ANTIMICROBIAL RESISTANCE: EXAMINING AN EMERGING PUBLIC HEALTH THREAT

HEARING

BEFORE THE

SUBCOMMITTEE ON OVERSIGHT AND INVESTIGATIONS

OF THE

COMMITTEE ON ENERGY AND COMMERCE

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C O N T E N T S

ANTIMICROBIAL RESISTANCE: EXAMINING AN EMERGING PUBLIC HEALTH THREAT

FRIDAY, APRIL 28, 2023

HOUSE OF REPRESENTATIVES,
SUBCOMMITTEE ON OVERSIGHT AND INVESTIGATIONS,
COMMITTEE ON ENERGY AND COMMERCE,
Washington, DC.

The subcommittee met, pursuant to call, at 9:00 a.m. in the John D. Dingell Room 2123, Rayburn House Office Building, Hon. H. Morgan Griffith (chairman of the subcommittee) presiding.

Members present: Representatives Griffith, Burgess, Guthrie, Palmer, Lesko, Armstrong, Cammack, Rodgers (ex officio), Castor (subcommittee ranking member), Schakowsky, Tonko, Ruiz, and Pallone (ex officio).

Also present: Representative Carter.

Staff present: Kate Arey, Digital Director; Sean Brebbia, Chief Counsel, Oversight and Investigations; Lauren Eriksen, Clerk, Oversight and Investigations; Tara Hupman, Chief Counsel; Peter Kielty, General Counsel; Emily King, Member Services Director; Chris Krepich, Press Secretary; Karli Plucker, Director of Operations (shared staff); Gavin Proffitt, Professional Staff Member, Oversight and Investigations; John Strom, Counsel, Oversight and Investigations; Joanne Thomas, Counsel, Oversight and Investigations; Dray Thorne, Director of Information Technology; Austin Flack, Minority Junior Professional Staff Member; Waverly Gordon, Minority Deputy Staff Director and General Counsel; Tiffany Guarascio, Minority Staff Director; Liz Johns, Minority GAO Detailee; Will McAuliffe, Minority Chief Counsel, Oversight and Investigations; Christina Parisi, Minority Professional Staff Member; Harry Samuels, Minority Oversight Counsel; and Caroline Wood, Minority Research Analyst.

Mr. GRIFFITH. The Subcommittee on Oversight and Investigations will now come to order.

Housekeeping detail first. We expect votes to be called at 10:00. In an attempt to accommodate everybody's schedule, what we are going to do is we are going to have rolling votes. It is a single vote, so people can leave and then come back. But we will continue the questioning so that we can move this process along without folks having to have a half-an-hour or 45-minute break in the process.

All right. That being said, I now recognize myself for a 5-minute opening statement.

OPENING STATEMENT OF HON. H. MORGAN GRIFFITH, A REPRESENTATIVE IN CONGRESS FROM THE COMMONWEALTH OF VIRGINIA

Welcome to what I hope will be a productive fact-finding hearing on a subject I have long been interested in: antimicrobial resistance, or AMR.

We heard in yesterday's hearing that the risk of a pathogen escaping from a lab and causing a pandemic is very real. Just as real is the threat posed by an antimicrobial-resistant pathogens.

Prior to the discovery of penicillin, significant research was being done on bacteriophage, or phage therapy. Phage therapy is where we search for a virus to attack harmful bacteria. Ever since the discovery of penicillin, antibiotics have been developed to treat previously untreatable infections. And they truly are lifesavers. But unfortunately, as the development of antibiotics took off, attention to phage therapy fell to the wayside.

Recently, the CDC and NIH are studying and doing more research into phage therapy, but more is needed. The problem is, over time, pathogens become resistant to the commonly used classes of antibiotics. Accordingly, if a new way to kill the pathogen is not found, the patient is defenseless to the disease caused by the pathogens. As it stands right now, antibiotic-resistant infections can be extremely difficult to treat. AMR is often referred to as the silent pandemic and has become one of the biggest medical concerns today.

The pipeline for AMR drugs has slowly been drying up due to various reasons that deserve our attention and which we hope to highlight today. Despite the increased demand, there has been a significant reduction in investment and development of new antimicrobials. According to data, since 1990, 78 percent of major drug companies have cut or scaled back antibiotic research due to developmental challenges.

According to the Centers for Disease Control and Prevention, at least 2.8 million people—that is right, 2.8 million people—are infected with antibiotic-resistant bacteria in the United States each year, and more than 35,000 people will die as a result of such infection.

The rise of drug-resistant infections places a heavy burden on our Nation's healthcare system. The CDC suggests that approximately 30 percent of all antibiotics prescribed in the U.S. are for infections that do not necessarily require antibiotics, which amounts to about 47 million antibiotic courses prescribed in these settings each year. That said, often what happens is individual doctors, faced with perplexing symptoms while trying to save their patients, will understandably turn to antibiotics.

AMR is not just an issue that arises in a hospital or a healthcare setting. Antibiotic usage in humans and animals all have the possibility of developing antimicrobials with expanding resistance. And it is a problem that sometimes we don't understand everything that nature is doing.

I have recently met with a veterinarian and a professor from Virginia Tech, which is in my district, about her work in southern Africa. While there she came across abandoned mongoose who had an antimicrobial resistant to antibiotics that she had never seen be-

fore. This shows that the antibiotic antimicrobial resistance can appear anywhere and everywhere.

I look forward to hearing from our witnesses about potential innovative solutions like phage therapy. I expect we will also hear today from the GAO about deficiencies at the Department of Health and Human Services, the agency with the most responsibility for tackling the AMR problem.

One issue that I hope we can shine a light on and bring more oversight into is the number of Federal programs and initiatives the Government currently has to address antimicrobial resistance. While I am pleased to see we are addressing this silent pandemic, it is Congress' duty to provide oversight into how dollars are being spent. Have the various programs found any success yet? And which of these programs are duplicative?

As we consider potential solutions to confront these antimicrobials, we must consider the work that is already being done and the dollars already being spent to combat this crisis and look for ways that will yield more successful outcomes fighting these superbugs. While there is no easy solution to the problem of AMR, we are committed to exploring potential solutions to address this public health crisis.

I want to emphasize and be clear that this hearing is not about taking a position on any legislation introduced. But rather, as this committee usually does, it is to gather information and to find out the facts. Our goal today is to examine the AMR problem, assess the role of the Federal Government, and explore potential solutions. I look forward to hearing and learning from our great witnesses who are here with us today.

[The prepared statement of Mr. Griffith follows:]

Chair H. Morgan Griffith
House Energy and Commerce Committee
Oversight & Investigations Hearing
"Antimicrobial Resistance: Examining an Emerging Public Health Threat."
April 28, 2023

Welcome everyone to what I hope will be a productive, fact-finding hearing on a subject I have long been interested in – Antimicrobial Resistance, or AMR.

We heard in yesterday's hearing that the risk of a pathogen escaping from a lab and causing a pandemic is very real. Just as real is the threat posed by antimicrobial resistant pathogens.

Ever since the discovery of penicillin, antibiotics have been developed to treat previously untreatable infections – and they truly are life savers.

The problem is, over time, the pathogens become resistant to the antibiotics, and if a new way to kill the pathogen is not found, the patient will succumb to the pathogen.

As it stands right now, antibiotic resistance infections can be impossible to treat.

Despite the increased demand, there has been a significant reduction in investment and development of new antimicrobials. According to data, since 1990, 78% of major drug companies

have cut or scaled back antibiotic research due to development challenges.[1]

According to the Centers for Disease Control and Prevention, at least 2.8 million people are infected with antibiotic-resistant bacteria in the United States each year, and more than 35,000 people die as a result.[2]

The rise of drug-resistant infections places a heavy burden on our nation's health care system. The CDC suggests that approximately 30% of all antibiotics prescribed in the US are for infections that do not require antibiotics, which amounts to about 47 million antibiotic courses prescribed in these settings each year.[3]

I am curious to hear from our witnesses about potential solutions, including innovative solutions like phage therapy.

I expect we will also hear today from the GAO about deficiencies at Health and Human Services, the agency with the most responsibility for tackling the AMR problem than any other agency.

While there is no silver bullet solution to the problem of AMR, we are committed to exploring potential solutions to address this

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[1] Mary Palmer et al, *The importance of pharmacokinetics and pharmacodynamics in antimicrobial drug development and their influence on the success of agents developed to combat resistant gram negative pathogens: A review*, Frontiers in Pharmovology (Jul. 25, 2022) available from Nat'I Institutes of Health, National Library of Medicine, https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9359604/

[2] Center for Disease Prevention and Control, *About Antimicrobial Resistance*, (Oct. 5, 2022) https://www.cdc.gov/drugresistance/about.html

[3] Center for Disease Prevention and Control, *Antimicrobial Resistance Questions and Answers*, (Nov. 15, 2022) https://www.cdc.gov/antibiotic-use/community/about/antibiotic-resistance-faqs.html#two

public health crisis. I want to emphasize that this hearing is not about taking a position on any legislation introduced, but rather to gather information and fact-find.

