotics that enter the sewage system then flow to wastewater treatment plants where, if not removed during the treatment process, they are released into the environment, such as in rivers and streams, as wastewater effluent.[14] In addition, some areas may use onsite septic systems to treat wastewater and in these systems wastewater is discharged below the ground's surface.[15] Unused antibiotics that are disposed of in the trash could enter the environment if landfills were to leak. Although modern landfills are designed with liners and systems to limit this process by rerouting leachate, that is, liquid generated in landfills, to wastewater treatment plants, the antibiotics that are contained in the leachate may ultimately enter the environment. This can occur if antibiotics are not removed during the wastewater treatment process. In general, wastewater treatment plants are not designed to remove low concentrations of drug contaminants, such as antibiotics.[16,17]

In addition, antibiotics that have been used by humans to treat infections can also enter the environment. Most used antibiotics enter the sewage

[13]The guidance, available on the FDA Web site, states that consumers should follow these guidelines unless the drug's label directs consumers to flush the unused drug down the toilet. FDA recommends flushing for a small number of drugs to prevent life-threatening risks from accidental use. See http://www.fda.gov/forconsumers/consumerupdates/ucm101653.htm, downloaded on March 31, 2011.

[14]Wastewater that leaves a treatment plant is known as effluent. Solid, semisolid, or liquid organic materials that leave a wastewater treatment plant are known as sewage sludge or biosolids. Sewage sludge is often applied to land as fertilizer, subject to EPA regulations.

[15]Inadequately treated sewage from such septic systems can be a cause of groundwater contamination.

[16]In general, a contaminant is any substance or matter in the environment such as those that have an adverse effect on air, water, soil, or human health.

[17]For a discussion of wastewater treatment plants and their ability to remove low concentrations of antibiotics, see J.R. Lefkowitz and M. Duran, "Changes in Antibiotic Resistance Patterns of *Escherichia coli* during Domestic Wastewater Treatment," *Water Environment Research*, vol. 81 (2009), pp. 878-885.

systems after they are ingested and excreted by individuals because antibiotics are not fully absorbed by the human body.[18] Like unused antibiotics that enter the sewage systems, used antibiotics flow from sewage systems to wastewater treatment plants and may be released into the environment as wastewater effluent or biosolids. Agricultural manure is another potential source of antibiotics entering the environment; some antibiotics used for agriculture are similar to those used by humans.[19]

Federal Agency Responsibilities

Within HHS, the Centers for Disease Control and Prevention (CDC), FDA, and the National Institutes of Health (NIH) have responsibilities for protecting Americans from health risk, including risk associated with antibiotic-resistant infections. These agencies have a variety of responsibilities related to the surveillance, prevention, and research of infectious disease. CDC has a primary responsibility to protect the public health through the prevention of disease and health promotion. One of CDC's primary roles is to monitor health, and part of this role involves monitoring antibiotic-resistant infections and the use of antibiotics. CDC's statutory authority to conduct such surveillance derives from the Public Health Service Act.[20] Tracking the emergence of antibiotic resistance, and limiting its spread, is also part of CDC's mission. Consistent with this mission, CDC implements prevention strategies, such as educational programs, that are designed to limit the development and spread of antibiotic resistance and the agency monitors antibiotic prescriptions in humans to help reduce the spread of antibiotic resistance.

Part of FDA's responsibility for protecting the public health involves assuring the safety and efficacy of human drugs. FDA reviews and approves labels for antibiotics and provides educational information to consumers and healthcare providers about the appropriate use of antibiotics, and the risk of the development of antibiotic resistance associated with their inappropriate use. FDA also licenses vaccines for use

[18]Antibiotics can also enter sewage systems as a result of bathing and washing. Bathing and washing may release antibiotic ingredients remaining on the skin from the use of topical applications or from excretion to the skin through sweating.

[19]Antibiotics may also enter the environment as a result of their use in aquaculture and orchards (e.g., antibiotics may be sprayed on apple or pear trees to prevent certain infections).

[20]CDC officials told us that the act has been interpreted broadly to include CDC's surveillance of antibiotic-resistant infections and the use of antibiotics. See Public Health Service Act, as amended, § 301(a), codified at 42 U.S.C. § 241(a) (2011).

in humans to prevent bacterial infections—including certain antibiotic-resistant infections—as well as viral infections and has the authority for the review of diagnostics, including tests to detect bacterial infections. As the nation's medical research agency, NIH is responsible for conducting and funding medical research to improve human health and save lives. According to its research agenda on antibiotic resistance, NIH supports and conducts research on many aspects of antibiotic resistance, including studies of how bacteria develop resistance, the development of diagnostic tests for bacterial infections that are or are likely to become resistant to antibiotics, as well as clinical trials such as those to study the effective duration for antibiotic treatments.

CDC, FDA, and NIH are also co-chairs of the Interagency Task Force on Antimicrobial Resistance (Task Force)[21] and released A Public Health Action Plan to Combat Antimicrobial Resistance (Action Plan) in 2001.[22] The Action Plan identified actions needed to address the emerging threat of antibiotic resistance and highlighted the need to improve federal agencies' ongoing monitoring of antibiotic use and of antibiotic-resistant infections. Specifically, the Action Plan stated that establishing a national surveillance plan for antibiotic-resistant infections should be a high priority, and that improved monitoring of such infections was needed to identify emerging trends and assess changing patterns of antibiotic resistance as well as to target and evaluate prevention and control efforts. The Action Plan also specifically stated that surveillance of antibiotic use in humans should be a high priority and was needed to better understand the relationship between antibiotic use and antibiotic resistance. For example, identifying a specific pattern of antibiotic use associated with increased antibiotic resistance could support a response from

[21]The Public Health Improvement Act required that the Secretary of HHS establish the Task Force to provide advice and recommendations related to antibiotic resistance. Under the act, the secretary—in consultation with the Task Force and state and local public health officials—is required to develop, improve, coordinate, or enhance participation in a surveillance plan to detect and monitor emerging antibiotic resistance. The act also states that the secretary, in consultation with the Task Force and others, shall develop and implement educational programs for the general public to increase awareness of the appropriate use of antibiotics and to instruct healthcare professionals in the prudent use of antibiotics. See 42 U.S.C. § 247d-5 (2011).

[22]The Task Force includes eight other federal agency members. These members are the Agency for Healthcare Research and Quality, Centers for Medicare & Medicaid Services, Health Resources and Services Administration, HHS Office of the Assistant Secretary for Preparedness and Response, Department of Agriculture, Department of Defense, Department of Veterans Affairs, and EPA.

policymakers, such as to affect change in antibiotic use practices. Further, improved antibiotic use monitoring would help identify prevention activities and anticipate gaps in the availability of existing antibiotics effective in treating bacterial infections. A revised draft Action Plan was published for public comment on March 16, 2011.[23]

EPA's mission includes protecting Americans from significant environmental health risks. As part of its role, EPA sets national standards for the disposal of solid and hazardous waste and the quality of drinking water. EPA generally regulates the disposal of waste, including some unused or expired drugs, under the Resource Conservation and Recovery Act (RCRA).[24] EPA also promulgates national requirements for drinking water quality of public water systems under the Safe Drinking Water Act (SDWA). EPA conducts research on topics related to human health and the environment, including research aimed at understanding drug disposal practices and the potential human and ecological health risks of drugs, such as antibiotics, found in the environment.

Within DOI, USGS is responsible for providing scientific information to better understand the health of the environment, including our water resources. USGS conducts large-scale studies to gather information that can provide a basis for evaluating the effectiveness of specific policies; these studies can also be used to support decision making at the local and national levels—for example, decisions related to protecting water quality. In 1998, USGS initiated the Emerging Contaminants Project to improve the scientific understanding of the release of emerging contaminants to the environment, including where these contaminants originate and whether they have adverse effects on the environment. As part of the project, USGS has conducted national studies to measure the presence of unregulated contaminants, including antibiotics, in the environment, and conducts targeted local studies to assess the impact of specific pathways by which antibiotics can enter the environment.

[23]The revised draft Action Plan includes the same focus areas—surveillance, prevention and control, research, and product development—as the 2001 Action Plan, along with specific projects or implementation steps for many of the action items. The revised draft Action Plan includes expected completion dates for projects or implementation steps, unlike the 2001 Action Plan.

[24]Hazardous waste has properties, such as being toxic, that make it dangerous or potentially harmful to human health or the environment.

CDC's Monitoring of Antibiotic Resistance in Healthcare and Community Settings

CDC has six surveillance systems that provide information to monitor antibiotic resistance that occurs in healthcare and community settings. According to CDC, public health surveillance is the ongoing and systematic collection, analysis, and interpretation of data for use in the planning, implementation, and evaluation of public health practice.[25] The surveillance systems collect information about antibiotic resistance among certain bacteria that cause infections in humans, and the infections are transmitted either in healthcare settings or in the community. For example, CDC's National Healthcare Safety Network (NHSN) monitors infections that occur in healthcare settings, including those that are resistant to antibiotics, such as MRSA, while CDC's Active Bacterial Core Surveillance (ABCs) system monitors bacterial infections such as meningitis and pneumonia that are spread in the community or in healthcare settings.[26] Table 1 provides information about the purpose of each CDC surveillance system that monitors antibiotic resistance and summarizes the settings in which the monitored infections are spread. (See app. III for additional information about each of the six systems.)

[25]Surveillance systems include the timely dissemination of data to persons who can undertake effective prevention and control activities, such as public health personnel and clinicians.

[26]MRSA infections can also spread in the community, for example, by having close skin-to-skin contact or by exposure to contaminated items and surfaces. ABCs monitors MRSA that is spread in the community as well as in healthcare settings.

Table 1: CDC's Six Surveillance Systems that Provide Information to Monitor Antibiotic Resistance, by System Purpose and Infection Transmission Setting

Surveillance system	Purpose of surveillance system and role in monitoring antibiotic resistance	Infection transmission setting
National Healthcare Safety Network (NHSN)	To provide a database for healthcare facilities to report their healthcare-associated infection (HAI) and antibiotic resistance surveillance data to allow them to estimate the occurrence of such events, monitor trends, and identify patient safety problems.[a] CDC compiles data on antibiotic resistance across participating facilities.	Spread in healthcare settings, such as from healthcare personnel to patient or from patient to patient.
Active Bacterial Core Surveillance (ABCs) [of the Emerging Infections Programs (EIP) Network][b]	To monitor trends in disease and deaths caused by invasive bacterial infections of public health importance, such as meningitis caused by *Neisseria meningitidis*. ABCs is also used to monitor trends in antibiotic resistance, track new resistance mechanisms, and evaluate the effect of public health interventions.	Spread in the community, from person to person (e.g., by exchange of respiratory secretions), or in healthcare settings, such as from healthcare personnel to patient or from patient to patient.
National Antimicrobial Resistance Monitoring System: Enteric Bacteria (NARMS: EB)	To monitor trends in antibiotic resistance among enteric bacteria from humans and to conduct research to better understand the emergence, persistence, and spread of antibiotic resistance.[c] NARMS: EB is also used to provide data to assist FDA in making decisions related to the approval of safe and effective antibiotic drugs for animals and to promote interventions to reduce resistance.	Spread in the community and in other settings, such as through eating food contaminated with fecal matter or eating undercooked poultry.
Gonococcal Isolate Surveillance Project (GISP)	To monitor trends in antibiotic resistance in *Neisseria gonorrhoeae*—the bacterium that causes gonorrhea—in order to establish a basis for selecting treatment guidelines for gonorrhea.	Spread in the community, from person to person, through sexual contact.
National Tuberculosis Surveillance System (NTSS)	To monitor national trends in tuberculosis (TB), including groups at risk for TB, and to evaluate outcomes of TB cases. CDC also uses NTSS to monitor antibiotic resistance in *Mycobacterium tuberculosis*—the bacterium that causes tuberculosis.	Spread in the community, from person to person, by breathing infected air during close contact.
National Notifiable Diseases Surveillance System (NNDSS)	To monitor certain infectious diseases, such as human immunodeficiency virus infection and measles. CDC also uses NNDSS to monitor antibiotic resistance in the bacteria *Streptococcus pneumoniae*, with a focus on assessing the impact of immunization against invasive *Streptococcus pneumoniae* infection. *Streptococcus pneumoniae* causes infections such as pneumonia and meningitis.	Spread in the community, from person to person, such as by exchange of respiratory secretions.

Source: GAO analysis of CDC information and scientific literature.

[a]NHSN also allows facilities to report on 'laboratory-identified' event surveillance data for certain HAIs that are resistant to multiple drugs—such as multidrug-resistant *Klebsiella* infections—as well as *Clostridium difficile* infections; such data are more easily obtained because they come primarily from laboratory test results without clinical evaluation of patients. *Clostridium difficile* infections may develop due to the prolonged use of antibiotics during healthcare treatment.

[b]As part of EIP's Healthcare Associated Infections Surveillance, CDC has monitored *Clostridium difficile* infections in healthcare and community settings since 2009.

[c]FDA coordinates the NARMS program and works with CDC to manage NARMS: EB, the human component of the program. FDA and the United States Department of Agriculture test for antibiotic-resistant enteric bacteria in retail meats and food animals, respectively. Enteric bacteria are found in the intestinal tracts of humans and animals.

Federal Agencies Do Not Routinely Quantify Amount of Antibiotics Produced for Human Use, but Sales Data Show Over 7 Million Pounds of Antibiotics Were Sold in 2009

Federal agencies do not routinely quantify the amount of antibiotics that are produced in the United States for human use, but sales data, which can be used to estimate the quantity of antibiotic production, show that over 7 million pounds of antibiotics were sold in 2009 for human use in the United States. These data indicate that most of the antibiotics sold have common characteristics, such as belonging to five antibiotic classes.

