



Testimony

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Representatives

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ANTIBIOTIC RESISTANCE

Federal Agencies Have Taken Steps to Combat the Threat, But Additional Actions Needed

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Chair Griffith, Ranking Member Castor, and Members of the Subcommittee:

We appreciate the opportunity to be here today to discuss what is considered to be one of the greatest global public health threats of our time: antibiotic resistance. As you know, since the discovery of penicillin, nearly 100 years ago, many life-saving antibiotics have been developed that have allowed previously incurable infections to be easily treated. However, many types of infections have become more difficult or impossible to treat as bacteria have developed resistance to most—or, in some cases, all—currently available antibiotics. Each year, antibiotic-resistant infections have caused 2.8 million people to get sick and at least 35,900 to die in the United States, according to estimates from the Centers for Disease Control and Prevention (CDC).¹

While bacteria naturally develop resistance to antibiotics over time, this problem has been accelerated by the overuse and misuse of antibiotics in human health, food animals, and the environment. The World Health Organization (WHO) has warned that the world urgently needs to change the way antibiotics are prescribed and used, and CDC has highlighted the need for antibiotics to be used more appropriately—a concept called antibiotic stewardship—to preserve their effectiveness and help slow the development of antibiotic resistance.² CDC officials noted that poor infection control and limited communication between health care facilities also contribute to the spread of antibiotic resistance.

Furthermore, WHO and others warned that the pipeline of antibiotics in development is insufficient to tackle the growing threat of antibiotic resistance.³ Additionally, diagnostic testing used to identify antibiotic-

¹Department of Health and Human Services, Centers for Disease Control and Prevention, *Antibiotic Resistance Threats in the United States, 2019* (Atlanta, Ga.: Dec. 2019).

²World Health Organization, “Antibiotic Resistance,” accessed April 18, 2023, <https://www.who.int/en/news-room/fact-sheets/detail/antibiotic-resistance>. WHO is the Geneva-based coordinating authority on international health within the United Nations system.

CDC defines antibiotic stewardship as the effort to measure and optimize antibiotic use with the goal of optimizing the treatment of infections while reducing the adverse events associated with antibiotic use. Antibiotic stewardship aims to have all patients treated with the right antibiotic at the right time, in the right dose, and for the right duration for a given diagnosis.

³World Health Organization, *2019 Antibacterial Agents in Clinical Development: An Analysis of the Antibacterial Clinical Development Pipeline* (Geneva, Switzerland: 2019).

resistant bacteria is not available for all bacteria of concern. These gaps may hinder the correct diagnosis of antibiotic-resistant infections, which could delay treatment with appropriate antibiotics, contribute to antibiotic overuse, and impede overall surveillance efforts.⁴

Our statement today describes federal efforts and challenges related to

- (1) surveillance of antibiotic resistance,
- (2) the development and use of diagnostic testing to identify antibiotic resistance,
- (3) the development of treatments for resistant infections, and
- (4) appropriate antibiotic use.

This statement is based on our most recent report on antibiotic resistance, which was issued in March 2020, and selected updates.⁵ In that report we made eight recommendations, and this statement includes updates on the status of agency efforts to address them.

For our March 2020, report, we reviewed literature and agency documents; interviewed agency officials and health care industry, drug industry, and other stakeholders; and held a meeting of international and U.S. experts to obtain their views. Our March 2020 report includes a full description of our scope and methodology. To update the status of that report's recommendations and provide selected updates to the information we previously reported, we reviewed publicly available information from the Department of Health and Human Services (HHS) and WHO.

We conducted the work on which this statement is based 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

⁴Disease surveillance is the process of reporting, collecting, analyzing, and exchanging information related to cases of infectious diseases.

⁵GAO, *Antibiotic Resistance: Additional Federal Actions Needed to Better Determine Magnitude and Reduce Impact*, [GAO-20-341](#) (Washington, D.C.: Mar. 30, 2020).

provides a reasonable basis for our findings and conclusions based on our audit objectives.

Background

CDC identified bacterial pathogens that the agency considers to be “urgent,” “serious,” or “concerning” because they have developed enough resistance to antibiotics to be considered a threat to human health.⁶ (See fig. 1.) CDC also identified one type of fungus—*Candida auris*—that it considered to be a serious threat (see text box).