Our goal is to examine the AMR problem, assess the role of the federal government, and explore potential solutions.

I look forward to hearing and learning from our witnesses today.

Mr. GRIFFITH. With that, I yield back and now recognize Ms. Castor, the ranking member of the subcommittee, for her 5 minutes for an opening statement.

OPENING STATEMENT OF HON. KATHY CASTOR, A REPRESENTATIVE IN CONGRESS FROM THE STATE OF FLORIDA

Ms. CASTOR. Well, good morning, and thank you, Mr. Chairman, for holding this important hearing on the urgent public health issue of antimicrobial resistance.

If we have learned anything from the COVID–19 pandemic, it is that we must dedicate sufficient resources to prepare for the public health threats that we know of, while also working to prepare for the new and emerging threats. CDC's 2019 Threat Assessment Report identified 18 bacteria and fungi that are showing evidence of resistance to currently available treatments, and that trend is expected to rise.

The U.S. Government has been aware of this threat for some time and has taken steps to address it. In 2015, for example, President Obama, the Federal Government—in accordance with an Executive order issued by President Obama, the Federal Government released a National Action Plan for combating antibiotic-resistant bacteria that outlined the framework for the Federal response to this growing health threat.

While we have made some strides in preventing and treating antibiotic resistance, there is ground to regain as we emerge from 3 years of a pandemic that put unprecedented strains on the entire healthcare system and rolled back some of that progress. The effort to combat antibiotic resistance requires a strong, coordinated response involving both private- and public-sector stakeholders to advance new technologies, effectively collect data on incidents of antibiotic-resistant infections, and make resources available for hospitals and providers to practice sound antibiotic stewardship. We have got to foster scientific research on new treatments and therapies and implement prevention measures.

At yesterday's hearing, some Republicans on the subcommittee expressed real skepticism about the value of pandemic research. Today we are hearing all about the importance of addressing antimicrobial resistance, which will require a strong, supported medical and scientific workforce. While the tones of these back-to-back hearings are certainly intentioned, I hope we can come out of them with a better appreciation for the work of our scientific community.

Let me make an obvious but important point here. While there are many fronts on which to have—we—on which we have to fight these serious threats, we make no progress without consistent investment in scientific research. If the Republicans proceed with appropriations in accordance with the Default on America Act that they passed this week, scientific research will suffer greatly.

We need scientists to study these threats to help us prepare against them, and they should be able to do so free of political interference designed to malign or ban certain types of public health research. Our important oversight responsibilities include pressing for improvements across the scientific and research enterprise, and in doing so to build trust and confidence in the agencies that are at the forefront of a national response, like the CDC and the NIH.

I am pleased that the GAO is testifying today on its thorough report that was coincidentally completed right at the start of the COVID–19 pandemic. It is an excellent resource to build from as we enter pandemic recovery and turn our attention to the broader array of public health threats—hopefully, with a new appreciation for the importance of preparedness.

I would also like to thank our other witnesses for being here to share your expertise on the several different angles of this complex issue. Antimicrobial resistance is a problem for patients, for healthcare professionals, and researchers across the healthcare system. And it is also important to emphasize that there are environmental and agricultural aspects contributing to the rise in resistance that we have to address, as well.

A multipronged issue requires a multiprong solution, so I look forward to the discussion today and coming out of this hearing with a deeper understanding of the nature and scope of the threat of antimicrobial resistance so we can make more informed policy decisions to help combat it.

[The prepared statement of Ms. Castor follows:]

Committee on Energy and Commerce

Opening Statement as Prepared for Delivery
of
Subcommittee on Oversight and Investigations Ranking Member Kathy Castor

Hearing on "Antimicrobial Resistance: Taking on the Next Emerging Public Health Threat"

April 28, 2023

Thank you, Mr. Chairman, for holding this hearing on the urgent public health issue of antimicrobial resistance.

If we have learned any lesson from the COVID-19 pandemic, it is that we must dedicate sufficient resources to prepare for the public health threats we are aware of while also working to prepare for new and emerging health threats.

CDC's 2019 Threat Assessment Report identified 18 bacteria and fungi that are showing evidence of resistance to currently available treatments, and that trend is expected to rise.

Our government has been aware of this threat for some time, and has taken steps to address it. In 2015, for example, in accordance with an executive order issued by President Obama, the federal government released a National Action Plan for Combating Antibiotic-Resistant Bacteria that outlined the framework for the federal response to this growing health threat.

While we've made some strides in preventing and treating antibiotic resistance, there is ground to regain as we emerge from three years of a pandemic that put unprecedented strains on the entire health care system and rolled back some of that progress.

The effort to combat antibiotic resistance requires a strong coordinated response involving both private and public sector stakeholders to advance new technologies, effectively collect data on incidents of antibiotic resistant infections, make resources available for hospitals and providers to practice sound antibiotic stewardship, foster scientific research on new treatments and therapies, and implement prevention measures.

At yesterday's hearing, some of the Republicans on this subcommittee expressed real skepticism about the value of pandemic research. Today, we are hearing all about the importance of addressing antimicrobial resistance, which will require a strong, supported medical and scientific workforce. While the tones of these back-to-back hearings are certainly in tension, I hope we come out of them with a better appreciation for the work of our scientific community.

Let me make an obvious but important point here—while there are many fronts on which we have to fight these very serious threats, we make no progress without consistent investment in scientific research.

That was just as true yesterday as it is today, although that may be news to some of my colleagues.

We need scientists to study these threats to help us prepare against them, and they should be able to do so free of political interference designed to malign or ban certain types of public health research.

Our job is to maintain support for and trust in the agencies that are at the forefront of a national response, like the CDC and NIH.

I'm pleased that the GAO is testifying today on its thorough report that was coincidentally completed right at the start of the COVID-19 pandemic. It is an excellent resource to build from as we enter pandemic recovery and turn our attention to a broader array of public health threats – hopefully with a new appreciation for the importance of preparedness.

I'd also like to thank our other witnesses for being here to share their expertise from several different angles of this complex issue.

Antimicrobial resistance is a problem facing heath care professionals and researchers across the health care system. But it's also important to emphasize that there are environmental and agricultural aspects contributing to the rise in resistance that we have to address as well. A multi-pronged issue calls for a multi-pronged solution.

I look forward to the discussion today and coming out of this hearing with a deeper understanding of the nature and scope of the threat posed by antimicrobial resistance so we make more informed policy to help combat it.

Thank you again, Mr. Chairman, for holding this important hearing. I yield back.

Ms. CASTOR. Thank you again, Mr. Chairman, for holding this important hearing, and I yield back.

Mr. GRIFFITH. I thank the gentlelady for yielding back. I now recognize the Chair of the full committee, Mrs. McMorris Rodgers, for her 5-minute opening statement.

OPENING STATEMENT OF HON. CATHY MCMORRIS RODGERS, A REPRESENTATIVE IN CONGRESS FROM THE STATE OF WASHINGTON

Mrs. RODGERS. Thank you, Chair Griffith, for convening this hearing about the growing threat of antimicrobial resistance, or AMR, facing our Nation and, indeed, the world. And thank you to our panel of witnesses here today.

More than 2.8 million antibiotic-resistant infections occur in the United States each year, resulting in more than 35,000 deaths. In 2019 an estimated 1.3 million deaths globally were a direct result of drug resistance. AMR is a very real threat.

In recent days we have had eyedrop recalls due to contamination by an extensively drug-resistant strain of bacteria that has led to multiple deaths and loss of vision among patients in 16 States. This outbreak strain has never been reported in the United States prior to this outbreak. And just this week, a hospital in downtown Seattle announced an outbreak of antibiotic-resistant bacteria often found in healthcare settings which infected 31 people, 4 of whom have died.

This morning we seek to gain a better understanding of AMR, examine current efforts to address this ongoing public health threat, and explore innovative paths forward. Antibiotics are powerful, lifesaving drugs. Their discovery truly revolutionized modern medicine. In addition to their use to protect human lives, they are used in veterinarian care to treat animals and keep our food supply safe from harmful pathogens.

Globally and in the U.S., antimicrobials, particularly antifungals, are a relatively inexpensive way to control plant diseases and protect agricultural crops. Over time, however, through natural adaptation and use, microbes can develop into superbugs, making drugs ineffective against them. AMR is a complex web that can develop and spread through a variety of settings, including healthcare facilities, food production, the community, and the environment.

There is a need to learn more about AMR, its underlying causes, and innovative solutions to address this threat. We also must examine and understand the already existing efforts and initiatives underway, and assess how these programs are operating, including any successes and shortcomings.

In 2016, Congress appropriated an unprecedented 160 million of new investments for CDC to fight AMR. By fiscal year 2022, this appropriation had increased to more than 182 million. We are working to understand how this funding has been used, what initiatives CDC is undertaking, and how effective they have been.