Federal Agencies Do Not Routinely Quantify the Amount of Antibiotics Produced for Human Use

Federal agencies, including FDA and USITC, do not routinely quantify antibiotic production for human use.[27] FDA does collect annual information on the quantity of drugs that manufacturers distribute from new drug application (NDA) and abbreviated new drug application (ANDA) holders, but the data are not readily accessible.[28] For each approved drug, NDA and ANDA holders are required to report annually to FDA the total number of dosage units of each strength or potency of the drug that was distributed (e.g., 100,000 5 milligram tablets) for domestic and foreign use.[29] This information must be submitted to FDA each year—

[27]In contrast, FDA recently issued a report summarizing data on antibiotics sold or distributed for use in food-producing animals, as required by the Animal Drug User Fee Amendments of 2008. This report indicated that 28.7 million pounds of antibiotics were sold or distributed for use in food-producing animals in the United States in 2009. This number includes the antibiotic class ionophores, which are not used in human medicine. Excluding ionophores, the total amount of pounds of antibiotics that were sold or distributed for use in food-producing animals in the United States in 2009 was 20.5 million pounds. According to FDA, these data are limited because they combine therapeutic and subtherapeutic uses of antibiotics and all species of animals. Further, these data do not take into account the dose size, which varies by individual antibiotic and species of animal, or the total number of animals that received antibiotics. Due to such limitations in the data, FDA officials noted that comparisons of antibiotic use between food-producing animals and humans are problematic. See FDA, *2009 Summary Report on Antimicrobials Sold or Distributed for Use in Food-Producing Animals* (Rockville, Md: 2010). Available at http://www.fda.gov/downloads/ForIndustry/UserFees/AnimalDrugUserFeeActADUFA/UCM231851.pdf.

[28]NDAs and ANDAs are submitted to FDA by drug sponsors to obtain approval for their drug to be marketed in the United States.

[29]21 C.F.R. §§ 314.81(b)(2)(ii)(a), 314.98(c) (2011). Generally, only aggregated drug distribution data can be made publicly available. 21 C.F.R. § 314.430(g)(2) (2011).

within 60 days of the anniversary date of approval of the drug application—for as long as the NDA or ANDA is active. The data that NDA and ANDA holders submit to FDA on the quantity of distributed drugs are not readily accessible because, according to an FDA official, they are submitted as part of an annual report in the form of a table and the agency does not enter the data electronically. In addition, because the anniversary dates of approval vary by NDA and ANDA, the reporting periods are not comparable. For drugs with an active ingredient for which there are multiple NDA and ANDA applications, FDA officials stated that one would also need to aggregate the data across multiple applications in order to determine the total quantity of the particular active ingredient. An FDA official told us that the agency rarely uses these data for analyses of drug utilization, drug safety, and drug shortages because other sources of data provide FDA information that is more detailed and timely about the quantities of certain drugs that are available in the market. For example, FDA uses drug sales data, which are available on a monthly basis, to evaluate and address drug safety and drug shortage problems.[30] USITC no longer collects and quantifies antibiotic production, but did so until 1994.[31]

Over 7 Million Pounds of Antibiotics Were Sold in 2009 for Human Use and Most Antibiotics Sold Share Common Characteristics

Most of the 7.4 Million Pounds of Antibiotics Sold Fell into Five Antibiotic Classes

In 2009, approximately 7.4 million pounds of antibiotics were sold for human use—which can be used as an estimate of the quantity of antibiotics produced for human use in the United States—and most sold share common characteristics, such as antibiotic classes. Most of the

[30]In April 2011, in response to a request from a Member of Congress, FDA used drug sales data to provide information about the amount of antibiotics that were sold in the United States in 2009 for human use, which it provided in correspondence to the Member.

[31]The USITC data on antibiotic production reflected the amount of antibiotics that were produced—for human and animal use—in the United States and for sale within or outside of the United States. USITC began reporting on the production of antibiotics, and other organic chemicals at the request of the House Committee on Ways and Means. In 1995, the committee requested that USITC stop its data collection on production because it determined that this effort was no longer cost effective or essential for ensuring the competitiveness of the U.S. industry.

7.4 million pounds, or about 89 percent, of antibiotics that were sold in 2009 fell into five antibiotic classes: penicillins, cephems, folate pathway inhibitors, quinolones, and macrolides (see table 2). The class of penicillins was the largest group of antibiotics sold in 2009.[32] About 3.3 million pounds of penicillins were sold, which represents 45.2 percent of all antibiotics sold in 2009. Penicillins, such as amoxicillin, are used to treat bacterial infections that include pneumonia and urinary tract infections.

Table 2: Amount of Antibiotics Sold in 2009 and Additional Information, by Antibiotic Class

Antibiotic class	Amount sold (in pounds)	Amount sold (in kilograms)	Percentage of total antibiotics sold	Examples of drugs within antibiotic class	Examples of bacterial infections treated by some drugs within antibiotic class
Penicillins	3,336,890	1,516,768	45.2	Penicillin, Amoxicillin, Oxacillin, Piperacillin	Group A Streptococcal infections, some pneumonia infections caused by *Streptococcus pneumoniae*, bacterial ear infections, some urinary tract infections caused by *Escherichia coli*, and some *Staphylococcus aureus* infections.
Cephems	1,094,681	497,582	14.8	Cephalexin, Cefuroxime, Cefotetan, Cefixime, Ceftriaxone	Skin infections, respiratory tract infections, intra-abdominal infections, gonorrhea, and bacterial meningitis.
Folate Pathway Inhibitors	1,064,456	483,843	14.4	Sulfonamides, Trimethoprim-Sulfamethoxazole	Urinary tract infections and other types of infections.
Quinolones	664,894	302,225	9.0	Ciprofloxacin, Levofloxacin	Urinary tract infections, respiratory tract infections, and other infections.
Macrolides	382,139	173,700	5.2	Erythromycin, Azithromycin	Some respiratory tract infections.
Other	844,467	383,849	11.4	Tetracyclines, Oxazolidinones, Aminoglycosides, and other classes	Skin infections and other infections.
Total	**7,387,527**	**3,357,967**	**100.0**		

Source: GAO analysis of IMS Health data and summary of CDC and NIH information.

Notes: Classes are identified according to the Clinical and Laboratory Standards Institute classification system. According to this classification system, certain antibiotic classes can be further classified into subclasses. For example, the cephem class includes the subclass of cephalosporins. The total amount of antibiotics sold does not take into account the dose, which varies by individual antibiotic, or the total number of individuals who were prescribed or treated with antibiotics.

[32]A limitation of comparing total weights across antibiotic classes is that dosages for antibiotics can vary by antibiotic class. According to FDA officials, comparing weights within antibiotic class may also be difficult, but the degree to which antibiotic dosages may vary within the same class is less than that across classes.

The Majority of Antibiotics Sold for Human Use in 2009 Were for Oral Administration and for Use in Outpatient Settings

Most of the antibiotics that were sold for human use in 2009 were for oral administration and for use in outpatient settings. As shown in table 3, about 6.5 million pounds, or 87.4 percent, of all antibiotics sold for human use in 2009 were intended for oral administration, for example, in the form of pills.[33] Oral forms of antibiotics and injectable forms, such as intravenous injections, together accounted for 99 percent of the total pounds sold.

Table 3: Amount of Antibiotics Sold in 2009, by Route of Administration

Route of administration	Amount sold (in pounds)	Amount sold (in kilograms)	Percentage of total antibiotics sold
Oral	6,454,670	2,933,941	87.4
Injection	854,281	388,310	11.6
Other[a]	78,576	35,717	1.1
Total	**7,387,527**	**3,357,967**	**100.0**

Source: GAO analysis of IMS Health data.

Note: Individual entries may not sum to totals because of rounding.

[a]Examples of other routes include administration by ear drops or inhalation.

About 5.8 million pounds, or 78.6 percent, of all antibiotics sold for human use in 2009 were purchased by chain store pharmacies, independent pharmacies, food store pharmacies, and clinics (see table 4). This suggests that most of the antibiotics that were purchased in 2009 were intended for use in outpatient settings.

[33]A drug is delivered to the body through oral administration when taken by mouth (e.g., a pill) and by injectable administration when delivered to the body through a needle.

Table 4: Amount of Antibiotics Sold in 2009, by Type of Purchaser

Type of purchaser	Amount sold (in pounds)	Amount sold (in kilograms)	Percentage of total antibiotics sold
Chain store pharmacies[a]	3,906,132	1,775,515	52.9
Independent pharmacies[b]	923,770	419,896	12.5
Nonfederal hospitals	852,247	387,385	11.5
Food store pharmacies[c]	745,526	338,876	10.1
Clinics	232,672	105,760	3.1
Long-term care facilities	228,662	103,937	3.1
Federal facilities[d]	219,533	99,788	3.0
Other[e]	278,984	126,811	3.8
Total	**7,387,527**	**3,357,967**	**100.0**

Source: GAO analysis of IMS Health data.

[a]Chain store pharmacies include businesses that consist of four or more stores with the same name that are owned and operated by the same organization.

[b]Independent pharmacies are privately owned pharmacies that operate fewer than four stores.

[c]Food store pharmacies include pharmacies that are located in grocery stores.

[d]Federal facilities include, for example, Department of Veterans Affairs hospitals and public health outpatient facilities.

[e]Other includes mail order pharmacies and pharmacies located in such entities as health maintenance organizations and prisons.

Data Gaps Remain Despite CDC's Efforts to Expand Its Limited Monitoring of Antibiotic Use; CDC, NIH, and FDA Have Implemented Efforts to Promote Appropriate Use

Although CDC annually collects certain national data on antibiotic prescriptions to monitor the use of antibiotics, these data have limitations and do not allow for important analyses. CDC is taking steps to improve its monitoring of antibiotic use by collecting and purchasing additional data, but gaps in information will remain. CDC's Get Smart program promotes the appropriate use of antibiotics and the agency has observed recent national declines in inappropriate antibiotic prescribing; however, it is unclear to what extent its program contributed to the recent declines. NIH and FDA activities have complemented CDC's efforts to promote the appropriate use of antibiotics.

CDC Annually Collects Certain National Data on Antibiotic Prescriptions to Monitor Antibiotic Use, but Data Do Not Allow for Important Analyses

CDC conducts two national health care surveys that gather data, annually, on antibiotic prescribing in outpatient settings—the National Ambulatory Medical Care Survey (NAMCS) and the National Hospital Ambulatory Medical Care Survey (NHAMCS).[34] NAMCS is based on a sample of visits to office-based physicians and community health centers.[35] NHAMCS is based on a sample of visits to emergency and outpatient departments and hospital-based ambulatory surgery locations.[36,37] Both surveys obtain data from healthcare provider records on patient symptoms, provider diagnoses, and the names of specific drugs, including antibiotics, that were prescribed during the patient visits.[38] CDC officials stated that, among their purposes, CDC uses NAMCS and NHAMCS to monitor antibiotic use in outpatient settings for patient conditions that do not usually require antibiotics for treatment, such as antibiotic prescribing rates for upper respiratory infections, such as the common cold.

NAMCS and NHAMCS are limited because they do not capture information about the use of antibiotics in inpatient settings. In inpatient settings, such as hospitals, antibiotics are often used, multiple antibiotics may be used in the same patient, and use may be prolonged. Monitoring overall antibiotic use (i.e., in inpatient and outpatient settings) over time is important for understanding patterns in antibiotic resistance. Information about overall antibiotic use in humans is also needed to routinely assess the contribution that human antibiotic use makes to the overall problem of antibiotic resistance in humans, relative to other contributing factors. For example, monitoring what portion of antibiotic use is attributed to humans

[34]NAMCS and NHAMCS are national probability sample surveys that are designed to provide information about medical care services in the United States.

[35]The NAMCS sample does not include visits to office-based physicians who are employed by the federal government.

[36]The NHAMCS sample includes nonfederal short-stay hospitals (i.e., average stay of fewer than 30 days) whose specialty is general (i.e., medical or surgical) or children's general. The NHAMCS sample also includes ambulatory surgery centers that are freestanding. Ambulatory surgery centers are medical facilities where surgical and other procedures not requiring an overnight hospital stay are performed.

[37]According to CDC officials, CDC is planning to merge NHAMCS with its current survey on inpatient care (i.e., the National Hospital Discharge Survey), into one survey called the National Hospital Care Survey, in 2011. In the integrated survey, data collection for antibiotic prescriptions will continue for outpatient visits.

[38]The surveys do not collect information on whether the prescriptions were filled or whether the prescribed treatment course was completed by the patient. According to CDC officials, this is because individual patients in the surveys are never identified or contacted.

versus animals is important to understanding antibiotic resistance. CDC officials told us that more complete information about antibiotic use by humans and animals is needed to help interpret trends from surveillance data and to inform on possible strategies to control the spread of antibiotic resistance, such as through changing antibiotic use practices.

NAMCS and NHAMCS data are further limited because they do not allow the agency to assess geographic patterns in antibiotic prescribing practices in outpatient settings. CDC officials told us that the survey samples were designed to obtain national, not state-level estimates. As a result, CDC cannot currently assess the potential effects of geographic variation at the state level in antibiotic prescribing rates on patterns of antibiotic resistance or identify states or other geographic areas in the United States, for instance, which have higher than average antibiotic prescribing for conditions that do not usually require antibiotics for treatment. Information about geographic variation in antibiotic prescribing would allow CDC to anticipate future patterns in antibiotic resistance, given that the use of antibiotics has a direct effect on antibiotic resistance. Such information, according to CDC officials, would also allow CDC to target prevention efforts, such as those aimed at reducing inappropriate antibiotic use.