Figure 1: Bacteria CDC Considers to Be Threats, 2019

 Urgent Threats	• Carbapenem-resistant <i>Acinetobacter</i> • <i>Clostridioides difficile</i>^a • Carbapenem-resistant Enterobacteriaceae • Drug-resistant <i>Neisseria gonorrhoeae</i>
 Serious Threats	• Drug-resistant <i>Campylobacter</i> • Extended-spectrum Beta-lactamase-producing Enterobacteriaceae • Vancomycin-resistant <i>Enterococcus</i> • Multidrug-resistant <i>Pseudomonas aeruginosa</i> • Drug-resistant Non-typhoidal <i>Salmonella</i> • Drug-resistant <i>Salmonella</i> serotype Typhi • Drug-resistant <i>Shigella</i> • Methicillin-resistant <i>Staphylococcus aureus</i> • Drug-resistant <i>Streptococcus pneumoniae</i> • Drug-resistant <i>Tuberculosis</i>
 Concerning Threats	• Erythromycin-resistant Group A <i>Streptococcus</i> • Clindamycin-resistant Group B <i>Streptococcus</i>
 Watch List	• Azole-resistant <i>Aspergillus fumigatus</i> • Drug-resistant <i>Mycoplasma genitalium</i> • Drug-resistant <i>Bordetella pertussis</i>

Source: Centers for Disease Control and Prevention (CDC); GAO (illustrations). | GAO-23-106776

⁶CDC, *Antibiotic Resistance Threats in the United States, 2019*.

Note: In addition to these bacteria, CDC also considers *Candida auris*, which is a fungus, as an urgent threat and drug-resistant *Candida* as a serious threat. CDC last updated this list in 2019.

***Candida auris* Is a Resistant Fungal Threat**

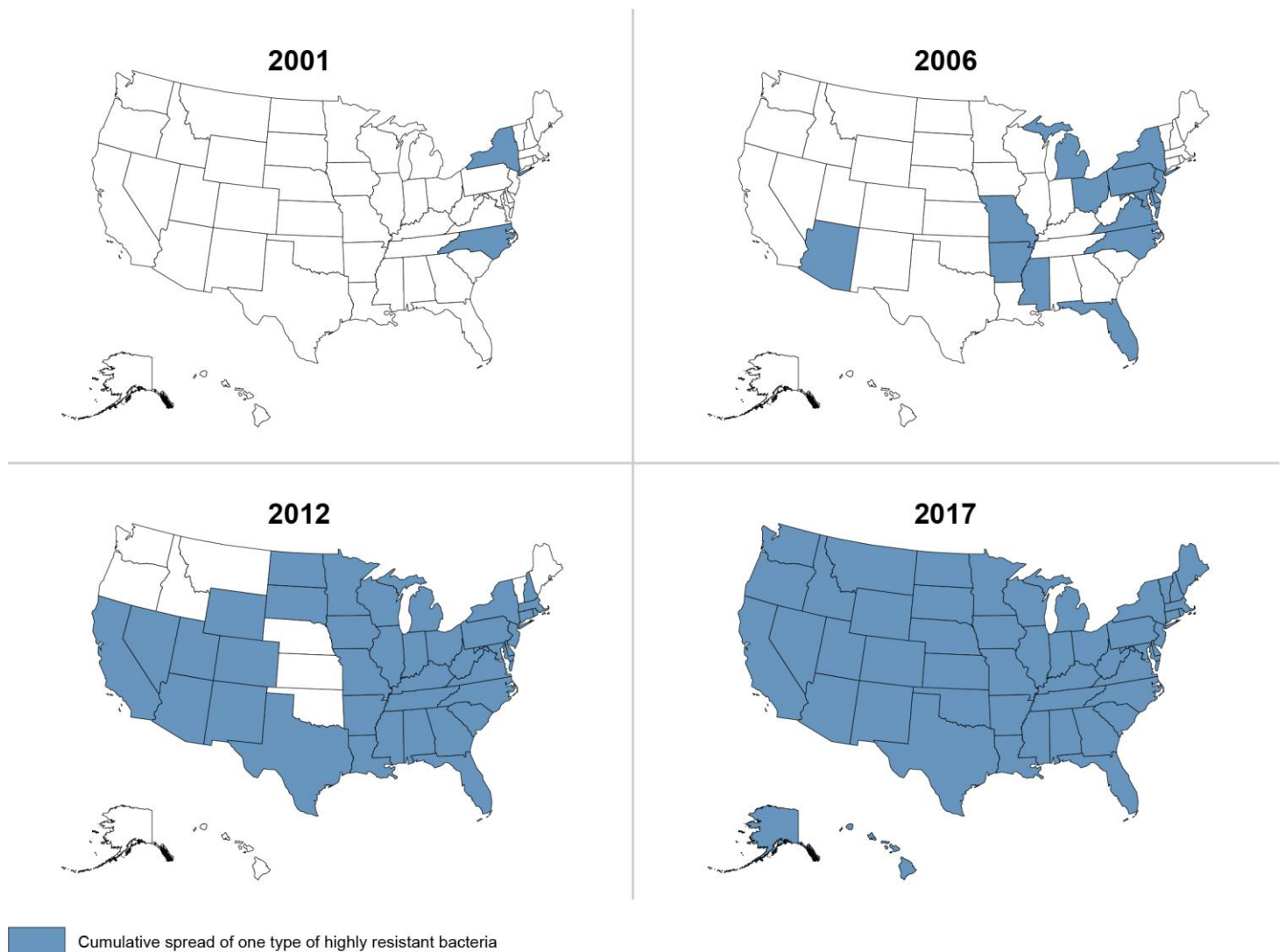
Candida auris (*C. auris*) is an emerging infectious fungus that, according to the Centers for Disease Control and Prevention (CDC), presents a global health threat in part because it is highly resistant to anti-fungal drugs and is challenging to address. In March 2023, CDC issued an alert regarding the increasing threat of spread of *C. auris* in health care facilities due to a rapid rise and geographic spread of cases. According to CDC, *C. auris* is highly transmissible and some commonly used hospital surface disinfectants appear to be less effective against *C. auris*. A CDC official told us *C. auris* is a good example of an emerging threat that requires more research and associated efforts to properly address.