In addition to CDC funding, there are a countless number of HHS interagency efforts focused on AMR, including the creation of numerous Federal task force and committees such as the Presidential Advisory Council on Combating Antibiotic Resistant Bacteria and the Combating Antibiotic Resistance Bacteria Task Force,

as well as an array of national plans, strategies, directives, data bases, and monitoring systems, guidance documents, toolkits, and guides.

And these efforts are not restricted to HHS. According to the Congressional Research Service, the USDA, DoD, State Department, EPA, USAID, VA, and Interior each have their own individual existing initiatives and programs. Several subagencies within these agencies also have separate programs. HHS has at least eight subagencies with individual initiatives.

The fact that AMR continues to be a growing threat and a health burden despite this heavy investment of resources is alarming. And I am hopeful our witnesses here today will be able to provide greater insight into why this is the case and how we can improve our ongoing efforts to address this problem.

Thank you to the Ranking Member Pallone, my colleagues across the aisle. Thank you to the chairman and the ranking member for working together on this. I look forward to today's hearing as we continue to explore the increasing burden and threat of AMR facing our Nation and world.

[The prepared statement of Mrs. Rodgers follows:]

Chair Cathy McMorris Rodgers
House Energy and Commerce Committee
Oversight & Investigations Hearing
"Antimicrobial Resistance: Examining an Emerging Public Health Threat"
April 28, 2023

Thank you, Chair Griffith, for convening this hearing about the growing threat of antimicrobial resistance, or AMR, facing our nation, and indeed, the world.

Thank you to our panel of witnesses here today.

More than 2.8 million antibiotic-resistant infections occur in the U.S. each year, resulting in more than 35,000 deaths. In 2019, an estimated 1.27 million deaths globally were a direct result of drug resistance.

AMR is a very real threat. In recent days, we've had eye drop recalls due to contamination by an extensively drug-resistant strain of bacteria that has led to multiple deaths and loss of vision among patients in 16 states.

This outbreak strain has never been reported in the United States prior to this outbreak.

And just this week, a hospital in downtown Seattle announced an outbreak of antibiotic-resistant bacteria often found in health care settings, which infected 31 people, 4 of whom have died.

This morning, we seek to gain a better understanding of AMR, examine current efforts to address this ongoing public health threat, and explore innovative paths forward.

Antibiotics, are powerful, life-saving drugs. Their discovery truly revolutionized modern medicine.

In addition to their use to protect human lives, they are used in veterinary care to treat illnesses in animals and keep our food supply safe from harmful pathogens.

Globally and in the U.S., antimicrobials, particularly antifungals, are a relatively inexpensive way to control plant diseases and protect agricultural crops.

Over time, however, through natural adaptation and use, microbes can develop into "super bugs," making drugs ineffective against them.

AMR is a complex web that can develop and spread through a variety of settings including health care facilities, food production, the community, and the environment.

There is a need to learn more about AMR, its underlying causes, and innovative solutions to address this threat.

We also must examine and understand the already existing efforts and initiatives underway … and assess how these programs are operating, including any successes and shortcomings.

In 2016, Congress appropriated an unprecedented $160 million of new investments for CDC to fight AMR. By fiscal year 2022, this appropriation has increased to more than $182 million.

We are working to understand how this funding has been used, what initiatives CDC is undertaking, and how effective they have been.

In addition to CDC funding, there are a countless number of HHS interagency efforts focused on AMR, including the creation of numerous federal taskforces and committees, such as the Presidential Advisory Council on Combating Antibiotic-Resistant Bacteria and the Combating Antibiotic-Resistant Bacteria Taskforce, as well as an array of national plans, strategies, directives, databases and monitoring systems, guidance documents, toolkits, and guides …

And these efforts are not restricted to HHS. By my count, the USDA, DOD, State Department, EPA, USAID, VA, and Interior each have their own individual currently existing initiatives and programs. Several subagencies within these agencies also have separate programs. HHS has at least 8 subagencies with individual initiatives

The fact that AMR continues to be a growing health burden despite such heavy investment of resources is alarming. I am hopeful our witnesses here today will be able to provide greater insight into why this is the case and how we can improve our ongoing efforts to address this problem.

CONCLUSION

Thank you, Ranking Member Pallone and my colleagues across the aisle, for continuing to work with us.

I look forward to today's hearing as we continue to explore the increasing burden and threat of AMR facing our nation and world.

Thank you, I yield back.

Mrs. RODGERS. Thank you. I yield back.

Mr. GRIFFITH. I thank the gentlelady for yielding back. I now recognize Mr. Pallone, the ranking member of the full committee, for his 5-minute opening statement.

OPENING STATEMENT OF HON. FRANK PALLONE, JR., A REPRESENTATIVE IN CONGRESS FROM THE STATE OF NEW JERSEY

Mr. PALLONE. Thank you, Mr. Chairman, and thank you to our witnesses for helping us better understand the serious threat that antimicrobial resistance poses to public health.

Antimicrobial resistance is not a new phenomenon. It has been vexing scientists and Congress for years. However, it has been increasing across the board and poses major health risks to the public. According to the Centers for Disease Control and Prevention, more than 2.8 Americans had an antimicrobial-resistant infection in 2019 and more than 35,000 Americans died from the infection, and these numbers are expected to grow as more and more dangerous organisms develop a resistance to the treatments available today. And that is a deeply concerning risk to our public health.

There does not seem to be one obvious solution to this issue. It cuts across the board from how we identify new drug-resistant threats to how we administer available drugs while also fostering the development of new treatments. Physicians face a challenging balance between withholding certain antibiotics from patients in order to avoid unintentionally promoting more resistant strains of bacteria and providing their patients with the best treatment available.

In terms of developing new treatments, normal market forces do not always encourage the development of new drugs in this space. We want antibiotics to be developed that are more powerful for those that really need them, but we want to use them as little as possible. And this is a challenge that is repeatedly addressed in our witnesses' testimony, and I look forward to all of your perspectives on how we might navigate this dilemma.

To address these challenges, we must continue to support our health agencies and public health infrastructure. Our health agencies in particular will play a central role in identifying and addressing antimicrobial resistance. The CDC will increasingly be responsible for identifying and monitoring new threats resulting from antimicrobial resistance.

The Food and Drug Administration plays a role in reviewing and approving new diagnostic and pharmaceutical tools to stay ahead of the threat.

And the National Institutes of Health will need to continue to support good research into the risks that are posed and how we combat those risks.

We also need to ensure that our health and research workforce are strong enough to address these challenges. From physicians and nurses to microbiologists, the whole spectrum of the health workforce has a role to play here, and we need to make sure that our health centers and research labs are equipped.

While the threat of antimicrobial resistance is increasingly on the radar for the general public, it presents a constant threat for

some individuals with certain health conditions, such as cystic fibrosis, who—they rely on antibiotics to prevent and treat ongoing risks of infection. And the patients know all too well the serious threat that antibiotic resistance bacteria can pose to your health if you have cystic fibrosis.

So the public health challenges posed by antimicrobial resistance are serious, and they are growing. I thank the chairman for holding this hearing and look forward to the discussion with our witnesses this morning.

[The prepared statement of Mr. Pallone follows:]

Committee on Energy and Commerce

Opening Statement as Prepared for Delivery
of
Ranking Member Frank Pallone, Jr.

Hearing on "Antimicrobial Resistance: Taking on the Next Emerging Public Health Threat"

April 28, 2023

Thank you, Mr. Chairman. And thank you to our witnesses for helping us better understand the serious threat that antimicrobial resistance, or AMR, poses to public health.

Antimicrobial resistance is not a new phenomenon –it's been vexing scientists and Congress for years. However, AMR has been increasing across the board, and poses major health risks to the public. According to the Centers for Disease Control and Prevention (CDC), more than 2.8 million Americans had an antimicrobial-resistant infection in 2019 and more than 35,000 Americans died from the infection. These numbers are expected to grow as more and more dangerous organisms develop resistance to the treatments available today. That is a deeply concerning risk to our public health.

There does not seem to be one obvious solution to this issue. It cuts across the board from how we identify new drug-resistant threats, to how we administer available drugs while also fostering the development of new treatments.

Physicians face a challenging balance between withholding certain antibiotics from patients in order to avoid unintentionally promoting more resistant strains of bacteria and providing their patients with the best treatment available.

In terms of developing new treatments, normal market forces do not always encourage the development of new drugs in this space. We want antibiotics to be developed that are more powerful for those that really need them, but we want to use them as little as possible. This is a challenge that is repeatedly addressed in our witnesses' testimony, and I look forward to all of your perspectives on how we might navigate this dilemma.

To address these challenges, we must continue to support our health agencies and public health infrastructure. Our health agencies in particular will play a central role in identifying and addressing AMR.