CDC Is Taking Steps to Improve Its Monitoring of Antibiotic Use in Outpatient and Inpatient Settings, but Gaps in Information Will Remain

CDC is taking steps to improve its monitoring of antibiotic use, but gaps in information about the use of antibiotics will remain. To address the agency's lack of data on inpatient antibiotic use, CDC is planning to gather information on antibiotic use with a prevalence survey of U.S. acute care hospitals in 2011.[39] The survey will be conducted during a single time period on a single day and will collect some patient information about the reasons for the antibiotic use, which include treating an active infection or using antibiotics to prevent infection associated with a medical or surgical procedure.[40] According to CDC officials, these data will fill in the gap in its data by providing information about the prevalence of inpatient antibiotic use. CDC officials further stated that having data on the baseline amount of inpatient antibiotic use, and the reasons for that use, will allow the

[39]Acute care hospitals provide inpatient medical care and other related services for surgery, acute medical conditions, or injuries, usually for a short-term illness or condition.

[40]Some antibiotics are used to prevent infections, such as prior to having certain kinds of surgery that carry a high risk of infection.

agency to target and evaluate its own prevention efforts.[41] However, the survey findings will not be representative of hospitals nationwide, because the survey sample is limited to selected hospitals located within five entire states and urban areas in five other states.[42] Furthermore, CDC officials do not know if the survey will be repeated.[43] Without periodic data collection and monitoring, CDC cannot assess trends in inpatient antibiotic use or evaluate the effects that changes in antibiotic use may have on antibiotic resistance.

Additionally, in 2011, CDC officials told us that the agency plans to reinstate a module of NHSN that will allow participating facilities to report their inpatient antibiotic use, which will provide CDC with some inpatient antibiotic use data, but these data will not be nationally representative.[44] In 2009, CDC temporarily discontinued this module because, according to CDC officials, it was not sustainable due to the high burden on facilities to report such data.[45] CDC has redesigned the module to reduce the reporting burden on facilities; for example, CDC officials told us that, instead of relying on manual entry, facilities will be able to electronically capture and automatically send their data to NHSN.[46] While the module will allow facilities in NHSN to monitor their own antibiotic use, the data will not provide the agency with information about the prevalence of inpatient antibiotic use because NHSN is not based on a nationally representative sample of facilities.

[41]CDC officials also stated that information about inpatient antibiotic use could inform recommendations about antibiotic treatment by professional groups, such as the Infectious Diseases Society of America.

[42]The survey is based on a sample of acute care hospitals located within the 10 EIP surveillance areas (also known as 'catchment' areas). According to a CDC official, the survey will be representative of hospitals within the EIP surveillance areas.

[43]CDC officials stated that a decision to repeat the survey will depend on available resources, and would be better made after the original survey has been completed. CDC expects to begin data collection in 2011 and complete its analysis in 2012.

[44]In NHSN, similar types of surveillance information are grouped into modules. For example, there is a module that captures surgical site infections.

[45]To illustrate, facilities reported on about 75 commonly used antibiotics as well as combinations of these antibiotics.

[46]CDC officials also told us that with the redesigned module, facilities will be able to immediately use their data to evaluate antibiotic use rates for antimicrobial stewardship activities. Antimicrobial stewardship includes interventions and programs designed to improve antibiotic use.

To improve CDC's monitoring of antibiotic use in outpatient settings, CDC officials told us that they are finalizing a contract with a private data vendor to obtain 5 years of national data on antibiotic prescribing in outpatient settings by antibiotic drug, county, and type of provider. According to CDC officials, these data will help the agency understand relationships between antibiotic use and antibiotic resistance in certain geographic areas. CDC officials further stated that these data would help guide the agency's prevention efforts. With preliminary data on outpatient prescriptions for the antibiotic subclass of fluoroquinolones, CDC has shown wide variation in prescribing across states. Further, CDC plans to increase the size of the NAMCS sample at least fourfold in 2012, which would allow CDC to produce antibiotic prescribing rates for some states that year.[47]

CDC's Get Smart Program Promotes Appropriate Antibiotic Use to Providers and Patients

CDC's Get Smart: Know When Antibiotics Work (Get Smart) program promotes appropriate antibiotic use, which is aimed specifically at healthcare providers, patients, and parents of young children.[48] CDC launched its Get Smart program in 1995 with the overall goal of reducing the increasing rate of antibiotic resistance.[49] The program is primarily focused on upper respiratory infections because, according to CDC, such infections account for over half of all antibiotics prescribed by office-based physicians. The Get Smart program works with partners, such as certain health insurance companies, to develop and distribute educational materials.[50] With the goal of educating healthcare providers and the public, the Get Smart educational materials are aimed directly at these populations. For example, the Get Smart program supported the development of an online training program for healthcare providers to improve their knowledge and diagnosing of middle ear disease. The Get

[47]CDC officials stated that there are no plans to provide state-level estimates with NHAMCS.

[48]Otherwise healthy adults under 50 years old are an additional target audience.

[49]According to CDC officials, the program was originally named the National Campaign for Appropriate Antibiotic Use in the Community and was renamed Get Smart in 2003.

[50]In addition to health insurance companies, other Get Smart partners include businesses, pharmaceutical companies, foundations, and professional associations. As an example of how CDC collaborates with its partners, a health insurance company mailed Get Smart promotional materials to 320,000 of its customers with children ages 3 to 10 years old. CDC also provided technical support to this company to develop educational kits that were sent to about 30,000 pediatric, family practice, and internal medicine offices.

Smart program developed and launched a national media campaign in 2003, in partnership with FDA, to provide a coordinated message on appropriate antibiotic use to the public and this message has been disseminated through print, television, radio, and other media.[51] For example, CDC developed a podcast for parents of young children, available on CDC's Web site, to communicate its message. In the podcast, a pharmacist counsels a frustrated mother about appropriate antibiotic use and symptomatic relief options for her son's cold. Some materials are aimed at healthcare providers with the goal of educating their patients; for example, the Get Smart program developed a prescription pad for symptoms of viral infections. Healthcare providers can use the communication tool to acknowledge patient discomfort and recommend strategies to their patients for the relief of symptoms associated with viral illnesses—without prescribing an antibiotic unnecessarily. The prescription sheet includes the Get Smart logo and provides information for patients about the appropriate use of antibiotics to treat bacterial infections.

CDC has continued to update and expand its materials for the Get Smart program. For example, CDC officials stated that the agency has expanded its educational materials by partnering with Wake Forest University to develop a curriculum for medical students related to appropriate antibiotic prescribing, and the impact of antibiotic use and its inappropriate use on antibiotic resistance, and the agency has developed a continuing education course for pharmacists. CDC officials told us that pharmacists serve as one of the most important health care professionals in promoting appropriate antibiotic use, for example by educating patients about the importance of taking antibiotics exactly as directed. In November 2010, CDC launched another Get Smart program, called Get Smart for Healthcare. This program focuses on improving antibiotic use in inpatient healthcare settings—including hospitals and nursing homes—through antimicrobial stewardship.

[51]In 2005, CDC launched two additional components of the national media campaign. These include materials for healthy adults, Spanish speakers, and American Indians. In 2008, the campaign coordinated its first national observance, Get Smart About Antibiotics Week, and through a variety of activities and resources, the messages of the Get Smart program were delivered to the public.

CDC Has Observed Declines in Inappropriate Antibiotic Prescribing, but It Is Unclear to What Extent Its Program to Promote Appropriate Antibiotic Use Contributed to Recent Trends

CDC has observed declines in inappropriate antibiotic prescribing in outpatient settings since its Get Smart program began in 1995, but it is unclear to what extent this program contributed to these trends. For example, using NAMCS and NHAMCS data, CDC found about a 26 percent decline in the number of courses of antibiotics prescribed per 100 children younger than 5 years old for ear infections between 1996-1997 and 2006. Further, CDC reported about a 53 percent decrease in the antibiotic prescription rate for the common cold among all persons between 1996-1997 and 2006.[52] A similar trend in antibiotic prescribing among children has also been observed with data from the National Committee for Quality Assurance (NCQA). NCQA monitors trends in antibiotic prescribing for the purpose of comparing the performance of healthcare plans.[53] NCQA monitors the percentage of children 3 months to 18 years of age who were diagnosed with an upper respiratory infection and did not receive an antibiotic prescription within 3 days of the office visit, and this measure has shown improvement (i.e., percentage increases in appropriate treatment) between 2003 and 2008.[54]

The measures that CDC uses to evaluate the effectiveness of the Get Smart program do not necessarily reflect the effect of the program because they do not capture information about individuals who were exposed to the Get Smart program, compared to those who were not. As a result, it is unclear if the declines in the inappropriate antibiotic prescribing were due to exposure to Get Smart messages and educational materials or from other factors, such as efforts to measure healthcare performance with antibiotic prescribing indicators (e.g., NCQA measures) or the recommended use of influenza vaccines among young children, since 2004.[55] CDC officials told

[52]Both measures are used by HHS, as part of Healthy People 2010, to assess national progress related to disease prevention.

[53]NCQA is a private organization whose mission is to improve healthcare quality. As part of its mission, NCQA develops quality standards and performance measures for a broad range of healthcare entities. The NCQA measures are used by more than 90 percent of U.S. health plans to measure performance. CDC officials helped NCQA write the measures on antibiotic prescribing.

[54]NCQA also measures the percentage of healthy adults (18 to 64 years of age) who did not receive an antibiotic prescription with a diagnosis of acute bronchitis, characterized by a cough that can last for up to 3 weeks. Performance on this measure declined between 2005 and 2008 because the percentage decreased.

[55]The American Academy of Pediatrics has recommended influenza vaccination for healthy children 6 through 24 months of age since 2004. Currently, the American Academy of Pediatrics recommends the influenza vaccination for healthy children 6 months of age and older.

us that they believe the NCQA measures have helped to improve appropriate antibiotic prescribing by improving knowledge of treatment guidelines by physicians and practitioners. In addition, reducing the number of cases of influenza among children is likely to have contributed to declines in inappropriate antibiotic prescriptions because antibiotics are often prescribed in patients with influenza symptoms. The measures that CDC uses to evaluate the effectiveness of the Get Smart program also do not allow CDC to determine, for example, whether declines in inappropriate antibiotic prescribing are attributable to a decrease in demand for antibiotics by patients, or to improved adherence to appropriate prescribing guidelines by healthcare providers. The measures are further limited because they do not allow CDC to determine whether the observed declines are consistent across the United States or are due to decreases in certain geographic areas.

CDC officials told us that they rely on other indicators to demonstrate the effectiveness of the Get Smart Program, such as interest in CDC's Get Smart Web site and media materials. According to these officials, studies examining the impact of educational materials, including Get Smart materials, further demonstrate the effectiveness of the Get Smart program. For example, CDC officials cited a study in Massachusetts where educational materials, including Get Smart materials, were distributed to physicians and their patients in several communities.[56] Findings indicate that in communities where educational and promotional materials about appropriate antibiotic use—including Get Smart materials—were distributed, antibiotic prescribing rates for children declined. Declines were also observed in communities where these educational and promotional materials were not distributed.[57] These findings indicate that factors other than educational and promotional materials focused on the appropriate use of antibiotics may also have led to declines in inappropriate antibiotic prescribing. Without information about which are the most effective ways to reduce inappropriate antibiotic prescribing in

[56]See J.A. Finkelstein et al., "Impact of a 16-Community Trial to Promote Judicious Antibiotic Use in Massachusetts," *Pediatrics*, vol. 121 (2008), pp. e15-e23.

[57]Antibiotic prescribing rates decreased in all three age groups of children included in the study, regardless of whether educational and promotional materials were distributed. For example, rates decreased by 14.5 percent among children 2 years old to less than 4 years old in communities with educational and promotional materials, and by 10.3 percent in communities without such materials. The greater declines in antibiotic prescribing rates in communities with educational and promotional materials were statistically significant in two of the three age groups.

outpatient and inpatient settings, CDC cannot target its resources on these preventive approaches.

NIH and FDA Activities Have Complemented CDC's Efforts to Promote Appropriate Antibiotic Use

NIH and FDA have complemented CDC's efforts to promote the appropriate use of antibiotics in humans through various activities. NIH supports research specifically aimed at decreasing the inappropriate use of antibiotics as part of its research agenda to target antibiotic resistance. NIH-funded studies focus on establishing appropriate antibiotic treatment courses, using off-patent antibiotics to treat infections, and developing rapid diagnostic tests to help healthcare providers choose an appropriate antibiotic for treatment.[58] For example, in 2009, NIH began funding a clinical trial to determine whether the standard 2-week antibiotic treatment course for children with urinary tract infections can remain effective if shortened, thereby decreasing the likelihood of antibiotic resistance and preserving the effectiveness of existing antibiotics.[59] In 2007, NIH awarded two 5-year contracts to study whether off-patent antibiotics such as clindamycin and a combination of the drugs trimethoprim and sulfamethoxazole can be used to treat certain skin infections instead of the more recently developed antibiotics, such as Linezolid and Vancomycin, in order to preserve the newer drugs' effectiveness.[60] Further, since 2002, NIH has supported the development of a new test to rapidly diagnose TB. It currently takes up to 3 months to accurately diagnose TB and to determine its resistance to antibiotics, according to NIH officials. Findings from a recent clinical trial study reported that, within 2 hours, the new test can diagnose a TB infection and determine if it is resistant to the antibiotic rifampin, which is commonly used to treat TB.[61] NIH officials stated that the test is being recommended by the World Health Organization for the early diagnosis of TB and NIH is

[58]When a medication is first sold, the drug manufacturer has exclusive rights, or a patent, to produce that drug for a certain number of years. After the patent has expired, the drug becomes an off-patent medication and can be reproduced by other drug manufacturers.