Addressing *C. auris* is challenging for reasons including the rise of resistance and limitations in diagnostic tests. According to CDC, there are three classes of antifungals available to treat *C. auris*. However, CDC has identified strains that are resistant to all three classes. A CDC official noted that getting new antifungals to market is challenging because, among other things, the demand for antifungals, relative to antibiotics, is low. Additionally, according to the Food and Drug Administration (FDA), although reliable tests for identifying *C. auris* exist, commonly used laboratory tests may misidentify this fungus, posing a barrier to correct diagnosis.

Source: GAO summary of CDC and FDA information. | GAO-23-106776

CDC is concerned about rising resistant infections in health care settings and in the community. For example, one type of bacteria, carbapenem-resistant Enterobacteriaceae—which CDC calls a “nightmare bacteria”—is resistant to nearly all available antibiotics and can survive in sink drains at health care facilities and spread to patients and to the environment through wastewater. According to CDC, these bacteria had spread to all 50 states by 2017. (See fig. 2.)

Figure 2: 2001-2017 Cumulative Spread of One Type of Highly Resistant Bacteria in the United States



Source: Centers for Disease Control and Prevention (CDC). | GAO-23-106776

Note: This figure tracks a type of carbapenem-resistant Enterobacteriaceae. Shading indicates CDC confirmed the presence of these bacteria within that state in that year or a previous one.

Recognizing the growing threat of antibiotic resistance, the President established via Executive Order the Task Force for Combating Antibiotic-Resistant Bacteria (CARB Task Force) in 2014, co-chaired by the Secretaries of the Departments of Health and Human Services, Defense,

Federal Efforts and Challenges Related to Surveillance of Antibiotic Resistance

and Agriculture.⁷ In 2015, the White House issued the *National Action Plan for Combating Antibiotic-Resistant Bacteria* (hereafter referred to as the National Action Plan), setting forth goals over 5 years to slow the development of resistant bacteria, strengthen national surveillance efforts, advance the development and use of diagnostic tests, and accelerate the development of new treatments, among other things.⁸ In 2020, the CARB Task Force issued an updated plan, the *National Action Plan for Combating Antibiotic-Resistant Bacteria, 2020-2025*.⁹

As we reported in March 2020, the precise magnitude of the problem of antibiotic resistance is unknown. While CDC had made progress in expanding surveillance of infections from certain antibiotic-resistant bacteria in the United States and abroad, the agency faced several general challenges in tracking and reporting trends in antibiotic resistance.¹⁰ For example, CDC faced challenges obtaining data on infections and testing to track antibiotic resistance across health care settings. CDC also faced challenges in reporting complete and timely information on the magnitude of and trends in antibiotic resistance.