The CDC will increasingly be responsible for identifying and monitoring new threats resulting from AMR. The Food and Drug Administration plays a role in reviewing and approving new diagnostic and pharmaceutical tools to stay ahead of the threat. And the National Institutes of Health will need to continue to support good research into the risks that AMR poses and how we can combat those risks.

We also need to ensure that our health and research workforce is strong enough to address these challenges. From physicians and nurses, to microbiologists, the whole spectrum of the health workforce has a role to play here, and we need to make sure that our health centers and research labs are equipped.

While the threat of AMR is increasingly on the radar for the general public, it presents a constant threat for some individuals with certain health conditions, such as cystic fibrosis, who rely on antibiotics to prevent and treat ongoing risk of infection. These patients know all too well the serious threat that antibiotic resistant bacteria can pose to our health.

The public health challenges posed by AMR are serious and they are growing. I thank the Chairman for holding this hearing and look forward to the discussion with our witnesses today.

Mr. PALLONE. Thank you again, and I yield back, Mr. Chairman.

Mr. GRIFFITH. I thank you for yielding back. And that concludes Members' opening statements.

I would remind all Members that, pursuant to the committee rules, the Members' opening statements will be made a part of the record.

I want to thank our witnesses for being here today and taking the time to testify before our subcommittee.

Each witness will have the opportunity to give an opening statement, followed by a round of questions from Members.

Our witnesses today are Mary Denigan-Macauley, Director of Health Care, U.S. Government Accountability Office; Kevin Outterson, professor of law and executive director of CARB–X, Boston University; Amanda Jezek—I hope I said that right—senior vice president, Infectious Disease Society of America; Amy Mathers, associate professor of medicine and pathology, University of Virginia School of Medicine.

We appreciate all of you being here today, and I look forward to hearing from you on this important issue.

You all are aware that the committee is holding this oversight hearing, and when we hold oversight hearings we have the practice of taking testimony under oath. Do any of you have an objection to testifying under oath?

Seeing no objections, we will proceed.

You are also advised that you have the right to have counsel present, should you wish to do so pursuant to House rules. Do any of you desire to be advised by counsel during your testimony today?

Seeing that none require, would you all please rise and raise your right hand?

[Witnesses sworn.]

Mr. GRIFFITH. Seeing all witnesses answered in the affirmative, you are now sworn in and under oath, subject to penalties set forth in title 18, section 1001 of the United States Code.

You may be seated. With that we will now recognize Mary Denigan-Macauley for her 5-minute opening statement.

STATEMENTS OF MARY DENIGAN-MACAULEY, PH.D., DIRECTOR, HEALTH CARE, GOVERNMENT ACCOUNTABILITY OFFICE; KEVIN OUTTERSON, AUSTIN B. FLETCHER PROFESSOR, BOSTON UNIVERSITY SCHOOL OF LAW, AND EXECUTIVE DIRECTOR, CARB-X; AMANDA JEZEK, SENIOR VICE PRESIDENT, PUBLIC POLICY AND GOVERNMENT RELATIONS, INFECTIOUS DISEASES SOCIETY OF AMERICA; AND AMY J. MATHERS, M.D., ASSOCIATE DIRECTOR OF CLINICAL MICROBIOLOGY AND ASSOCIATE PROFESSOR OF MEDICINE AND PATHOLOGY, UNIVERSITY OF VIRGINIA SCHOOL OF MEDICINE

STATEMENT OF MARY DENIGAN-MACAULEY, Ph.D.

Dr. DENIGAN-MACAULEY. Thank you very much. Chairs Griffith, Rodgers, and Ranking Members Castor and Pallone, and members of the subcommittee, thank you for the opportunity to discuss GAO's work on antibiotic resistance.

As we address the COVID–19 pandemic, another pandemic has been quietly brewing. Not one from a single disease, but rather one of resistance. Since the discovery of penicillin less than 100 years ago, many lifesaving antibiotics have been developed and become essential to the practice of modern medicine. However, the rising prevalence of antibiotic resistance threatens these gains.

Today, many of infections have become more difficult, if not impossible, to treat because of an increasing number of microbes that have developed resistance to most or, in some cases, all currently available antibiotics. According to the WHO, if nothing changes by 2050, 10 million people are expected to die from drug-resistant diseases—infections every year. Resistance can also complicate the response to a public health emergency, with secondary infections exasperating a crisis. The CDC and WHO consider antibiotic resistance to be one of the greatest public health threats of our time.

The solution to resistance is not simple. It is a complex issue involving the movement of not only bacteria, but fungi, viruses, and other microbes between humans, animals, and our environment. Today I will focus my statement on GAO's most recent work related to Federal efforts, human health, and antibiotics. While many Federal efforts are underway, I would like to focus on four key areas where we believe more can be done.

First, the precise magnitude of this problem is not known. While we have estimates that antimicrobial resistance has killed more than a million people worldwide and infected many more, the true extent of the problem is not known because data here in the U.S. and overseas is not complete or timely.

Second, there are limitations with tests for diagnosing antibiotic-resistant infection. Rapid and accurate diagnostic tests help doctors identify cases of resistant infections and help them to know which antibiotic to prescribe. However, more studies are needed to develop tests and demonstrate their benefits to encourage their use.

Further, because bacteria are always changing, their resistance to antibiotics also changes. Therefore, it is important to monitor tests and update them to ensure that they can accurately detect these resistant infections.

Third, according to experts, the pipeline of antibiotics in development is insufficient to tackle this growing threat, notably because of the inadequate return on investment for drug companies. This is concerning because we reported in 2020 that no new classes of antibiotics approved for human use had been approved since the mid-1980s, despite Government incentives. Experts believe there may be potential for other incentives, particularly those that would help newly developed drugs remain on the market to reduce costs and potentially save lives. Some experts also believe that nontraditional therapies such as phage are promising.

Finally, more is needed to monitor and promote the appropriate use of antibiotics. The WHO has warned that the world urgently needs to change the way antibiotics are prescribed and how they are used in order to preserve their effectiveness and help slow the development of resistance. However, Federal efforts to promote appropriate use are limited. For example, reporting on antibiotic use has, to date, only been required for VA and DoD healthcare facilities. Greater reporting and monitoring are critical, because behav-

ior can be challenging to change. For example, a doctor may feel pressured to prescribe antibiotics to satisfy a patient's demand, even when it is not warranted, such as for a viral respiratory infection which we know the antibiotic will not work.

As we emerge from COVID–19, while it is fresh on our minds and before a new crisis emerges, I wanted to share some parallels with antimicrobial resistance that may help us understand the importance of preparedness for a public health threat. For example, both are complex global issues exacerbated by supply disruptions and poor hygiene and a lack of medical countermeasures.

Better data and diagnostic tools are needed to understand the magnitude and monitor progress. Public-private partnerships, investments, and innovation drive solutions. Clear communication and education are key. And finally, action saves lives now and for our future generations.

Chairmans and ranking members, this concludes my prepared statement. I look forward to our discussion today on this important issue.

[The prepared statement of Dr. Denigan-Macauley follows:]

United States Government Accountability Office

Testimony

Before the Subcommittee on Oversight and Investigations, Committee on Energy and Commerce, House of Representatives

For Release on Delivery
Expected at 9:00 a.m. ET
Friday, April 28, 2023

ANTIBIOTIC RESISTANCE

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

Statement of Mary Denigan-Macauley, Director, Health Care, and Karen L. Howard, Acting Chief Scientist and Director, Science, Technology Assessment, and Analytics

GAO-23-106776

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-

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

[2]World 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.

[3]World 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

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

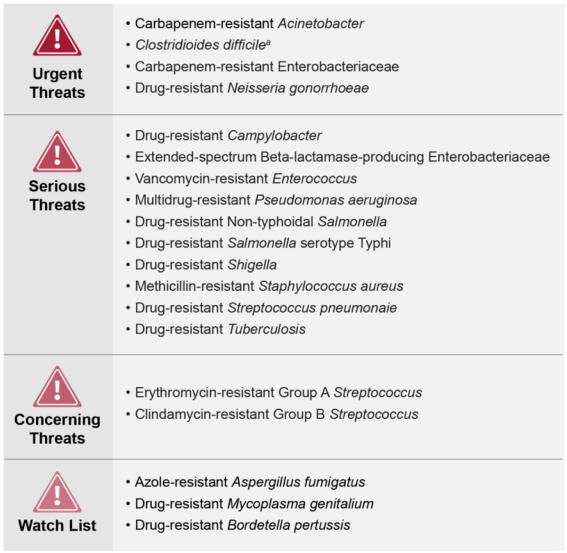
[5]GAO, *Antibiotic Resistance: Additional Federal Actions Needed to Better Determine Magnitude and Reduce Impact,* GAO-20-341 (Washington, D.C.: Mar. 30, 2020).