[59]As of March 2011, this study is ongoing, according to an NIH official.

[60]As of March 2011, both studies are ongoing and continue to enroll participants, according to an NIH official.

[61]See C.C. Boehme et al., "Rapid Molecular Detection of Tuberculosis and Rifampin Resistance," *New England Journal of Medicine*, vol. 363, no. 1 (2010), pp. 1005-1015.

currently supporting research to improve the test and expand its capabilities.[62]

Research on the development of vaccines for bacterial and viral infections is also part of NIH's research agenda to decrease the inappropriate use of antibiotics, according to an NIH official. An NIH official stated that the agency has funded the discovery and development of several staphylococcal vaccine candidates, for example, through investigator-initiated grants.[63] In addition, an NIH official told us that NIH conducted preclinical animal studies that provided data for the development of a multivalent staphylococcal vaccine candidate, which allowed the candidate to advance to clinical testing.[64] NIH also supports the development of vaccines for viral infections. According to an NIH official, decreasing the occurrence of influenza infections with influenza vaccines may decrease the inappropriate use of antibiotics. Many healthcare providers inappropriately treat viral respiratory infections with antibiotics, so preventing influenza reduces the opportunities for unnecessary antibiotic treatment.[65]

FDA activities also complement CDC's efforts to promote the appropriate use of antibiotics in humans. According to an FDA official, the agency collaborated with CDC on certain Get Smart activities, such as developing an appropriate antibiotic use message for the national media campaign, and amended its drug labeling regulations in 2003 to require that all oral or intravenous antibiotics for human use include additional information on

[62]The test is also being recommended for the early diagnosis of multidrug-resistant TB and TB in individuals infected with human immunodeficiency virus.

[63]As part of this effort, NIH has funded basic research, proof-of-concept studies, and preclinical research, according to an NIH official.

[64]This candidate is currently in the first phase of clinical testing, which is supported by a company. A multivalent staphylococcal vaccine would provide broader protection against a variety of *Staphylococcus aureus* strains.

[65]An NIH official further explained that the influenza virus causes lung damage that often predisposes individuals to bacterial pneumonia. Thus, fewer cases of influenza would lead to fewer secondary bacterial infections requiring antibiotic treatment.

their appropriate use.[66,67] FDA's labeling requirement is intended to encourage physicians to prescribe antibiotics only when clinically necessary and to encourage them to counsel their patients about the proper use of such drugs and the importance of taking them exactly as directed. For example, the amended regulation requires that antibiotic labeling include the statement that "prescribing [the antibiotic] in the absence of a proven or strongly suspected bacterial infection is unlikely to benefit the patient and increases the risk of the development of drug-resistant bacteria."

CDC's Monitoring of Antibiotic-Resistant Infections Has Limitations in Assessing the Overall Problem of Antibiotic Resistance

CDC's monitoring of antibiotic-resistant infections has limitations in assessing the overall problem of antibiotic resistance. The agency's monitoring of antibiotic-resistant infections in healthcare facilities has data gaps that limit CDC's ability to produce accurate national estimates of such infections. For some of these infections monitored by CDC in community settings, in comparison, CDC can provide accurate national estimates. CDC is taking steps to improve its monitoring of antibiotic-resistant infections in healthcare settings, but these efforts will not improve CDC's ability to assess the overall problem of antibiotic resistance.

Data Gaps in CDC's Monitoring of Antibiotic-Resistant Infections in Healthcare Settings Limit Its Ability to Produce Accurate National Estimates

A sample of healthcare facilities that is not representative—and incomplete information about the entire scope of healthcare-associated infections (HAIs) that are resistant to antibiotics—present data gaps that limit CDC's ability to produce accurate national estimates of antibiotic resistant HAIs in healthcare settings. Some infections are acquired as a result of medical treatment in a healthcare setting, such as a hospital or outpatient unit, while others are transmitted in the community, such as respiratory infections that are spread in schools and the workplace. According to CDC officials, healthcare settings contribute to the development of antibiotic resistance because of their high volume of susceptible patients, large number of disease-causing bacteria, and high

[66]See 21 § CFR 201.24 (2011), 68 *Fed. Reg.* 6081 (Feb. 6, 2003). The amended drug labeling requirement applies only to antibiotics that are administered orally or intravenously. Antibiotics that are administered via a different route, such as those that are applied topically, are excluded from the labeling requirement.

[67]For FDA information related to antibiotic use, see http://www.fda.gov/NewsEvents/PublicHealthFocus/ucm235649.htm (downloaded on March 17, 2011).

antibiotic usage. CDC uses NHSN to monitor HAIs,[68] including antibiotic-resistant HAIs, at a national level, but the facilities that participate are not a nationally representative sample. Facility enrollment and participation in NHSN[69] is either voluntary, required because of a state mandate, or obligated as a condition of participation in HHS' Centers for Medicare & Medicaid Services (CMS) Hospital Inpatient Quality Reporting program.[70] According to CDC officials, as of January 2011, 23 states and territories required, or had plans to require, healthcare facilities to use NHSN for their reporting mandate.[71] As of January 1, 2011, all acute care hospitals participating in the CMS Hospital Inpatient Quality Reporting Program are obligated to report into NHSN central-line associated bloodstream infections for certain procedures[72] from their intensive care units.[73] Although the number of participating facilities has increased substantially, because healthcare facilities enroll voluntarily or by mandate, this group of facilities is not representative of facilities nationwide, as a random sample would be. Participating healthcare facilities in states with mandated participation are more likely to be overrepresented in the

[68]With laboratory-identified event surveillance data from NHSN, CDC also monitors certain HAIs caused by multidrug-resistant organisms (MDRO) as well as *Clostridium difficile* infections.

[69]Enrollment in NHSN is open to all types of healthcare facilities in the United States, including acute care hospitals, psychiatric hospitals, rehabilitation hospitals, outpatient dialysis centers, ambulatory surgery centers, and long-term-care facilities.

[70]CMS is the agency that, among other activities, administers Medicare, a health insurance program that helps pay for inpatient care in hospitals.

[71]CDC officials said that as of January 2011, approximately 4,000 hospitals and other healthcare facilities participated in NHSN. In comparison, we reported in 2008 that approximately 1,000 hospitals were participating in NHSN, as of December 2007. See GAO, *Health-Care-Associated Infections in Hospitals: Leadership Needed from HHS to Prioritize Prevention Practices and Improve Data on These Infections*, GAO-08-283 (Washington, D.C.: Mar. 31, 2008). NHSN opened enrollment to all types of healthcare facilities in 2008. According to the American Hospital Association's 2009 annual survey of hospitals, there are approximately 5,800 hospitals in the United States.

[72]The procedures include, for example, coronary artery bypass graft and other cardiac surgery, and hip or knee arthroplasty.

[73]Acute care hospitals electing to participate in the Hospital Inpatient Quality Reporting Program are obligated to report certain quality data measures to CMS; those that do not participate are penalized by a reduction in the increase they would otherwise receive to their annual payments for providing inpatient services to Medicare beneficiaries. Under the Hospital Inpatient Quality Reporting Program, NHSN was designated by CMS to serve as the reporting mechanism for certain HAIs.

sample, while facilities in states without mandates are more likely to be underrepresented.

The data that participating healthcare facilities supply to NHSN do not reflect the full scope of HAIs that occur within these facilities, further limiting CDC's ability to provide accurate national estimates about antibiotic-resistant HAIs.[74] Participating facilities may submit data about different types of HAIs, and this includes information about whether the HAIs are resistant to antibiotics.[75] For example, some facilities report data to NHSN on central-line associated bloodstream infections but not other infection types, such as catheter-associated urinary tract infections.[76] Further, participating healthcare facilities may report HAI data to NHSN for certain units within facilities. For example, participating facilities may report data to NHSN on infections that occur in intensive care units but not those that occur in specialty care areas. CDC depends on the microbiology data provided by participating facilities to determine, among reported cases, the number and percentage of certain types of HAIs with resistance to certain antibiotics.[77] Without an accurate national estimate of antibiotic-resistant HAIs, CDC cannot assess the magnitude and types of such infections that occur in all patient populations (i.e., facilitywide) within healthcare settings.

[74]In 2008, we similarly stated that NHSN was limited in terms of its inability to produce reliable national estimates on the frequency of all HAIs—not just antibiotic-resistant HAIs. This is because NHSN data do not reflect the full scope of HAIs and the sample is not representative of facilities nationwide. See GAO-08-283.

[75]Facilities may report on different types of HAIs for which NHSN has developed detailed definitions and protocols. As part of the protocols, facilities submit microbiological data for each HAI identified, provided by the facility's designated clinical microbiology laboratory. These data include information about the type of bacteria causing the infection and test results regarding antibiotic resistance. NHSN also has a protocol for reporting MDROs and *Clostridium difficile* infections as laboratory-identified events and, according to CDC officials, the test results regarding antibiotic resistance are used to determine whether such cases should be reported.

[76]Central line-associated bloodstream infections, catheter-associated urinary tract infections, and ventilator-associated pneumonia are device-associated infections that can be reported through NHSN. Surgical site infections and postprocedure pneumonia are procedure-associated infections that can also be reported. MDRO and *Clostridium difficile* infections can be reported into NHSN as HAIs or as laboratory-identified events.

[77]Laboratory-identified event surveillance data from NHSN also allow CDC to determine, among reported cases, the number of MDRO and *Clostridium difficile* infections.

CDC's Monitoring of Antibiotic-Resistant Infections in Community Settings Can Provide Accurate National Estimates for Some Infections

CDC's monitoring of antibiotic-resistant infections in community settings can provide accurate national estimates of antibiotic-resistant infections that are caused by 5 of the 12 bacteria that the agency monitors. These 5 are captured by two surveillance systems, the National Antimicrobial Resistance Monitoring System for Enteric Bacteria (NARMS: EB) and the National Tuberculosis Surveillance System (NTSS), which collect nationally representative data about certain antibiotic-resistant infections; these infections can occur in community settings.

Both systems employ sampling strategies that can provide accurate national estimates by collecting representative case information from all 50 states.[78] For NARMS: EB, health departments in all 50 states submit a representative sample of four of the five bacteria it monitors—non-typhoidal *Salmonella*, typhoidal *Salmonella*, *Shigella*, and *Escherichia coli* O157 cases to NARMS: EB for antibiotic susceptibility testing. To ensure adequate sample size and a random sample for testing, the health departments systematically select and submit to NARMS: EB every 20th non-typhoidal *Salmonella*, *Shigella*, and *Escherichia coli* O157 case as well as every typhoidal *Salmonella* case received at their laboratories. NARMS: EB cannot produce an accurate national estimate for one of the five bacteria it monitors—*Campylobacter*—because according to CDC officials, the system collects a sample of the bacteria in 10 states.[79] CDC uses NTSS to collect information about each newly reported case of tuberculosis infection in the United States, including information on drug susceptibility results for the majority of cases that test positive for tuberculosis.

CDC's monitoring of other bacteria that cause antibiotic-resistant infections in community settings cannot provide estimates that are nationally representative because they are derived from samples that do not accurately represent the entire United States. Through ABCs, CDC

[78]NARMS: EB also collects cases from the District of Columbia, and NTSS reporting includes the District of Columbia, Puerto Rico, and other U.S. jurisdictions in the Pacific and Caribbean.

[79]NARMS: EB collects every case, every other case, or every fifth case of *Campylobacter* from each of the 10 state health departments, depending on the number of cases each health department receives.

conducts antibiotic resistance surveillance of five[80] infection-causing bacteria—group A and B *Streptococcus*, *Neisseria meningitidis*, *Streptococcus pneumoniae*, and MRSA.[81,82] According to CDC officials, these bacteria cause bloodstream infections, sepsis, meningitis, and pneumonia. ABCs is a collaboration between CDC, state health departments, and universities in 10 states.[83] CDC officials told us that for each identified case of infection within their surveillance populations, the ABCs sites conduct a chart review to collect a variety of information, such as underlying disease and risk factors, vaccination history, and demographic information. This information is entered into a case report form and submitted to CDC along with bacterial isolates for additional testing, including tests for antibiotic resistance.[84]

ABCs' monitoring of cases of resistant infections is limited to surveillance areas in 10 states, and the surveillance areas vary somewhat depending on the infection-causing bacterium that is monitored. For example, *Neisseria meningitidis* is monitored in 6 entire states and in primarily urban areas in 4 other states while MRSA is monitored in 1 entire state and primarily urban areas in 8 other states.[85] According to CDC's Web site, the

[80]CDC also monitors *Haemophilus influenzae* with ABCs, but CDC officials stated that they do not routinely collect antibiotic susceptibility testing data for cases of *Haemophilus influenzae* infection, in part, because of constraints on time and resources at CDC's laboratories, but that the agency does conduct some testing for clusters of cases.

[81]CDC uses ABCs to monitor community- and healthcare-associated cases of MRSA. CDC also monitors healthcare-associated MRSA through NHSN.

[82]In addition to ABCs, CDC monitors cases of *Streptococcus pneumoniae* through NNDSS. CDC officials told us that NNDSS is used to monitor cases in areas not covered by ABCs' surveillance. NNDSS relies on the voluntary submission of case reports and it is considered a passive surveillance system. In comparison, ABCs is considered an active surveillance system because it relies on the active identification and collection of cases on a regular basis.