As an example of the challenge of reporting complete information, CDC's primary surveillance system for antibiotic resistant gonorrhea—which CDC classified as an urgent antibiotic resistance threat affecting over half a million patients annually—represented only an estimated 1 to 2 percent of all reported U.S. cases and only in males. In March 2020, we reported

⁷Exec. Order No. 13676, *Combating Antibiotic-Resistant Bacteria*, 79 Fed. Reg. 56,931 (Sept. 23, 2014).

⁸The White House, *National Action Plan for Combating Antibiotic-Resistant Bacteria* (Washington, D.C.: March 2015).

The CARB Task Force was tasked with providing annual updates to the President on, among other things, plans for addressing any barriers to full implementation of the National Action Plan. Our March 2020 report included a recommendation that the CARB Task Force should include these plans in its annual updates and, as appropriate, make recommendations for new or modified actions. HHS concurred with this recommendation and has taken steps to implement it. See the [GAO website](#) for more information on this recommendation and its status.

⁹The Federal Task Force on Combating Antibiotic-Resistant Bacteria, *National Action Plan for Combating Antibiotic-Resistant Bacteria, 2020-2025* (October 2020).

¹⁰Public health surveillance is the ongoing, systematic collection, analysis, and interpretation of health-related data essential to planning, implementation, and evaluation of public health practice.

that CDC had not fully evaluated the representativeness of the gonorrhea surveillance system's results.

As a result of our findings, in our March 2020 report, we recommended that CDC ensure that its evaluation of its surveillance system for antibiotic-resistant gonorrhea includes measures of its representativeness, such as comparison of the trends in the sample population with those in the overall U.S. population, using specially designed studies if needed. CDC agreed with our recommendation and has begun taking steps to implement it. For example, in March 2023, HHS stated CDC was developing methods to implement molecular surveillance of gonorrhea in additional populations that will allow them to assess the representativeness of its surveillance efforts for antibiotic-resistant gonorrhea. Once CDC has evaluated its surveillance system, we will assess whether CDC has fully implemented this recommendation.

In addition, our report included three other recommendations to address CDC efforts regarding (1) surveillance related to antibiotic resistance infection reporting from hospitals, (2) information on uncertainties around estimates of resistant infections, and (3) timely, comprehensive reports on antibiotic resistance. CDC agreed with these recommendations and has taken some steps to implement the first by working with the Centers for Medicare & Medicaid Services (CMS) to require certain hospitals to report data on antibiotic resistant infections to CDC's national surveillance system. We will assess the effect of these new requirements once they take effect in 2024. CDC has not taken significant steps toward the other two recommendations. Doing so would improve the information that CDC reports on antibiotic resistance. See GAO's website for more information about these three recommendations and their status.¹¹ GAO will continue to monitor CDC's progress towards implementing them.

Federal Efforts and Challenges Related to Diagnostic Tests for Antibiotic Resistance

As we reported in March 2020, according to experts, tests for antibiotic resistance not only help clinicians decide what antibiotics to use, but they also provide important information for surveillance, including the number of cases of resistant infections in a population.

We also reported that federal agencies had taken steps to advance the development and use of diagnostic tests to identify antibiotic-resistant bacterial infections, but these efforts had limitations. For example, HHS agencies, including the National Institutes of Health, had funded some

¹¹<https://www.gao.gov/products/gao-20-341>.

studies to assess the extent to which testing patients to identify whether they have antibiotic-resistant infections leads to improved clinical outcomes, such as more effective treatment for patients or more judicious use of antibiotics. However, in 2020, we reported that more such studies were needed, according to experts and agency officials. Without information to guide test usage, clinicians may not be able to select appropriate treatments for their patients.

In our March 2020 report, we reported that one reason for the insufficient number of studies is that HHS agencies that are in a position to conduct or fund such studies—such as CDC and the Biomedical Advanced Research and Development Authority—disagreed about what each agency’s role should be. By clarifying roles and responsibilities, HHS agencies could more effectively address the need for more studies. The resulting studies could help demonstrate the value of diagnostic tests for antibiotic resistance, potentially increasing their use and improving patient care.