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



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

[6]CDC, *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**

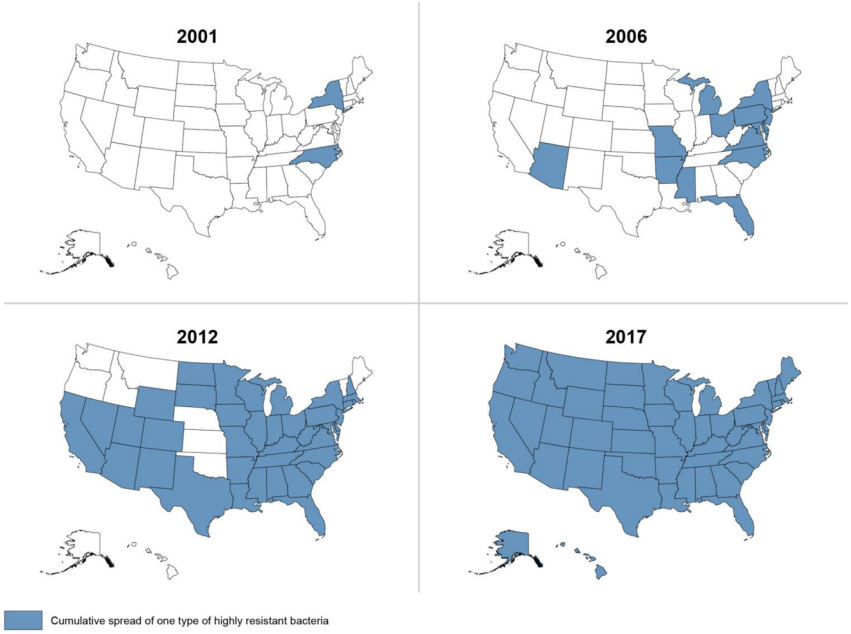
Candida auris (*C. auris*) is an emerging infectious fungus that, according to the Centers for Disease Control and Prevention (CDC), presents a global health threat in part because it is highly resistant to anti-fungal drugs and is challenging to address. In March 2023, CDC issued an alert regarding 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,

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]

Federal Efforts and Challenges Related to Surveillance of Antibiotic Resistance

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

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

[8]The 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.

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

[10]Public 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

[12]Because 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.

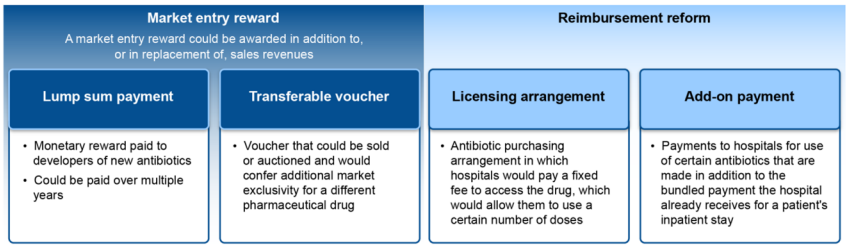
[14]World Health Organization, "Antimicrobial Resistance: Analysis of the Antibacterial Pipeline," accessed April 12, 2023, https://www.who.int/observatories/global-observatory-on-health-research-and-development/analyses-and-syntheses/antimicrobial-resistance/analysis-of-the-antibacterial-pipeline.

[15]The 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



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

[16]Market 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

[17]In 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

For further information about this statement, please contact Mary Denigan-Macauley at (202) 512-7114 or deniganmacauleym@gao.gov or Karen L. Howard at (202) 512-6888 or howardk@gao.gov. Contact points for our Offices of Congressional Relations and Public Affairs may be found on the last page of this testimony. In addition to the contacts named above, key contributors to this statement were William Hadley (Assistant Director), Kaitlin Farquharson, Hayden Huang, Amber Sinclair, Laura Tabellion, and Cathleen Whitmore. Additional support was provided by Emily Bippus, Xiaoyi Huang, Anne K. Johnson, and Ethiene Salgado-Rodriguez.

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Mr. GRIFFITH. Thank you so much.
Mr. Outterson, you are now recognized for your 5 minutes.

STATEMENT OF KEVIN OUTTERSON

Mr. OUTTERSON. To the Chairs Griffith and Rodgers, and to the Ranking Members Castor and Pallone, and the other members of this committee—subcommittee, good morning. I am Kevin Outterson, professor of law at Boston University. I am also the executive director of CARB–X, which is the global nonprofit accelerator for antibacterial innovation created under the U.S. National Action Plan by BARDA. I have spent most of my academic career in the topics we are discussing today, and thank you for the opportunity to speak with you at the hearing.

Americans rely on effective antibiotics and antifungals. Every hospital in your district, every cancer patient, every new mom that gets a C-section, and even people my age who are thinking about hip or knee replacement, all of us depend on antibacterials and antifungals in order to enable modern medicine. But resistance is eating away at this miracle just like rust eats away at a bridge.

Antibiotics are valuable, but this market is really broken. FDA approval should be a celebration, but for new antibiotics, the payday and the celebration never comes. Because of resistance, doctors are doing the right thing by being careful with the newest antibiotics. They put them on the shelf behind glass like a fire extinguisher.

And let me tell you, the fire extinguisher company gets paid at the moment that that fire extinguisher hangs on the wall. You get paid at the moment the preparedness starts, not when the fire starts. But for antibiotics, we are paying for them only after the fire starts. A new drug that isn't used much in the early years cannot make money. In the last decade, seven antibiotics have come to the market sponsored by small companies. Seven. All of those companies, 100 percent of them, have gone either bankrupt, or the economic equivalent of their R&D investors losing their shirts, even after approval from the FDA.

No wonder that every expert report agrees that the clinical pipeline of antibiotics is in terrible shape. There's a couple dozen antibiotics in the clinical pipeline being tested in humans, more than a thousand for cancer. Cancer drugs make money, so future cures are always moving towards the patient. Antibiotics lose money, with a predictable result in innovation.

Now is a great time to respond to this national security crisis. We must change the way we pay for antibiotics. After more than a decade of studying this problem, G7 governments, the wealthy governments of the world, are creating antibiotic pull incentives to reward innovation while allowing the antibiotic to be used carefully. If Congress creates a subscription program, Americans will get the new antibiotics we need. They will be sitting on the shelf, ready to go like that fire extinguisher, but the companies will also get what they need, which is not bankruptcy.

Antibiotic subscriptions should be carefully crafted to ensure that taxpayers get a good deal. They must focus only on the most promising new drugs. The required size of these antibiotic subscriptions is well understood, as well as the fair share that other wealthy

countries should pay. Subscription payments can start at an appropriate point and increase over time if stronger evidence is presented on the importance of the new drug.

Subscriptions will be remarkably good value for the U.S. taxpayer. The Centers for Global Development forecast a financial return on investment for Americans of six to one over a decade. From recent data that I published in the Nature journal, we know that a U.S. subscription would cost less than what we spend on patent antibiotics just a few years ago. This is affordable to do what we need to do, because we did it ourselves 5 to 10 years ago. It is time to invest in the future of antibiotics again.

By restoring some common sense to the market for antibiotics, subscriptions will bend the curve towards innovation. Globally, the health impact of a subscription program is remarkable: 9.9 million lives will be saved over the next 10—next 2 decades, an amazing legacy.

Now, I know all of this not just because of academic work or the work of other experts. I know it because, in a sense, I have seen the future. At CARB–X we see the most promising antibiotic candidates 10 to 15 years before potential FDA approval. Let me tell you, that future is bright so long as you continue to support push incentives like CARB–X and BARDA and complement them with a new pull incentive like the antibiotic subscription. And I know it is not a legislative hearing, but the example would be the PASTEUR Act.

At CARB–X, we mainly work with very small startup companies with highly innovative new products, including three phages, minidiagnostics, microbiome, vaccines, and many first-in-class products. A dozen of these CARB–X companies have initiated first-in-human testing, which is really the measure of our success. Push incentives like CARB–X are working, but these companies need a future other than bankruptcy. A program—a subscription program will finish the job.

Threats to bacteria and fungi are bad today and will be worse tomorrow. If you want a steady stream of lifesaving innovation, let's do something about it. And I think the path is clear.

Thank you for your time. I look forward to your questions.

[The prepared statement of Mr. Outterson follows:]

Written Testimony
Kevin Outterson, Austin B Fletcher Professor
Boston University School of Law
Executive Director, CARB-X[1]

The House Energy & Commerce Committee
Subcommittee on Oversight and Investigations
Friday April 28, 2023

Summary

- Bacterial and fungal infections are serious and growing health and fiscal threats.
- Unlike other drugs, antibiotics and antifungals lose their effectiveness when used, as microorganisms become resistant. Continuous innovation is needed, just to avoid falling behind.
- When new antibiotics receive FDA approval, they are mostly held in reserve, with low sales. As a result, $150 billion in on-patent revenues have been lost from the market since 2001. Larger companies have mostly ceased their own R&D programs, leaving most of the innovation in the hands of very small companies. One hundred percent of the small companies with an approved antibiotic in the past decade have suffered economically, despite the success of FDA approval.
- Push incentives like CARB-X have successfully advanced new products but pull incentives like subscriptions are now needed. The combination will sustainably restore antibacterial innovation at an affordable price, based on the consensus from two decades of academic and policy work.