[83]The 10 states are California, Colorado, Connecticut, Georgia, Maryland, Minnesota, New Mexico, New York, Oregon, and Tennessee. CDC's surveillance of *Streptococcus pneumoniae*, *Neisseria meningitidis*, and group A and B *Streptococcus* is based on geographic areas located in these 10 states and surveillance of MRSA is based on geographic areas located in 9 of the 10 states.

[84]Bacterial isolates are sent to CDC and other laboratories for testing. CDC officials told us that antibiotic susceptibility testing is conducted on all cases of *Neisseria meningitidis*, *Streptococcus pneumoniae*, group A *Streptococcus*, and MRSA, as well as a subset of group B *Streptococcus* cases that are submitted to ABCs from 8 of the 10 sites.

[85]To illustrate the population sizes covered by ABCs surveillance, the population for *Neisseria meningitidis* surveillance is about 41 million and the population for MRSA surveillance is about 19 million, as of January 2010.

population included in the ABCs surveillance areas is roughly representative of the U.S. population on the basis of certain demographic characteristics (e.g., race and age) and urban residence. However, ABCs cannot provide estimates that are nationally representative for rural residence, and some experts have raised concerns because of the underrepresentation of rural areas.[86,87] Further, since surveillance is critical to providing early warning of emerging resistance problems, limited geographic coverage among monitored infection-causing bacteria impedes CDC's ability to detect emerging problems.

The Gonococcal Isolate Surveillance Project (GISP), which CDC uses to monitor antibiotic resistance in *Neisseria gonorrhoeae*, the bacterium that causes gonorrhea, cannot provide accurate national estimates of cases of antibiotic-resistant gonorrhea because it collects information only on selected patient populations. Each month, GISP collects case samples from the first 25 men diagnosed with urethral gonorrhea in each participating sexually transmitted disease clinic. The clinics are located in 24 states and they send these samples to designated laboratories for antibiotic susceptibility testing.[88] However, according to CDC officials, most cases of gonorrhea in the United States are not treated in sexually transmitted disease clinics, and are more likely treated in a variety of healthcare settings, such as primary care physicians' offices. Further, since GISP collects information on cases of gonorrhea from male patients only, the data cannot represent the total U.S. population in order to provide an accurate national estimate of resistant gonorrhea cases.[89]

[86]CDC uses ABCs data to calculate national estimates of certain diseases, based on race and age information from ABCs surveillance areas and the 2009 U.S. population.

[87]CDC officials stated that the selection of catchment areas in urban areas allows the agency to capture a significant percentage of the population in the state.

[88]GISP surveillance collects information about gonorrhea cases from more locations in the West because CDC officials said they expect antibiotic resistance in gonorrhea to emerge first in the western United States and then to spread eastward.

[89]A CDC official told us that he does not believe there are significant differences between men and women in the frequency of antibiotic resistance among cases of gonorrhea.

CDC Is Taking Steps to Improve Its Monitoring of Antibiotic-Resistant Infections in Healthcare Facilities, but These Steps Will Not Improve CDC's Ability to Assess the Overall Problem of Antibiotic Resistance

CDC is taking steps to improve its monitoring of antibiotic-resistant infections in healthcare facilities, but CDC's ability to assess the overall problem of antibiotic resistance will not be improved. With a prevalence survey, CDC is planning to collect additional data in 2011 about HAIs, which may provide more comprehensive information about certain types of HAIs that are resistant to antibiotics. According to CDC officials, the survey of U.S. acute care hospitals—which will also provide data on antibiotic use, as described previously—will allow the agency to more accurately assess the burden of HAIs and antibiotic resistance among those HAIs in healthcare settings.[90] Unlike NHSN, the survey is designed to allow CDC to assess the magnitude and types of HAIs occurring in all patient populations within the sample of acute care hospitals. The survey will collect information about types of infection (e.g., urinary tract infection, bloodstream infection), bacteria causing HAIs, and test results regarding antibiotic resistance. The survey will not collect resistance information for all bacteria that cause HAIs. However, according to CDC officials, the survey will collect resistance information for some of the most common bacteria that cause HAIs, including *Acinetobacter*, *Enterococcus faecalis*, *Enterococcus faecium*, *Escherichia coli*, *Klebsiella*, *Pseudomonas aeruginosa*, and *Staphylococcus aureus*.[91] While the survey may provide more comprehensive information about certain types of HAIs that are resistant to antibiotics because it is designed to cover all patient populations in the sampled hospitals, the survey will not be able to provide information about the prevalence of all antibiotic-resistant HAIs that occur in U.S. acute care hospitals. A further limitation is that the sample is not representative of U.S. acute care hospitals. As described earlier, this is because the survey is based on a sample of acute care hospitals located within the EIP surveillance areas, according to CDC officials.

CDC also plans to enhance its monitoring of HAIs by expanding the geographic coverage of its surveillance of *Clostridium difficile* infections and CDC officials told us that the agency is piloting additional surveillance for gram-negative infections through the EIP network.[92] According to CDC,

[90]The survey will also be used to inform decision making regarding, for example, appropriate targets and strategies for preventing HAIs and the emergence of antibiotic-resistant infections.

[91]The survey will collect information about different species of *Acinetobacter* and *Klebsiella*.

[92]Gram-negative infections include those caused by *Klebsiella*, *Acinetobacter*, *Pseudomonas aeruginosa*, and *Escherichia coli*, and are increasingly resistant to most available antibiotics.

the agency began monitoring *Clostridium difficile* infections through EIP in 2009 in 7 surveillance areas, to obtain more comprehensive and representative information about this infection, including for antibiotic resistance.[93] CDC officials stated that the agency plans to expand its *Clostridium difficile* monitoring to 10 surveillance areas by summer 2011. In 2 of the 10 surveillance areas (i.e., Oregon and Minnesota), surveillance will occur in rural areas only. CDC officials stated that the data will allow the agency, among other things, to detect *Clostridium difficile* infections that occur prior to admission to a healthcare facility and to identify new populations at risk.[94] CDC officials also told us that the agency is piloting surveillance for gram-negative infections that are resistant to multiple antibiotics, through the EIP network, as an exploratory effort and feasibility study on how to improve the agency's monitoring of these infections in healthcare settings.

In addition, CDC anticipates that the number of acute care hospitals participating in NHSN will expand in 2011 stemming from the CMS Hospital Inpatient Quality Reporting Program obligation to do so. The expanded participation will, CDC officials believe, result in more representative data about certain HAIs and antibiotic-resistant infections.[95] CMS has expanded its quality data measures to include two HAI measures that will be reported through NHSN. As stated previously, as of January 1, 2011, hospitals are obligated to report on central-line bloodstream infections associated with certain procedures from their intensive care units and on January 1, 2012, hospitals will be obligated to report on surgical site infections.[96] Hospitals will also need to report on antibiotic resistance associated with these two types of infections, given NHSN's reporting requirements for participation. As part of CDC's protocols, facilities submit microbiological data for each HAI identified, which

[93]CDC also monitors *Clostridium difficile* infections through NHSN.

[94]CDC officials also stated that these data will complement the data on *Clostridium difficile* infections that are collected through NHSN.

[95]CDC officials noted that since more than 90 percent of acute care hospitals (excluding critical access hospitals) participate in CMS's Hospital Inpatient Quality Reporting Program, NHSN data will be more representative by 2012.

[96]See 75 *Fed. Reg.* 50042 (Aug. 16, 2010). Collection and reporting of data on bloodstream infections associated with central lines is required for the fiscal year 2013 payment determination and collection and reporting of surgical site infections is required for the fiscal year 2014 payment determination.

includes the type of bacteria causing the infection and test results regarding antibiotic resistance.

Federal Agencies Do Not Monitor Antibiotic Disposal, but Have Examined the Presence of Antibiotics in the Environment, and Studies Find that Such Antibiotics Can Increase the Population of Resistant Bacteria

Federal agencies do not collect data regarding the disposal of most antibiotics intended for human use, but EPA and USGS have measured the presence of certain antibiotics in the environment due, in part, to their disposal. Studies conducted by scientists have found that antibiotics that are present in the environment at certain concentration levels can increase the population of resistant bacteria due to selective pressure.

Federal Agencies Do Not Monitor the Disposal of Most Antibiotics Intended for Human Use, but Have Measured the Presence of Antibiotics in the Environment

EPA does not monitor the disposal of most antibiotics intended for human use, but EPA and USGS have measured the presence of antibiotics in the environment, including water, soil, and sediment.[97] According to EPA, antibiotics enter the environment through various pathways into water, soil, and sediment, such as wastewater discharged from treatment plants.[98] The disposal of hazardous waste, such as chemicals that are harmful to human health when ingested, is regulated by EPA. Under RCRA, EPA has established a system by which hazardous waste is regulated from the time it is produced until it is disposed.[99] Under this system, EPA receives information from hazardous waste generators through the Biennial

[97]GAO has ongoing work on pharmaceuticals in drinking water.

[98]Treatment plants include, for example, municipal treatment plants that treat domestic sewage as well as healthcare and pharmaceutical manufacturing facility treatment plants.

[99]RCRA's implementing regulations define hazardous waste as including those wastes specifically listed by EPA as well as those wastes exhibiting any of several characteristics.

Reporting System.[100] EPA officials told us that antibiotics in general do not fall under RCRA's definition of hazardous waste; as a result, EPA does not generally receive information about the disposal of antibiotics. EPA officials further stated that the agency would receive limited information about antibiotics if they fell under RCRA's definition of hazardous waste. However, in part because it is the responsibility of the person disposing of a waste to determine whether or not it is hazardous, agency officials could not identify any specific antibiotics that fall under EPA's regulatory definition of hazardous waste and therefore concluded that it would be a rare occurrence for the agency to receive information on the disposal of antibiotics.

Under SDWA, EPA is authorized to regulate contaminants in public drinking water systems. EPA generally requires public water systems to monitor certain contaminants for which there are national primary drinking water regulations—standards limiting the concentration of a contaminant or requiring certain treatment. EPA has not promulgated any drinking water regulation for an antibiotic. EPA is required to identify and publish a list every 5 years of unregulated contaminants that may require regulation, known as the Contaminant Candidate List (CCL). EPA generally uses this list to select contaminants for its periodic regulatory determinations, by which the agency decides whether to regulate a contaminant, but contaminants may remain on the CCL for many years before EPA makes such a decision.[101] Erythromycin is the only antibiotic on the third CCL list (CCL 3)—the current CCL that was published in October 2009.[102] According to EPA officials, the agency is in the process of evaluating CCL 3 contaminants, including erythromycin, and plans to determine whether or not regulation is required for at least five contaminants from the CCL 3 by 2013. EPA's determination to promulgate a national primary drinking water regulation for a contaminant is made based on three criteria established under SDWA, including that the

[100]A hazardous waste generator is any person whose processes and actions produce hazardous waste.

[101]For many contaminants, EPA lacks sufficient information to allow EPA to make a regulatory determination. See GAO, *Safe Drinking Water Act: EPA Should Improve Implementation of Requirements on Whether to Regulate Additional Contaminants*, GAO-11-254 (Washington, D.C.: May 27, 2011).

[102]74 *Fed. Reg.* 51,850, 51,852 (Oct. 8, 2009).

contaminant may have an adverse effect on human health.[103] To provide information such as that needed to determine whether to regulate the contaminant, EPA has the authority to require a subset of public water systems to monitor a limited number of unregulated contaminants, which the agency has implemented through the Unregulated Contaminant Monitoring Rule (UCMR). On March 3, 2011, EPA proposed the list of contaminants (primarily from the CCL 3) to be monitored under the third UCMR (UCMR 3). Erythromycin was not included on the proposed UCMR 3 list of contaminants, because according to EPA officials, further development of an analytical method that can be used for national monitoring of erythromycin is needed. EPA officials stated that the agency is in the initial stages of development of an analytical method for a number of pharmaceuticals, including erythromycin, and will evaluate the readiness of this analytical method for future UCMR efforts. EPA officials further stated that the agency will continue to evaluate unregulated contaminants, such as erythromycin, for future CCLs and will utilize any new data that become available.[104]

EPA and USGS have conducted several studies to measure the presence of antibiotics in the environment, which results partly from their disposal. According to EPA and USGS officials, there is no specific statutory mandate requiring the agencies to collect information about the presence of antibiotics in the environment. However, from 1999 through 2007, the agencies conducted five national studies measuring the presence and concentration of certain antibiotics in streams, groundwater, untreated drinking water, sewage sludge, and wastewater effluent as part of their efforts to study emerging contaminants.[105,106] (See table 5.) These studies

[103]The other two criteria are: "the contaminant is known to occur, or there is a substantial likelihood that the contaminant will occur, in public water systems with a frequency and at levels of public health concern" and "in the sole judgment of the Administrator, regulation of such a contaminant presents a meaningful opportunity for health risk reduction for persons served by public water systems." 42 U.S.C. §§ 300g-1(b)(1)(A),(b)(1)(B)(ii) (2011).

[104]EPA expects to publish the next CCL by 2014.

[105]In addition, USGS has completed a national study of streambed sediment in about 50 streams that are located in 17 states but the results have not been made available. USGS officials told us that the agency expects to issue a report in 2012. However, some of the data have been published and show, for example, that trimethoprim, an antibiotic, occurred in higher concentrations in streambed sediment, compared to the overlying stream water. See E.T. Furlong et al., "Distributions of Organic Wastewater Contaminants between Water and Sediment in Surface-Water Samples in the United States," *Proceedings of the 3rd International Conference on Pharmaceuticals and Endocrine Disrupting Chemicals in Water* (2003), pp. 60-62.

were generally designed to determine whether certain contaminants, including antibiotics, were entering the environment and as a result, some study sites were selected based on being susceptible to contamination.[107] For example, the study examining the presence of antibiotics, and other contaminants, in streams in 30 states was designed to determine whether these contaminants were entering the environment. Therefore, USGS purposely selected study sites susceptible to contamination by humans, industry, and agricultural wastewater.