We recommended in March 2020 that HHS identify leadership and clarify roles and responsibilities among HHS agencies to assess the clinical outcomes of diagnostic testing for identifying antibiotic-resistant bacteria. HHS agreed with this recommendation and has taken some steps to implement it. The CARB Task Force introduced an objective within the updated 2020-2025 National Action Plan to support research into appropriate use of diagnostic tests. While this plan identified agency responsibilities for this objective at a high level, it lacked specificity on actions each agency will take to meet the objective. To fully implement our recommendation, HHS needs to provide more specific details on how each agency will effectively support studies into diagnostic tests.

In addition, our March 2020 report included a recommendation to the Food and Drug Administration (FDA) to conduct additional monitoring and evaluation of authorized tests needing updates.¹² FDA agreed with our recommendation and has begun taking steps to implement it. These steps include encouraging test manufacturers to check the FDA website

¹²Because bacteria can develop increasing resistance to antibiotics, it is sometimes important to change a critical testing threshold, known as a breakpoint, used for determining whether or not bacteria are resistant to a given antibiotic. Using tests with out-of-date breakpoints could result in misidentifying a resistant infection as non-resistant, which can lead to treating a patient with an ineffective antibiotic and the further spread of the infection.

for information and guidance regarding test updates. See GAO's website for information about this recommendation and its status.¹³

Federal Efforts and Challenges Related to Development of Novel Antibiotics

Experts warn that the current pipeline of antibiotics in development is insufficient to meet the threat of resistance. For example, according to WHO, in 2021, only 46 antibiotics were in clinical development globally—meaning clinical trials were being conducted to test their safety and efficacy in humans—and only 28 of them targeted bacteria on WHO's priority list.¹⁴

In March 2020, we reported that several challenges impede the development of new treatments for antibiotic resistant infections. Most notable, according to experts, antibiotic developers, and federal officials we spoke with, is the inadequate return on investment for drug companies largely due to low prices and a limited patient population for whom these treatments would be appropriate. In our report, we noted that many large pharmaceutical companies had discontinued their antibiotic development in recent years. According to The Pew Charitable Trusts and other published sources we reviewed, four large pharmaceutical companies worldwide had antibiotics in clinical development in 2018, compared to 1990, when 18 were involved in antibiotic research and development.¹⁵ Two antibiotic companies declared bankruptcy in 2019; in the case of one, the company filed for bankruptcy only 10 months after its antibiotic, which targets resistant bacteria, received FDA approval.

Multiple federal agencies have supported the development of new antibiotic treatments, including providing funding for antibiotic research and development. For example, HHS and Department of Defense agencies have provided premarket financial incentives to support antibiotic research and development. However, experts and antibiotic developers told us that premarket incentives alone are not sufficient to sustain antibiotic development. Two antibiotic developers we spoke with

¹³<https://www.gao.gov/products/gao-20-341>.

¹⁴World Health Organization, "Antimicrobial Resistance: Analysis of the Antibacterial Pipeline," accessed April 12, 2023, <https://www.who.int/observatories/global-observatory-on-health-research-and-development/analyses-and-syntheses/antimicrobial-resistance/analysis-of-the-antibacterial-pipeline>.

¹⁵The Pew Charitable Trusts, "Tracking the Global Pipeline of Antibiotics in Development," accessed November 29, 2019, <https://www.pewtrusts.org/en/research-and-analysis/issue-briefs/2019/03/tracking-the-global-pipeline-of-antibiotics-in-development>; and P. Sharma and A. Towse, Office of Health Economics, *New Drugs to Tackle Antimicrobial Resistance: Analysis of EU Policy Options* (London, United Kingdom: April 2011).

for our March 2020 report explained that while these types of incentives provided needed funding for conducting research and development, they will not help cover the costs to manufacture and market the product once it is approved.

As we reported in March 2020, experts, federal officials, and antibiotic developers agree that more postmarket incentives are needed to overcome the economic challenges to developing new antibiotics. Postmarket incentives offer financial benefit, either directly or indirectly, to developers of successful antibiotics after they reach the market. Advisory groups, including a presidential advisory council, and others have called for new postmarket incentives and identified multiple options for their design, including market entry rewards and reimbursement reform (see fig. 3).¹⁶ However, we reported that HHS had not developed a strategy to further incentivize development of new treatments for antibiotic-resistant infections, and it may need to request authority and appropriations to create and implement certain types of incentives.