[1] I testify today in my personal capacity as an academic. My testimony is not necessarily the opinion of Boston University, CARB-X, or any CARB-X funder.

Written Testimony

Superbugs have long been the enemies of civilization. From the Black Death in the Middle Ages (plague bacteria), to the recognition that cholera was caused by something in the water at the Broad Street pump, to modern bacterial and fungal infections – we have been locked in a ceaseless struggle with these microscopic foes.

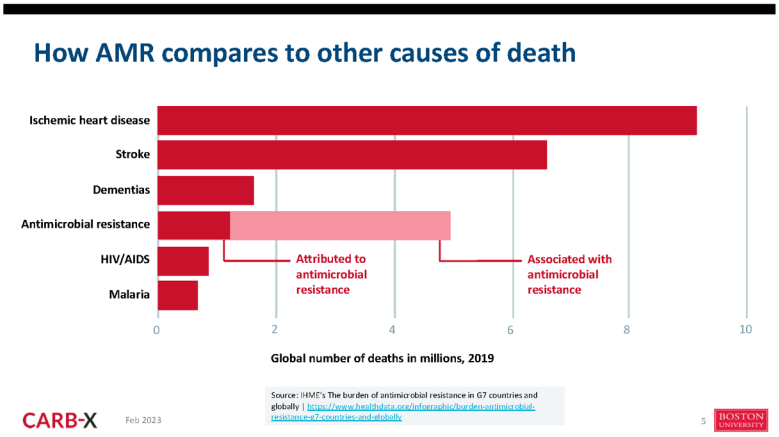
For a brief period in the 20th Century, it looked like we had the upper hand. Antibiotics like penicillin were life savers – beginning with soldiers in World War 2. But even at the celebration for the Nobel Prize for penicillin in 1945, we knew that every time we use these drugs, we reduce their effectiveness for future patients. Unlike any other drug class, anti-infectives[2] decline in effectiveness through use. Genetic mutations and transfers amongst microbial life eventually result in superbugs immune to our best drugs.

For superbugs, today's drugs aren't enough. We must continually innovate to remain one step ahead.

The global death toll today is staggering: the world's most comprehensive study estimated 4.95 million people who died in 2019 suffered from drug-resistant bacterial infections, and at least 1.27 million of these deaths were directly caused by superbug bacteria.[3] The US and other countries mounted impressive efforts in past decades to reduce death and suffering from HIV,

[2] Including antibacterials, antifungals, antiretrovirals, antivirals, and antiparasitics.
[3] IHME. The burden of antimicrobial resistance in G7 countries and globally. https://www.healthdata.org/infographic/burden-antimicrobial-resistance-g7-countries-and-globally.

tuberculosis, and malaria. Through PEPFAR, The Global Fund, and other programs, death rates are declining for these diseases. Hard-fought progress saves lives (Fig. 1).



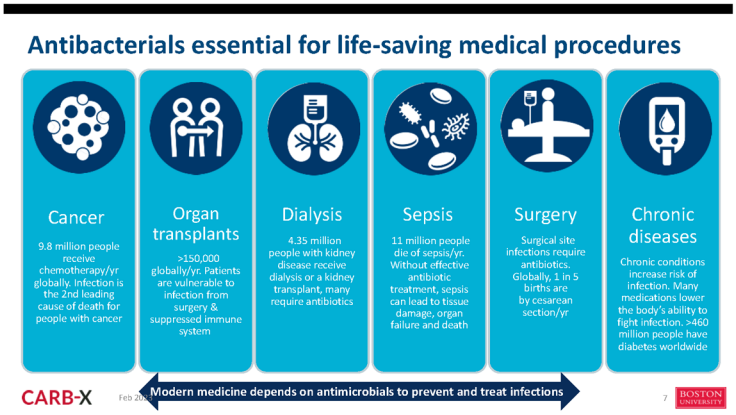
We have not made similar scale commitments against bacteria, and we are falling behind. As bad as the problem is today, a decade from now we could be unprepared against an even larger threat. These problems are exacerbated by conflict, displacement of people, and climate change.

In the US, resistant bacteria kill 48,000 Americans per year, and sicken many more of our people who survive.[4] The trend is moving in the wrong direction for the last few years, with an increase of at least 15% during the first year of the pandemic.[5] The economic damage is also serious –

[4] https://www.cdc.gov/drugresistance/national-estimates.html
[5] https://www.cdc.gov/drugresistance/pdf/covid19-impact-report-508.pdf

more than $4.6 billion each year in additional costs to our healthcare system, especially from longer hospital stays and more intensive services.[6] This economic estimate does not include productivity losses in economic activity and does not put any price on the human lives lost. These estimates are only from drug-resistant bacteria and don't yet include estimates from other superbugs like the fungi on the CDC threat list.

Americans rely on effective antibiotics and antifungals. Every hospital in your district, every cancer patient, every new mom with a C-section, any soldier with infections, or even folks my age thinking about knee or hip surgery – all of us depend on effective antibiotics and antifungals to enable modern medicine. But resistance eats away at the effectiveness of these wonderful drugs, like rust weakens a bridge. When antibiotics become less effective, everything in modern medicine becomes more difficult and less safe (Fig. 2).

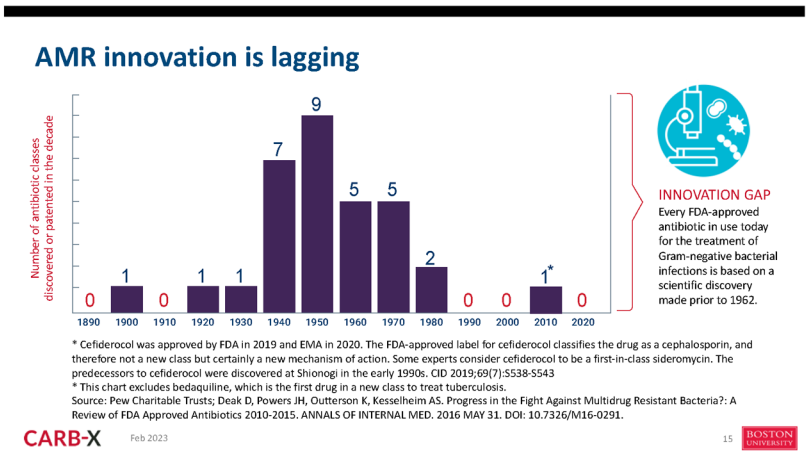


[6] https://www.cdc.gov/drugresistance/solutions-initiative/stories/partnership-estimates-healthcare-cost.html

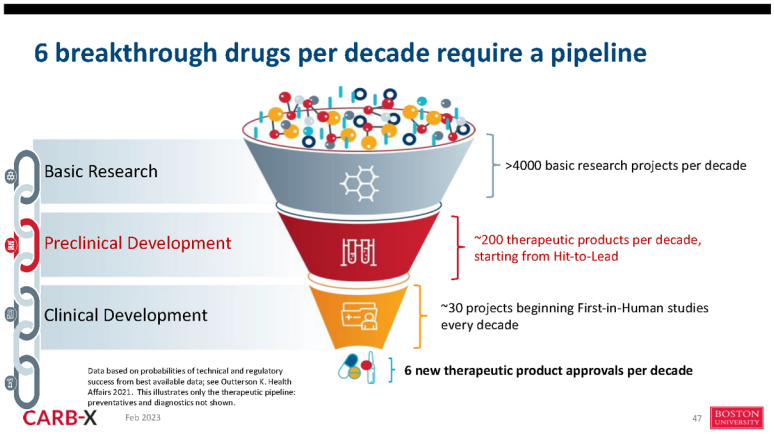
This is a national security issue, threatening the readiness of the American workforce and health care system and imposing needless death, suffering, and expense on our people. But remember that antibiotic and antifungal drugs used today are gradually losing effectiveness. They must be continuously replaced to avoid falling behind.

Superbugs need new drugs

For the past two decades, I have studied the pipeline for new drugs. I have some good news and bad news. First, the bad news. For drugs already in human testing, there is an embarrassing shortfall: about four dozen antibiotics compared to more than a thousand cancer drugs. Cancer drugs make money, so future cures are always moving towards patients. Antibiotics lose money in our current reimbursement system, with predictable results on innovation (Fig. 3).