Table 5: Five National Studies that Measured the Presence of Antibiotics in the Environment, Conducted by EPA and USGS

Name of study (agency that conducted the study)	Year(s) study was conducted	Description of study sites	Examples of antibiotics detected[a]
Pharmaceuticals, Hormones, and Other Organic Wastewater Contaminants in U.S. Streams, 1999-2000: A National Reconnaissance (USGS)	1999-2000	139 streams across 30 states.	Ciprofloxacin, Erythromycin, Tetracycline
A National Reconnaissance of Pharmaceuticals and Other Organic Wastewater Contaminants in the United States – I) Groundwater (USGS)	2000	47 groundwater sites across 18 states.	Lincomycin, Sulfamethazine, Sulfamethoxazole
A National Reconnaissance for Pharmaceuticals and Other Organic Wastewater Contaminants in the United States – II) Untreated Drinking Water Sources (USGS)	2001	25 ground- and 49 surface-water sources of drinking water in 25 states and Puerto Rico.	Azithromycin, Ciprofloxacin, Erythromycin
Targeted National Sewage Sludge Survey (EPA)	2006-2007	74 publicly owned plants that treat wastewater in 35 states.	Azithromycin, Ciprofloxacin, Erythromycin
Transport of Chemicals from Wastewater Effluents (EPA and USGS)	2002	10 wastewater treatment plants in 10 states.	Erythromycin, Sulfamethoxazole, Trimethoprim

Source: GAO analysis and summary of EPA and USGS information.

[a]Detected antibiotics include those used for treatment by both animals and humans.

In all five studies antibiotics were found to be present. For example, erythromycin was detected in multiple samples tested in four studies and

[106]The five national studies also measured the presence of the antiseptic active ingredient triclosan in the environment. (For more information on triclosan, see app. IV).

[107]In comparison, EPA's targeted national sewage sludge study sample was designed to be representative of U.S. publicly owned treatment plants that treat more than one million gallons of wastewater per day.

ciprofloxacin was detected in three studies.[108] According to EPA and USGS officials, the antibiotic concentrations detected in streams, groundwater, and untreated drinking water are low relative to the maximum recommended therapeutic doses approved by FDA for most antibiotics. In contrast, antibiotics were found in relatively higher concentrations in sewage sludge. For example, the maximum concentration level of ciprofloxacin that was detected in streams or untreated drinking water sources was .03 micrograms per liter of water.[109] In comparison, ciprofloxacin was detected in sewage sludge sampled from large publicly owned treatment plants at concentrations ranging from 74.5 to 47,000 micrograms per kilogram of sewage sludge.[110] The maximum recommended therapeutic dose for ciprofloxacin is about 13,000 micrograms per kilogram of weight. According to USGS officials, waste from humans and domestic animals that receive antibiotics (i.e., therapeutic or subtherapeutic doses) are likely to contain antibiotics as a substantial portion of such antibiotic treatments are not fully absorbed through the body.[111]

EPA and USGS also have two ongoing studies that measure the presence of antibiotics in wastewater and drinking water. First, EPA is assessing the concentration of pharmaceuticals and other contaminants in municipal

[108]Few antibiotics were detected in groundwater. For example, neither ciprofloxacin nor erythromycin was detected in groundwater. According to USGS officials, while antibiotics were generally less likely to be detected in groundwater compared to surface water systems, the USGS groundwater study's findings document that at least some antibiotics are able to enter groundwater.

[109]Among the national studies of streams, groundwater, and untreated drinking water, the maximum antibiotic concentration level detected was 1.9 micrograms per liter of water—for sulfamethoxazole detected in streams. A concentration level of 1 microgram per liter of water is also referred to as 1 part per billion and a detection level of 1 milligram per liter of water is also referred to as 1 part per million.

[110]Ciprofloxacin was not detected in the wastewater effluent study. Other antibiotics were detected in the treated effluent samples, including sulfamethoxazole and trimethoprim; the maximum concentration level for sulfamethoxazole was .589 micrograms per liter of water and the maximum concentration level for trimethoprim was .353 micrograms per liter of water.

[111]In addition to the wastewater effluent study, USGS has conducted other, generally smaller-scale studies that examined levels of antibiotics in various sources of human and animal waste. For example, in one study USGS found chlortetracycline concentrations ranging from 68 to 1000 micrograms per liter of swine waste lagoon samples. See Campagnolo et al., "Antimicrobial residues in animal waste and water resources proximal to large-scale swine and poultry feeding operations," *The Science of the Total Environment*, vol. 299 (2002), pp. 89-95.

wastewater because past studies have suggested that municipal wastewater is a likely source of human pharmaceuticals entering the environment. According to EPA officials, EPA is collecting samples from 50 of the largest municipal wastewater plants in the United States and testing their treated effluents for contaminants, including 12 antibiotics.[112] The study's findings are expected to be made available sometime in 2012 and may help EPA develop new standards for municipal wastewater treatment, according to EPA officials. Second, EPA and USGS are collaborating on a study to measure the presence of several antibiotics (e.g., erythromycin) and other contaminants in raw and finished drinking water to better determine human exposures to these contaminants through drinking water.[113] During 2011, researchers will take samples from between 20 and 25 drinking water treatment plants across the United States and according to EPA officials, the information will be used to inform EPA decision making about the focus of future monitoring efforts. EPA and USGS officials anticipate the study's findings to be made available sometime in 2012.

Studies Find Antibiotics Present in the Environment at Certain Concentration Levels Can Increase the Population of Resistant Bacteria Due to Selective Pressure

Scientific evidence gathered in our literature review shows that, at certain concentration levels, antibiotics present in the environment—in water and soil—can increase the population of resistant bacteria, due to selective pressure. Of the 15 studies we identified that examined this association, 5 examined water-related environments and 10 examined soil-related environments. Among these 15 studies, 11 provided evidence to support the association. Support for this association means that antibiotics present in these environments increased the population of resistant bacteria

[112]EPA officials stated that they selected wastewater treatment plants that primarily receive wastewater from municipal sources and that discharge effluent to surface water.

[113]EPA officials stated that while this study will provide the agency with information that will be useful in terms of the occurrence frequency and concentration of erythromycin, additional method development work will be required to produce a method that can be used for regulatory purposes.

through selective pressure because bacteria containing resistance genes survived and multiplied.[114]

Results for the five studies examining water-related environments generally support an association between the presence of antibiotics and an increase in the population of resistant bacteria caused by selective pressure, although only one tested concentration levels of antibiotics as low as those that have been detected in national studies of U.S. streams, groundwater, and source drinking water. The results of this study were inconclusive as to whether low antibiotic concentration levels, such as levels measured at or below 1.7 micrograms per liter of water, led to an increase in the population of resistant bacteria.[115] Among the four other studies that supported an association between the presence of antibiotics and an increase in the population of resistant bacteria, the lowest concentration level associated with an increase was 20 micrograms of oxytetracycline per liter of water—over 50 times higher than maximum antibiotic concentration levels detected in stream water across the United States.[116] Another of these four studies found that chlortetracycline was associated with an increase in the population of resistant bacteria, but only at concentration levels over 1000 times higher than those that have been detected in streams across the United States.[117] According to USGS officials, scientists generally agree that the population of resistant bacteria would increase in water if the concentration levels of antibiotics that are present were to reach the minimum level that is known to induce

[114]Horizontal gene transfer—the process in which bacteria exchange genes that are coded for resistance—can also lead to an increase in the population of antibiotic-resistant bacteria in the environment because bacteria that were previously nonresistant become resistant. Studies have shown that concentrated animal feeding operations and wastewater treatment plants have high densities of antibiotics, as well as antibiotic-resistant bacteria, and that both characteristics facilitate gene transfer. For example, one study found that when swine waste was applied to fertilize soil, resistant bacteria found in the waste transferred their resistance genes to other bacteria in the soil. See H. Heuer et al., "Spreading antibiotic resistance through spread manure: characteristics of a novel plasmid type with low %G+C content," *Environmental Microbiology* (2009), vol. 11, pp. 937-949.

[115]See S. Castiglioni, et al., "Novel homologs of the multiple resistance regulator *mar*A in antibiotic-contaminated environments," *Water Research*, vol. 42 (2008), pp. 4271-4280.

[116]See C.W. Knapp et al., "Indirect Evidence of Transposon-Mediated Selection of Antibiotic Resistance Genes in Aquatic Systems at Low-Level Oxytetracycline Exposures," *Environmental Science & Technology*, vol. 42 (2008), pp. 5348-5353.

[117]See J. Munoz-Aguayo et al., "Evaluating the Effects of Chlortetracycline on the Proliferation of Antibiotic-Resistant Bacteria in a Simulated River Water Ecosystem," *Applied and Environmental Microbiology*, vol. 73 (2007), pp. 5421-5425.

antibiotic resistance in a clinical setting.[118,119] USGS officials further stated that higher concentrations of antibiotics have been found, for example, in waters near to pharmaceutical manufacturing facilities in countries outside of the United States.[120]

Results for the 10 studies examining antibiotic resistance in soil-related environments, such as soil and sediment, were more mixed, and we cannot draw comparisons between concentration levels tested in these studies and those that have been found in such environments across the United States. Seven of the 10 studies found evidence to support an association between the presence of antibiotics and an increase in the population of resistant bacteria due to selective pressure, and the association existed at all concentration levels studied. No association existed among the antibiotic concentration levels in the other 3 studies. Because national data about the presence and concentration levels of antibiotics in soil and sediment are not available, we cannot draw comparisons between concentration levels tested in these studies and those commonly found in such environments across the United States. As with water-related environments, USGS officials stated that scientists generally agree that the population of resistant bacteria would increase in soil if the concentration levels of antibiotics that are present were to reach the minimum level that is known to induce antibiotic resistance in clinical

[118]The antibiotic concentration level that is known to increase the population of resistant bacteria because of selective pressure is referred to as a minimum inhibitory concentration (MIC) level. MIC levels are determined for specific types of bacteria and antibiotics and a MIC level reflects the lowest concentration of an antibiotic that prevents visible growth of a bacterium in two types of laboratory tests. MIC levels are used to predict the success or failure of an antibiotic treatment in a clinical setting, and thus, guide healthcare providers' choice of antibiotics to treat bacterial infections. According to a USGS official, the low concentration levels of antibiotics in the environment that have been detected in national studies are generally characterized as such because they are below MIC levels.

[119]USGS officials further stated that there is evidence that antibiotic concentration levels lower than MIC levels can affect, among other things, bacterial growth in the environment. See J.C. Underwood et al., "Effects of the Antimicrobial Sulfamethoxazole on Groundwater Bacterial Enrichment," *Environmental Science and Technology*, vol. 45 (2011), pp. 3096-3101.

[120]For example, see J. Fick et al., "Pharmaceuticals and Personal Care Products in the Environment: Contamination of Surface, Ground, and Drinking Water from Pharmaceutical Production," *Environmental Toxicology and Chemistry*, vol. 28 (2009), pp. 2522-2527. This study showed high concentrations of certain antibiotics in rivers and lakes near a wastewater treatment plant in India that receives wastewater from approximately 90 drug manufacturers. USGS officials told us that they are currently designing a national study of pharmaceutical manufacturing facilities that will examine antibiotic concentration levels in areas proximal to such facilities.

settings. USGS officials further stated that antibiotic concentration levels in soils where human and animal waste have been applied as fertilizer are likely to be directly related to the antibiotic concentration levels in these sources.[121]

Conclusions

Antibiotics have been widely prescribed to treat bacterial infections in humans and their use contributes to the development of antibiotic resistance, which is an increasing public health problem in the United States and worldwide. Monitoring the use of antibiotics in humans and preventing their inappropriate use, such as prescribing an antibiotic to treat a viral infection, is critically important because the use of antibiotics for any reason contributes to the development and spread of antibiotic resistance. Establishing patterns of antibiotic use is necessary for understanding current—and predicting future—patterns of antibiotic resistance. Monitoring overall antibiotic use in humans, including in inpatient and outpatient healthcare settings, is also needed to evaluate the contribution of such use—relative to other causes, such as animal use—to the overall problem of antibiotic resistance. Such information could help policymakers set priorities for actions to control the spread of antibiotic resistance.

CDC is collecting data on antibiotic use and the occurrence of resistance, but the agency's data sources have limited ability to provide accurate national estimates and do not allow it to assess associations between use and resistance. CDC does not monitor the use of antibiotics in inpatient settings—where antibiotic use is often intensive and prolonged and thus, the risk of antibiotic resistance is greater—although the agency believes such information would help it target and evaluate its own prevention efforts to reduce the occurrence of resistance. Although the agency collects annual data in the United States about the use of antibiotics in outpatient settings, the data do not allow CDC to assess geographic patterns of use in those settings. Similarly, CDC's monitoring of antibiotic-resistant infections does not allow the agency to assess the overall problem of antibiotic resistance because of gaps in the data it collects. Without more comprehensive information about the occurrence of cases

[121]For example, one study, not conducted by USGS, has documented that triclocarban, an antiseptic active ingredient, persists and bioaccumulates in soils amended with treated sewage sludge. See C.P. Higgins et al., "Persistence of Triclocarban and Triclosan in Soils after Land Application of Biosolids and Bioaccumulation in *Eisenia Foetida*," *Environmental Toxicology and Chemistry*, vol. 30 (2010), pp. 556-563.

of antibiotic-resistant infections and the use of antibiotics, the agency's ability to understand the overall scope of the public health problem, detect emerging trends, and plan and implement prevention activities is impeded. Further, the lack of comprehensive information about antibiotic-resistant infections and antibiotic use, and the most effective ways to reduce inappropriate prescribing, impedes CDC's ability to strategically target its resources directed at reducing the occurrence of antibiotic-resistant infections.