Figure 3: Examples of Possible Postmarket Financial Incentive Options Identified by Advisory Groups and Others to Encourage the Development of Antibiotics

Market entry reward		Reimbursement reform	
A market entry reward could be awarded in addition to, or in replacement of, sales revenues			
Lump sum payment	Transferable voucher	Licensing arrangement	Add-on payment
• Monetary reward paid to developers of new antibiotics • Could be paid over multiple years	• Voucher that could be sold or auctioned and would confer additional market exclusivity for a different pharmaceutical drug	• Antibiotic purchasing arrangement in which hospitals would pay a fixed fee to access the drug, which would allow them to use a certain number of doses	• Payments to hospitals for use of certain antibiotics that are made in addition to the bundled payment the hospital already receives for a patient's inpatient stay

Source: GAO summary of publicly available proposals. | GAO-23-106776

We recommended in March 2020 that HHS develop a strategic framework to further incentivize the development of new treatments for antibiotic-resistant infections, including through the use of postmarket

¹⁶Market entry rewards can take the form of lump sum payments or transferable vouchers that could be sold to confer additional market exclusivity to other pharmaceutical drugs. Reimbursement reform could involve licensing arrangements or add-on payments for hospital-administered antibiotics.

financial incentives, and, if appropriate, make recommendations to Congress for necessary authority. Although HHS did not concur with our recommendation in 2020, it has nevertheless taken some steps to address it. In May 2022, HHS officials told us they had conducted an analysis of issues relating to the need to address the limited pipeline for antibacterial products, and that based on this analysis, HHS had developed a draft strategic framework that is under consideration by HHS leadership. HHS officials also said they relied on this analysis to develop a legislative proposal that could create a novel payment mechanism to stimulate future innovation. As of March 2023, HHS had not shared a copy of the strategic framework or the proposal with us; once HHS does so, we will review it to determine whether our recommendation has been implemented.

Federal Efforts and Challenges Related to Appropriate Use of Antibiotics

As we reported in March 2020, federal agencies have taken steps to promote the appropriate use of antibiotics across health care settings through what is known as antibiotic stewardship—giving patients the right antibiotic at the right time, in the right dose, and for the right duration. For example, CMS has required certain types of health care facilities—hospitals and nursing homes—to implement antibiotic stewardship programs and has developed incentives for clinicians to improve antibiotic use and stewardship programs.

However, we reported in 2020 that CDC is limited in its ability to monitor and improve appropriate antibiotic use, in part because of limited data on the extent of antibiotic use. CDC and experts said that more antibiotic use data would enable health care providers, federal agencies, and others to identify and target areas for improvement, track results over time, and adjust antibiotic stewardship activities as needed. In 2022, CMS finalized a rule stating that, beginning in 2024, certain hospitals must report antibiotic use and resistance data to a web-based surveillance system in order to meet certain program requirements.¹⁷ While the requirement may provide CDC with additional data, it has not yet taken effect, making it too early to determine the impact of this requirement on CDC's ability to assess antibiotic use.

In conclusion, antibiotic resistance poses a threat to public health, both globally and here in the United States. An adequate response will require

¹⁷In calendar year 2024, the Centers for Medicare & Medicaid Services will begin requiring hospitals participating in the Medicare Promoting Interoperability Program to report an antimicrobial use and resistance measure to CDC's National Healthcare Safety Network. See 87 Fed. Reg. 48,780, 49,335 (Aug. 10, 2022).

action on many fronts—ensuring surveillance and testing are in place to identify the threat, reducing the overuse and misuse of antibiotics, and ensuring a sufficient pipeline of new treatments. The federal government has an important role in driving this response. While it has taken many actions and made progress toward addressing many of our March 2020 recommendations, much work remains. Continued attention to this issue will be critical to ensuring that we are able to slow the development of antibiotic resistance and maintain an effective array of lifesaving drugs.

Chair Griffith, Ranking Member Castor, and Members of the Subcommittee, this concludes our statement. We would be pleased to respond to any questions you may have.

GAO Contacts and Staff Acknowledgments

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