But there is also good news. The preclinical pipeline is filled with outstanding products, the fruit of investments by the organization I lead, CARB-X, which has invested over $400 million dollars since 2017. CARB-X is supported by BARDA/ASPR, Wellcome, the United Kingdom, Germany, and the Gates Foundation. We have been successful these first 6 years in our primary mission, by delivering 18 therapeutic, diagnostic, and prevention products into first-in-human clinical testing. This preclinical pipeline is amazingly innovative, but fragile from the need for additional public push incentives and private investment. Data from the Global AMR R&D Hub suggests that push incentives are underfunded by several hundred million dollars per year globally if the goal is to bring 6 highly impactful new antibiotics to FDA approval in the next decade (Fig. 4).[7]

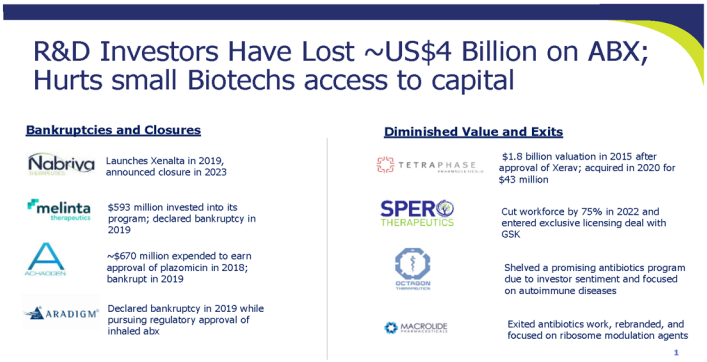


[7] Kevin Outterson, Presentation at the Meeting of the Global Leaders Group on Antimicrobial Resistance, Feb. 8, 2023.

Holding antibiotics in reserve drives companies into bankruptcy

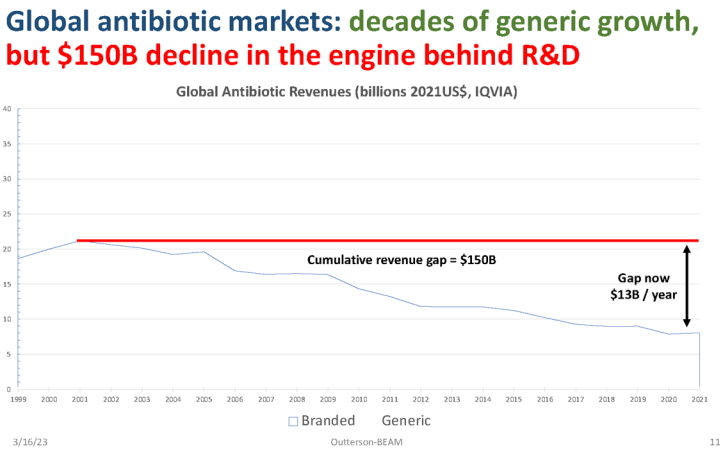
Antibiotics are valuable, but the market is broken: scientists work on new antibiotics for decades. Most fail because science is hard. FDA approval is a time for celebration in all other therapeutic areas – but for new antibiotics, the payday never comes. Because of resistance, doctors rightly want to reserve the newest antibiotic for the future, putting them on the shelf, behind glass like a fire extinguisher. The fire extinguisher company gets paid when preparedness starts, not when the fire starts. We are paying for new antibiotics only after the fire. A new drug that isn't used much in the early years can't make money.[8]

In the last decade, seven antibiotics have been approved by the FDA from small companies.[9] Every one of them has either gone bankrupt or their R&D investors lost their shirts, as non-generic sales of antibiotics are in free fall over the past two decades (Fig. 5).[10]



[8] https://amr.solutions/fire-extinguishers-of-medicine/ (John Rex).
[9] Lefamulin (2019, Nabriva), omadacycline (2019, Paratek), eravacycline (2018, Tetraphase), plazomycin (2018, Achaogen), meropenem/ vaborbactam (2017, Melinta), delafloxacin (2017, Melinta), oritavancin (2014, Melinta).
[10] Madden J, Outterson K. Trends in the global antibiotics market. Nat Rev Drug Disc. 2023 Mar; 22(3):174.

Data from my 2023 publication in *Nature Reviews Drug Discovery* demonstrates the $150 billion cumulative revenue gap in on-patent antibiotic sales since 2001, which has driven so many companies from the field (Fig. 6).



Subscription programs + push incentives will restore innovation at an affordable price

Now is the time to respond to this national security crisis. Push incentives alone will not be enough. We must also change the way we pay for antibiotics. After nearly two decades studying this problem,[11] G7 governments are creating antibiotic subscriptions to reward innovation while

[11] Major reports include Bad Bugs, No Drugs (IDSA, 2004), ASPE/HHS (2014), President's Council of Advisors on Science & Technology (2014), Chatham House (UK, 2015), AMR Review (UK, 2016), GUARD/BCG (German Federal Ministry of Health, 2017), PACCARB (2017), DRIVE-AB (EU, 2018), GAO (2020), Duke-Margolis (2020), BCG (2022), PwC for HERA (EU, 2022), London School of Economics for the Swedish Presidency of the Council of the European Union (2023, not yet released). I was a co-author of three of these reports (and a fourth underway for a G7 government but not yet public) and was interviewed or testified as an expert for eight others. Believe me when I say this problem has been adequately studied by governments and think tanks.

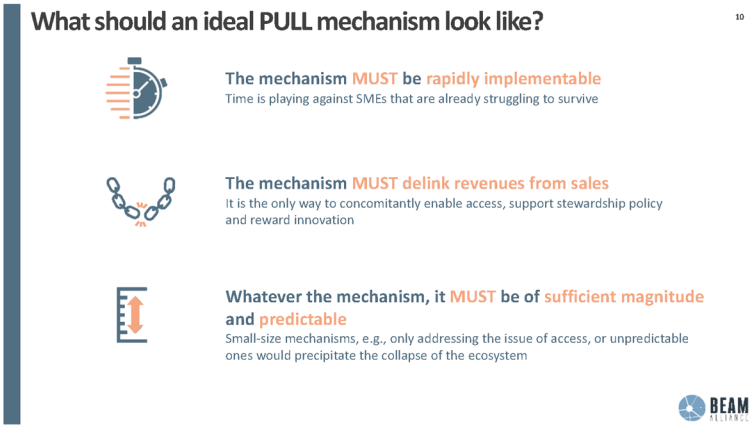
allowing the new antibiotic to be used sparingly at first.[12] If Congress creates a subscription program, Americans will get the new antibiotics we need – sitting on the shelf ready to go, like that fire extinguisher – and the companies will also get what they need to incentivize their R&D activities: reasonable profits instead of bankruptcy. Action by the US would also galvanize other G7 countries to contribute their fair share as well.

Antibiotic subscriptions should be crafted carefully to ensure that U.S. taxpayers get what they need without overpaying. For example, they must focus only on the most promising new drugs, which has been the consensus position since the Chatham House report in 2015. Creating a subscription asks drug developers to aim for a target; let's make sure we create high but attainable targets so that subscriptions result in *better* antibiotics and antifungals.

While earlier proposals suggested paying pull incentives in a lump sum (often called a market entry reward), the DRIVE-AB Report for the European Commission also recommended it could be paid over longer periods of time to reduce the risk of lemons or non-compliance. The UK subscription is moving to a 10-year payment period. The proposed PASTEUR Act in the previous 117th Congress spread the pull incentive over the longer of 10 years or the remaining patent and exclusivity period, which will incentivize the sponsor to minimize patent extensions and facilitate generic entry after the subscription contract is concluded.

[12] Subscription programs or revenue guarantees are officially launched or announced in England and Japan. The EC is expected to release a proposal for a pull incentive within weeks. Canada has announced a Council of Canadian Academies Panel to report back to the government on a pull incentive for Canada.

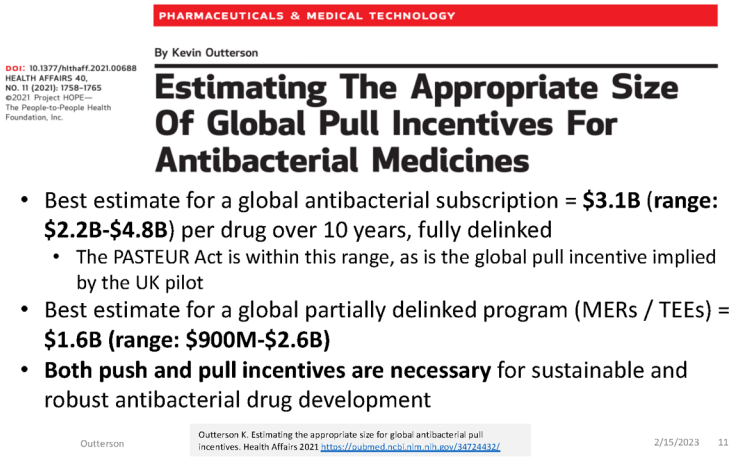
The BEAM Alliance, representing small antimicrobial companies in Europe, has proposed ideal features of pull incentives (Fig. 7).



- The call for **rapid implementation** reflects the urgency of the medical situation, as well as the business urgency for small companies with less than a year of cash on hand with which to fund R&D operations.