CDC is attempting to address the gaps in its data on antibiotic use in humans and on antibiotic-resistant infections by obtaining additional data, but it is not clear whether the steps it is taking will result in more comprehensive information from which the agency could assess the public health impact of antibiotic resistance. Further, it is not clear whether these steps will provide CDC with the information it needs to identify what actions are needed to reduce the occurrence of antibiotic-resistant infections.

Recommendations

To better prevent and control the spread of antibiotic resistance, we recommend that the Director of CDC take the following two actions:

- Develop and implement a strategy to improve CDC's monitoring of antibiotic use in humans, for example, by identifying available sources of antibiotic use information; and
- develop and implement a strategy to improve CDC's monitoring of antibiotic-resistant infections in inpatient healthcare facilities to more accurately estimate the national occurrence of such infections.

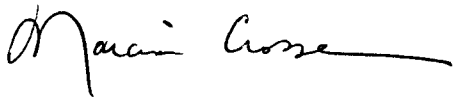
Agency Comments

We provided a draft of this report for review to HHS, EPA, and DOI. HHS provided written comments, which are reproduced in appendix V. HHS, EPA, and DOI provided technical comments, which we incorporated as appropriate.

In its written comments, HHS generally agreed with the actions we recommend it take to improve its monitoring of antibiotic use and resistance. HHS says that steps are being taken to address existing gaps in CDC's monitoring of antibiotic use and the occurrence of antibiotic-resistant infections, and HHS noted that such monitoring is critically important in preventing the development and spread of antibiotic resistance. HHS highlighted examples of the steps CDC is taking, or plans to undertake, to address gaps in CDC's monitoring of antibiotic use and antibiotic-resistant infections, such as a planned survey of acute care hospitals in the United States. HHS noted that other planned activities to improve the monitoring of antibiotic use and antibiotic-resistant infections are described in the revised draft Action Plan, developed by the Interagency Task Force on Antimicrobial Resistance. HHS stated that CDC believes that the successful, timely accomplishment of its planned and ongoing activities to improve monitoring will result in information that is sufficiently comprehensive for a full and complete assessment of the public health impact of antibiotic resistance, and that this assessment will provide federal agencies with appropriate information to identify necessary actions to reduce the occurrence of antibiotic-resistant infections. HHS stated that it would provide updates on its progress toward the accomplishment of its steps to improve monitoring in the 2010 annual progress report on the Action Plan, scheduled for public release this summer. HHS also commented that it has initiated the process of developing a strategic plan for preventing the emergence and spread of antibiotic-resistant infections, and a primary component of this strategic plan is the monitoring of antibiotic use and resistance. We support this effort and encourage HHS, as it develops its strategic plan, to continue to examine approaches for improving its monitoring of antibiotic use and antibiotic-resistant infections that will help provide the agency with information that is needed to more accurately estimate the national occurrence of antibiotic-resistant infections.

As agreed with your offices, unless you publicly announce the contents of this report earlier, we plan no further distribution until 30 days from the report date. At that time, we will send copies to the Secretaries of the Department of Health and Human Services and the Department of the Interior, the Administrator of the Environmental Protection Agency, and other interested parties. In addition, the report will be available at no charge on the GAO Web site at http://www.gao.gov.

If you or your staff have any questions about this report, please contact me at (202) 512-7114 or crossem@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 major contributions to this report are listed in appendix VI.



Marcia Crosse
Director, Health Care

Appendix I: Methodology for Reviewing Scientific Evidence on Antibiotic Resistance in the Environment

To describe the scientific evidence on the development of antibiotic-resistant bacteria in the environment, we conducted a literature review. We identified literature made available since 2007 that reported scientific findings on antibiotic concentrations that induce bacteria located in the environment to become resistant as well as the ability of bacteria to spread resistance. We conducted a key word search of 39 databases, such as Elsevier Biobase and MEDLINE that included peer-reviewed journals and other periodicals to capture articles published on or between January 1, 2007, and July 8, 2010. We searched these databases for articles with key words in their title or abstract related to both antibiotic resistance and the environment, such as combinations and variations of the words "resistance," "antibiotic," and "environment," and descriptive words for different environmental settings, such as "water," "sediment," "soil," and "sewage."[1] From these sources, we identified 241 articles, publications, and reports (which we call articles) published from January 1, 2007, through July 8, 2010. Of these 241 articles, we then excluded articles that (1) were not published in English, (2) were available only in an abstract form or in books or book chapters, (3) were not peer-reviewed, (4) contained only a review of past literature, or (5) were unrelated to antibiotic resistance found in the environment such as articles that focused on the effects of antibiotic resistance found mainly in clinical settings.[2] In total, we included 105 articles in our literature review. We supplemented the scientific findings analyzed in our literature review with contextual and background information gathered from articles that were identified as a result of our interviews with officials from the Environmental Protection Agency and the United States Geological Survey.

[1]A complete list of search terms was variations on the phrases "antibiotic resistance" or "antimicrobial resistance" found in combination with any of the following terms: "environment," "ground water," "surface water," "drinking water," "waste water," "effluent," "hospital effluent," "municipal sewage," "animal feeding operation," "ecotoxicity," "pharmaceutical plant," "sediment," and "soil."

[2]For the purposes of our literature review, we defined the environment as water, soil, and sediment, as well as certain wastewater treatment-related settings and certain agricultural-related settings that serve as pathways into water, soil, and sediment.

Appendix II: Bacteria and the Development of Antibiotic Resistance

Bacteria are single-celled organisms that live in water, soil, and in the bodies of humans, animals, and plants. Bacteria compete with each other for resources, such as nutrients, oxygen, and space, and those that do not compete successfully will not survive. Most bacteria that are present in humans, such as those found on the skin and in the intestines, are harmless because of the protective effects of the human immune system, and a few bacteria are beneficial. However, some bacteria are capable of causing disease. For example, *Escherichia coli* O157—which can be found in the feces of animals, such as cattle, and can transfer to people through contaminated undercooked meat—produce a toxin that causes severe stomach and bowel disorders, and death in some cases.[1] In addition, the same bacteria that may cause disease in one individual may not cause disease in another.[2] For example, *Streptococcus pneumoniae* is a bacterium that is often found in the noses and throats of healthy persons without causing disease, but it can also cause mild illness, such as sinus infections, as well as life-threatening infections such as meningitis. Furthermore, when the immune system is weakened, infection may be caused by certain bacteria that would not generally result in an infection in a healthy human.

Like other living things, as bacteria grow and multiply, they also evolve and adapt to changes in their surroundings. Bacteria adapt to their surroundings through selective pressure, which is created by, among other things, the presence of antibiotics.[3] Selective pressure means that when an antibiotic is introduced into a bacterial environment, some bacteria will be killed by the antibiotic while other bacteria will survive.[4] Bacteria are able to survive because they have certain genetic material that is coded for resistance—allowing them to avoid the effects of the antibiotic. The surviving bacteria that are resistant to antibiotics will multiply and quickly

[1]*Escherichia coli* O157 can also spread through human feces. In addition to consuming contaminated meat, exposure to *Escherichia coli* O157 can occur by consuming other contaminated foods (e.g., milk and lettuce) or by having direct contact with infected carriers.

[2]Bacteria that cause disease are referred to as pathogenic bacteria. In order to cause disease, pathogens must be able to enter the body, which can occur, for example, through the mouth, eyes, or wounds that tear the skin.

[3]Some bacteria have developed resistance to antibiotics naturally, long before the development of commercial antibiotics.

[4]Any use of antibiotics—appropriate and inappropriate—creates selective pressure among bacteria.

become the dominant bacterial type. Bacteria that are susceptible to the effects of antibiotics may become resistant to such antibiotics after acquiring resistant genetic material from bacteria that are resistant through horizontal gene transfer. Horizontal gene transfer is the movement of genetic material between bacteria, and can occur within a species of bacteria and can sometimes occur between certain species of bacteria.[5] Close proximity between bacteria, which allows certain genetic material to be shared, can facilitate gene transfer.

The movement of antibiotic-resistant bacteria around the world is accelerated because of international travel and global trade. Individuals can contract bacterial strains—that is, distinct types of bacteria—that are resistant to antibiotics abroad during travel, whether as active infections or as unaffected carriers, and then spread such strains to others at home.[6] The bacterial strains in different parts of the world may also contain different resistance genes than bacterial strains found domestically. For example, in 2010, the Centers for Disease Control and Prevention reported that three bacterial strains included a resistance gene identified for the first time in the United States. The emergence of the resistance gene was traced to patients who had received recent medical care in India.[7] Further, international trade of food and livestock may accelerate the movement of antibiotic-resistant bacteria because food and livestock also carry resistant bacterial strains that can be contracted by humans through consumption.

To determine whether bacteria are resistant, tests are performed that measure the susceptibility of pathogenic bacteria to particular antibiotics. The test results can predict the success or failure of an antibiotic treatment, and thus, guide healthcare providers' choice of antibiotics to treat bacterial infections. The test results include a numeric value, which is then interpreted according to established ranges.[8] For example, a value may be categorized as 'resistant,' meaning that the pathogenic bacterium is

[5]A species is a group of organisms—including bacteria—with common traits, such as similar genetic characteristics.

[6]As an example, *Escherichia coli* O157 is a strain of the *Escherichia coli* species.

[7]The resistance gene was found in cases of *Escherichia coli*, *Klebsiella pneumoniae*, and *Enterobacter cloacae* infections. The presence of this particular gene resulted in resistance to certain antibiotics including the carbapenems subclass; for certain bacterial infections, carbapenems are considered antibiotics of last resort.

[8]The Clinical and Laboratory Standards Institute, a nonfederal entity, establishes ranges for the interpretation of test results for antibiotic resistance.

not inhibited by the concentration of the antibiotic that usually results in growth inhibition.[9]

[9]Test values may also fall into ranges for the 'susceptible' and 'intermediate' categories.

Appendix III: Centers for Disease Control and Prevention's Surveillance Systems for Monitoring Antibiotic Resistance

Table 6: CDC's Surveillance Systems for Monitoring Antibiotic Resistance, by Bacteria, Geographic Coverage, and Examples of Data Use

Surveillance system	Bacteria monitored for antibiotic resistance	Geographic coverage of surveillance	Examples of how surveillance data were used
Active Bacterial Core Surveillance (ABCs) [of the Emerging Infections Programs (EIP) Network[a]]	group A and group B *Streptococcus*; *Neisseria meningitidis*; *Streptococcus pneumoniae*; methicillin-resistant *Staphylococcus aureus* (MRSA)[b]	10 surveillance areas in California, Colorado, Connecticut, Georgia, Maryland, Minnesota, New Mexico, New York, Oregon, and Tennessee for group A and B *Streptococcus*; *Neisseria meningitidis*; and *Streptococcus pneumoniae* 9 surveillance areas in California, Colorado, Connecticut, Georgia, Maryland, Minnesota, New York, Oregon, and Tennessee for MRSA	ABCs data were used to show that rates of invasive pneumococcal infections, including antibiotic-resistant infections among children and adults, have declined since a pneumococcal conjugate vaccine was introduced for children in 2000. ABCs data have also shown a decline in the incidence of pneumococcal meningitis resistant to antibiotics. ABCs data on MRSA, collected between 2005 and 2008, were used to identify the genetic makeup of MRSA strains showing unusual patterns of resistance. This information provided the Centers for Disease Control and Prevention (CDC) with evidence that mechanisms of resistance in MRSA were being transferred from healthcare-associated to community-associated strains.
Gonococcal Isolate Surveillance Project (GISP)	*Neisseria gonorrhoeae*	29 sexually transmitted disease clinics located in the West, Midwest, Northeast, and South	Based on GISP data, CDC announced in 2007 that fluoroquinolones were no longer recommended to treat gonorrhea because of antibiotic resistance and that the recommended treatment for gonorrhea was limited to only cephalosporin antibiotics. *Neisseria gonorrhoeae* isolates collected through GISP have been used to support research on the mechanisms used to resist the effects of antibiotics, according to a CDC official.
National Antimicrobial Resistance Monitoring System: Enteric Bacteria (NARMS: EB)	*Shigella*, *Escherichia coli* O157, *Campylobacter*, typhoidal *Salmonella*, and non-typhoidal *Salmonella*[c]	50 states for *Shigella*, typhoidal *Salmonella*, non-typhoidal *Salmonella*, and *Escherichia coli* O157 10 states for *Campylobacter*—California, Colorado, Connecticut, Georgia, Maryland, Minnesota, New Mexico, New York, Oregon, and Tennessee	NARMS: EB data were used in 2005 to support the Food and Drug Administration's (FDA) withdrawal of approval for the use of enrofloxacin in chickens and turkeys. Enrofloxacin, a fluoroquinolone, marketed under the trade name Baytril, had been approved for use in poultry production. In September 2005, FDA withdrew its approval because of concerns about the spread of fluoroquinolone-resistant *Campylobacter* from poultry to humans. NARMS: EB data from 1996-2006 were used to identify mechanisms of resistance to cephalosporins among specific types of *Salmonella*.

Surveillance system	Bacteria monitored for antibiotic resistance	Geographic coverage of surveillance	Examples of how surveillance data were used
National Healthcare Safety Network (NHSN)	Includes, among others, *Enterococcus faecalis*; *Enterococcus faecium*; *Staphylococcus aureus*; *Acinetobacter*; *Escherichia coli*; *Enterobacter*; *Klebsiella* oxytoca; *Klebsiella pneumoniae*; *Pseudomonas aeruginosa*; and *Clostridium difficile*	Participating healthcare facilities across the United States	Participating facilities have used NHSN data to assess their own healthcare-associated infection (HAI) rates, by comparing their rates with national rates. CDC also compiled 2006-2007 data on antibiotic resistance across participating facilities and reported, for example, that as many as 16 percent of all HAIs observed in NHSN were associated with nine multidrug-resistant bacteria, such as MRSA.
National Notifiable Diseases Surveillance System (NNDSS)	*Streptococcus pneumoniae*	Health departments in the 50 states, 5 territories, New York City, and the District of Columbia voluntarily report cases to CDC	CDC has determined that NNDSS data are likely to be used to assess the impact of a vaccine that was approved in 2010 to prevent additional strains of *Streptococcus pneumoniae*.
National Tuberculosis Surveillance System (NTSS)	*Mycobacterium tuberculosis*	CDC receives information on each newly reported case of tuberculosis (TB) in the United States.	In 2010, after expanding the NTSS data collection with the TB Genotyping Information Management System, CDC officials used genotypes identified with the system to assist an investigation of a TB outbreak among healthcare workers. As a result of the investigation, the probable source for the TB outbreak was identified.

Source: GAO analysis and summary of CDC information.

[a]Since 2009, CDC has monitored *Clostridium difficile* infections in healthcare and community settings through EIP (as part of its Healthcare Associated Infections Surveillance). CDC officials stated that these data complement the *Clostridium difficile* data that are captured through the National Healthcare Safety Network and will, among other things, inform vaccine development.

[b]*Haemophilus influenzae* are monitored for antibiotic resistance periodically.

[c]According to CDC officials, NARMS: EB collects data on *Enterococci* from 2 states and has a pilot study to monitor *Escherichia coli* in 1 state.

Appendix IV: Topical Antiseptics and Antibiotic Resistance

Topical antiseptics are products that are used to reduce the risk of infection by killing or inhibiting the growth of microorganisms, such as bacteria, on the skin. Topical antiseptic products are diverse, and include those targeted for healthcare settings, such as surgical hand scrubs and patient preoperative skin preparations; products targeted to consumers for general body cleansing include antibacterial soaps; and products specifically intended for use by food handlers. Topical antiseptics contain a variety of active ingredients; for example, triclosan and triclocarban are commonly used in antibacterial liquid and bar soaps, while alcohol is used in leave-on handwashes.[1] Because antiseptics are intended for use in or on humans or animals,[2] they are considered drugs and are approved and regulated as nonprescription drugs by the Food and Drug Administration (FDA) under the Federal Food, Drug, and Cosmetic Act.[3] There are concerns by public officials, and others, about the possibility that the use of, or exposure to, topical antiseptics causes antibiotic resistance in bacteria. This process is called cross-resistance.[4]

FDA has conducted a review of the scientific literature regarding the relationship between exposure to active ingredients in topical antiseptics—including triclosan or triclocarban—and cross-resistance. According to the available scientific evidence that FDA has reviewed, bacteria are able to develop resistance to both antiseptics and antibiotics in the laboratory setting, but the relationship outside of the laboratory setting is not clear. For example, a laboratory study has shown that when certain strains of the bacteria *Escherichia coli* (E. coli) are exposed to triclosan, the E. coli not only acquire a high level of resistance to triclosan,

[1]Other active ingredients include iodine and chloroxylenol.

[2]In contrast, disinfectants are used on inanimate surfaces or objects to destroy or inactivate infectious microorganisms. Consequently, disinfectants, even if they contain the same active ingredient as an antiseptic, are regulated as chemicals by the Environmental Protection Agency.

[3]Federal Food, Drug, and Cosmetic Act of 1938, codified as amended at 21 U.S.C. § 301 & scattered sections (2011). To be considered a drug, a product must be intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease in humans or animals, or it must be intended to affect the structure or any function of the body of humans or other animals. Most antiseptic products are currently being marketed under the Tentative Final Monograph for over-the-counter Healthcare Antiseptic Drug Products, published in 1994. See 59 *Fed. Reg.* 31,402 (June 17, 1994).

[4]Since bacteria use similar mechanisms to resist the effects of antiseptics and antibiotics, scientists believe that it may be possible that exposure and development of resistance to antiseptics could also result in resistance to antibiotics.

but also demonstrate cross-resistance to various antibiotics, such as erythromycin and tetracycline.[5] However, a study that examined household use of certain antiseptic products did not show an association between their use and the development of antibiotic resistance.[6] According to FDA, the possibility that bacteria can develop cross-resistance to antibiotics from exposure to antiseptics warrants further evaluation. FDA will seek additional data regarding the safety of topical antiseptic products, for example, on the effects of antiseptics on cross-resistance, when it issues a proposed rule to amend the current monograph for antiseptic drug products. FDA officials told us that they expect the proposed rule to be published for public comment sometime in 2011.

The Environmental Protection Agency (EPA) and the United States Geological Survey (USGS) conducted five national studies between 1999 and 2007 that measured for the presence of the antiseptic active ingredients triclosan and triclocarban in the environment.[7] These studies tested for the presence and concentration of the antiseptic active ingredients along with other contaminants including antibiotics, in streams, groundwater, untreated drinking water, sewage sludge, and wastewater effluent.[8] (See table 6.) Each of the studies measured for the presence of triclosan, and the study involving sewage sludge also tested for triclocarban.[9] Triclosan was found to be present in 94 percent of

[5]M. Braoudaki and A.C. Hilton, "Adaptive Resistance to Biocides in *Salmonella enterica* and *Escherichia coli* O157 and Cross-Resistance to Antimicrobial Agents," *Journal of Clinical Microbiology*, Vol. 42 (2004), pp. 73-78.

[6]E.C. Cole, et al., "Investigation of antibiotic and antibacterial agent cross-resistance in target bacteria from homes of antibacterial product users and nonusers," *Journal of Applied Microbiology*, Vol. 95 (2003), pp. 664-676.

[7]Officials from FDA and the Centers for Disease Control and Prevention told us that they do not collect information about the amounts of antiseptics produced or used in the United States. According to FDA officials, however, FDA collects annual drug distribution data for chlorhexidine gluconate products, which are used as topical antiseptics, but are not covered under FDA's monograph for antiseptic drug products.

[8]In addition, USGS has completed a national study of streambed sediment in about 50 streams that are located in 17 states but the results have not been made available. USGS officials told us that the agency expects to issue a report in 2012. According to USGS officials, the national study of streambed sediment also tested for the presence of triclosan.

[9]As part of an ongoing study, EPA and USGS are measuring for the presence of triclosan and triclocarban in treated drinking water. According to EPA officials, findings are expected to be made available sometime in 2012.

sewage sludge samples, 100 percent of wastewater effluent samples, and 57.6 percent of stream samples tested from sites across the United States. It was also detected in 14.9 percent of groundwater samples and 8.1 percent of untreated drinking water samples.[10] Triclocarban was found to be present in all sewage sludge samples taken from wastewater treatment plants located across the United States.[11]

Table 7: Five National Studies that Measured the Presence of Antiseptic Active Ingredients in the Environment, Conducted by EPA and USGS

Name of study (agency that conducted the study)	Year(s) study was conducted	Description of study sites	Examples of antiseptic active ingredients tested
Pharmaceuticals, Hormones, and Other Organic Wastewater Contaminants in U.S. Streams, 1999-2000: A National Reconnaissance (USGS)	1999-2000	139 streams across 30 states	Triclosan
A National Reconnaissance of Pharmaceuticals and Other Organic Wastewater Contaminants in the United States – I) Groundwater (USGS)	2000	47 groundwater sites across 18 states	Triclosan
A National Reconnaissance for Pharmaceuticals and Other Organic Wastewater Contaminants in the United States – II) Untreated Drinking Water Sources (USGS)	2001	25 ground- and 49 surface-water sources of drinking water in 25 states and Puerto Rico	Triclosan
Targeted National Sewage Sludge Survey (EPA)	2006-2007	74 publicly owned plants that treat wastewater in 35 states	Triclosan and Triclocarban
Transport of Chemicals from Wastewater Effluents (EPA and USGS)	2002	10 wastewater treatment plants in 10 states	Triclosan

Source: GAO analysis and summary of EPA and USGS information.

[10]According to USGS officials, the laboratory method used for measuring triclosan in the agency's stream study was different than the method used in subsequent USGS studies. USGS officials further stated that this change in methodology resulted in higher triclosan detection frequencies in the stream study, compared to subsequent USGS studies.

[11]Triclosan has been detected in other USGS studies involving human waste sources. For example, see C.A. Kinney et al., "Survey of Organic Wastewater Contaminants in Biosolids Destined for Land Application," *Environmental Science and Technology*, vol. 40 (2006), pp. 7207-7215.

Appendix V: Comments from the Department of Health and Human Services

DEPARTMENT OF HEALTH & HUMAN SERVICES — OFFICE OF THE SECRETARY

Assistant Secretary for Legislation
Washington, DC 20201

MAY 13 2011

Marcia Crosse
Director, Health Care
U.S. Government Accountability Office
441 G Street N.W.
Washington, DC 20548

Dear Ms. Crosse:

Attached are comments on the U.S. Government Accountability Office's (GAO) draft report entitled, "ANTIBIOTIC RESISTANCE: Data Gaps Will Remain Despite HHS Taking Steps to Improve Monitoring" (GAO-11-406).

The Department appreciates the opportunity to review this report before its publication.

Sincerely,

Jim R. Esquea
Assistant Secretary for Legislation

Attachment

GENERAL COMMENTS OF THE DEPARTMENT OF HEALTH AND HUMAN SERVICES (HHS) ON THE GOVERNMENT ACCOUNTABILITY OFFICE'S (GAO) DRAFT REPORT ENTITLED, "ANTIBIOTIC RESISTANCE: DATA GAPS WILL REMAIN DESPITE HHS TAKING STEPS TO IMPROVE MONITORING" (GAO 11-406)

The Department appreciates the opportunity to review and comment on this draft report.

The Centers for Disease Control and Prevention (CDC) agrees with the GAO that monitoring and surveillance of antimicrobial use and the occurrence of resistant infections are critically important in preventing the development and spread of antibiotic resistance.

As GAO notes, CDC has previously recognized gaps in the monitoring and surveillance of antimicrobial use and resistance and is taking specific steps to address these gaps. As noted in the report, these steps include:

- The planned prevalence survey of U.S. acute care hospitals
- Addition of the antimicrobial use and resistance module to NHSN
- Increase in sample size of the National Ambulatory Medical Care Survey
- Acquisition of antimicrobial use data from private vendors
- Sharing of data among Federal agencies, including FDA, NIH and CMS, which is expanding its own data collections in collaboration with CDC's NHSN
- Continued growth of the NHSN and the enhancement of components which collect data from outpatient facilities

Additional CDC activities, not specifically mentioned in the GAO report, are described in the draft document A Public Health Action Plan to Combat Antimicrobial Resistance produced by the Interagency Task Force on Antimicrobial Resistance (http://www.cdc.gov/drugresistance/pdf/2010/Interagency-Action-Plan-PreClearance-03-2011.pdf). This document identifies over 50 specific actions being undertaken by Task Force members to improve monitoring and surveillance of antimicrobial use and resistant infections; for the majority of these actions, CDC is the lead agency. Among these actions are:

- Enhancements to the National Antimicrobial Monitoring System
- Enhancements to the Gonococcal Isolate Surveillance Project
- Enhancements to antimicrobial resistance monitoring conducted through the Emerging Infections Program
- Enhancements to the Active Bacterial Core Surveillance system
- Enhancements to the national tuberculosis reporting system
- Collaborations with non-Federal public health agencies (state and local health departments, the Conference of State and Territorial Epidemiologists, the Association of Public Health Laboratories), non-governmental organizations (e.g., the Clinical and Laboratory Standards Institute), and international organizations (e.g., World Health Organization) to improve monitoring and surveillance of antimicrobial resistance

1

GENERAL COMMENTS OF THE DEPARTMENT OF HEALTH AND HUMAN SERVICES (HHS) ON THE GOVERNMENT ACCOUNTABILITY OFFICE'S (GAO) DRAFT REPORT ENTITLED, "ANTIBIOTIC RESISTANCE: DATA GAPS WILL REMAIN DESPITE HHS TAKING STEPS TO IMPROVE MONITORING" (GAO 11-406)

Updates on CDC's progress toward successful accomplishment of these action steps will be further documented in the 2010 annual progress report on the Action Plan, scheduled for release this summer.

CDC believes that the successful, timely accomplishment of the numerous action steps currently in process and planned by CDC and in collaboration with Federal and non-Federal partners will result in the Federal agencies having sufficiently comprehensive information for a full and complete assessment of the public health impact of antibiotic resistance and will provide Federal agencies with appropriate information to identify necessary actions to reduce the occurrence of antibiotic-resistant infections.

Finally, CDC has initiated the process of developing a strategic plan for preventing the emergence and spread of antimicrobial resistant infections, of which a primary component is the monitoring and surveillance of antimicrobial use and resistance.

2

Appendix VI: GAO Contact and Staff Acknowledgments

GAO Contact

Marcia Crosse, (202) 512-7114 or crossem@gao.gov

Acknowledgments

In addition to the contact named above, Robert Copeland, Assistant Director; Elizabeth Beardsley; Pamela Dooley; Cathy Hamann; Toni Harrison; Elise Pressma; and Hemi Tewarson made key contributions to this report.

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