- **Delinking** revenues from sales solves the key R&D problem with antibiotics and antifungals by rewarding the sponsor for bringing a high-quality new drug to the market, even if it will be used only in modest volumes in the early years. Delinking also supports proper stewardship since incentives to oversell are no longer present.

- On the issue of "**sufficient magnitude**", *Health Affairs* published my comprehensive estimate of the appropriate size of antibacterial subscriptions in 2021, using only publicly available data in a fully transparent expected net present value model (Fig. 8).[13]



PHARMACEUTICALS & MEDICAL TECHNOLOGY

By Kevin Outterson

DOI: 10.1377/hlthaff.2021.00688
HEALTH AFFAIRS 40,
NO. 11 (2021): 1758–1765

Estimating The Appropriate Size Of Global Pull Incentives For Antibacterial Medicines

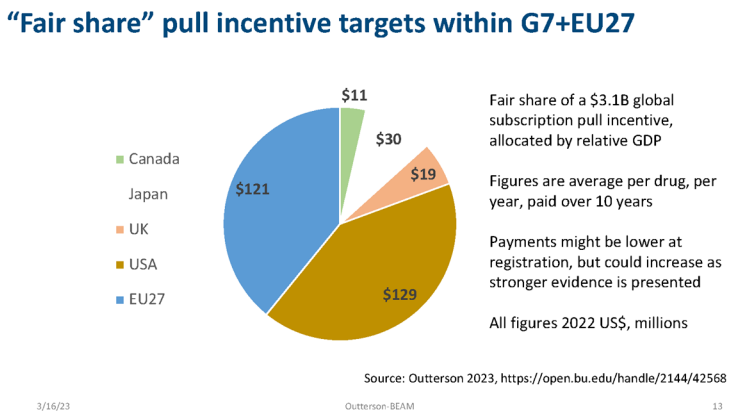
- Best estimate for a global antibacterial subscription = **$3.1B** (**range: $2.2B-$4.8B**) per drug over 10 years, fully delinked
  - The PASTEUR Act is within this range, as is the global pull incentive implied by the UK pilot
- Best estimate for a global partially delinked program (MERs / TEEs) = **$1.6B (range: $900M-$2.6B)**
- **Both push and pull incentives are necessary** for sustainable and robust antibacterial drug development

Outterson | Outterson K. Estimating the appropriate size for global antibacterial pull incentives. Health Affairs 2021 https://pubmed.ncbi.nlm.nih.gov/34724432/ | 2/15/2023 | 11

- The "fair share" of these costs that should be borne by each G7 government + the European Union has been presented in several conferences[14] and was adopted in a November 2019 analysis by the Center for Global Development.[15] As a result of this

[13] Outterson K. Estimating the appropriate size of a global antibacterial pull incentive. Health Affairs. 2021; 40(11):1758-1765.
[14] E.g., Outterson, K. ISPOR (Vienna, Austria, Nov. 8, 2022); HGPI (Tokyo, Japan, Sept. 22, 2022). Open access data: https://open.bu.edu/handle/2144/42568 (Fair Share).
[15] https://www.cgdev.org/blog/world-needs-new-antibiotics-proposed-us-program-develop-them-would-pay-281.

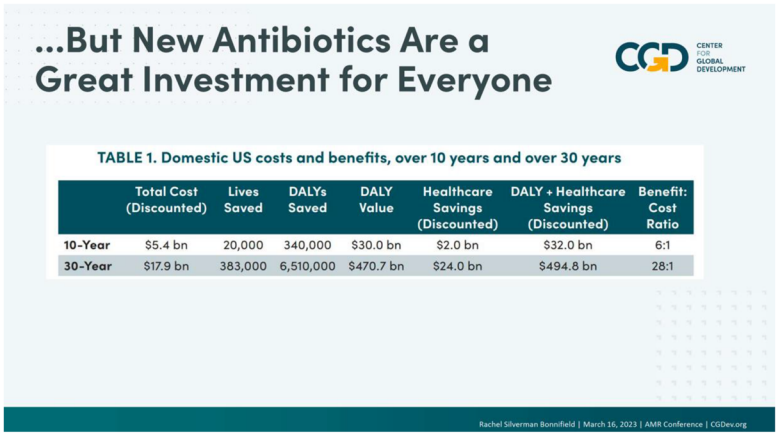
work, we now know the required size of an antibiotic subscription in the US, as well as the fair share for other wealthy countries (Fig. 9).



While the figure above are average amounts, ranges are appropriate for subscription payments, with higher payments going to drugs meeting higher standards. With the evidence available at FDA approval, qualifying drugs can start at an appropriate point and increase over time if stronger evidence is presented of the importance of the new drug.[16]

Subscriptions will be remarkably good value for the US taxpayer. The Center for Global Development forecasts a financial return on investment for Americans of 6:1 over a decade (Fig. 10).[17]

[16] Rex JH, & Outterson K (2016). Antibiotic reimbursement in a model delinked from sales: a benchmark-based worldwide approach. *LANCET INFECTIOUS DISEASES*, *16*(4), 500-505. doi:10.1016/S1473-3099(15)00500-9.
[17] https://www.cgdev.org/blog/world-needs-new-antibiotics-proposed-us-program-develop-them-would-pay-281.



From recent data I published in *Nature Reviews Drug Discovery*, we know that a US subscription would cost less than what we spent on on-patent antibiotics less than ten years ago.[18] This is affordable because we did it ourselves, very recently. It is time to invest in the future of antibiotics and antifungals once again.

By restoring some common sense to the market for antibiotics, subscriptions will bend the curve towards innovation. Globally, the health impact is striking: subscriptions will save 9.9 million lives over the next 3 decades, according to the Center for Global Development.[19]

[18] Madden J, Outterson K. Trends in the global antibiotics market. Nat Rev Drug Disc. 2023 Mar; 22(3):174.
[19] https://www.cgdev.org/blog/world-needs-new-antibiotics-proposed-us-program-develop-them-would-pay-281.

I know this not just based on the work of many experts, but because I have seen the future. At CARB-X, we see the most promising new antibiotic candidates 10 – 15 years before their potential FDA approval. That future is bright so long as you continue to support push incentives from CARB-X and BARDA and complement them with a new pull incentive like the antibiotic subscription in the PASTEUR Act. At CARB-X, we mainly work with very small start-up companies with highly innovative new products, including phages, diagnostics, vaccines, and many first-in-class products. Eighteen of these companies have initiated first-in-human testing. The future can be filled with a sustainable supply of new antibiotics. I am confident because at CARB-X we know this pre-clinical pipeline intimately. The key barriers today are economic, which is why we need both push and pull incentives.

Threats from bacteria and fungi are significant today and will be worse tomorrow. If you want a steady stream of life-saving innovation in a decade, you must act today. We need the fire extinguisher before the fire starts. Let's be well prepared, so bacteria and fungi don't steal a march on the health of Americans.

Thank you for your attention today. Additional information on CARB-X is found in the Appendix.

Professor Kevin Outterson

Boston, Massachusetts
April 28, 2023

Appendix A: CARB-X background

- The Combating Antibiotic Resistant Bacteria Biopharmaceutical Accelerator (CARB-X) is a global non-profit partnership based at Boston University that accelerates antibacterial research and development.[20] CARB-X awards non-dilutive funding and provides scientific, regulatory and business expertise to support early-stage development of innovative products that aim to prevent, diagnose and treat the drug-resistant infections caused by the most dangerous bacteria identified by the World Health Organization (WHO) and Centers for Disease Control and Prevention (CDC) priority lists.[21]
- The 2015 U.S. National Action Plan for Combating Antibiotic-Resistant Bacteria (CARB) called for a CARB product accelerator to bring "inventors and researchers together with start-up companies to explore creative ideas that could lead to the development of new antibiotics or non-traditional therapies."[22] The U.S. Department of Health and Human Services Biomedical Advanced Research and Development Authority (BARDA), part of the Administration for Strategic Preparedness and Response (ASPR), co-founded CARB-X with the Wellcome Trust and the U.S. National Institutes of Health (NIH) in 2016. Since then, Germany's Federal Ministry of Education and Research (BMBF), the United Kingdom Government's Global Antimicrobial Resistance Innovation Fund (UK GAMRIF), and the Bill & Melinda Gates Foundation have joined and supported the initiative. CARB-

[20] https://carb-x.org/.
[21] https://www.who.int/news/item/27-02-2017-who-publishes-list-of-bacteria-for-which-new-antibiotics-are-urgently-needed; https://www.cdc.gov/drugresistance/biggest-threats.html;
[22] https://www.cdc.gov/drugresistance/pdf/national_action_plan_for_combating_antibotic-resistant_bacteria.pdf.

X is hosted at Boston University. CARB-X has also been endorsed and mentioned in declarations from G7 and G20 governments alike.[23]

- CARB-X is the most successful global public-private partnership acting as a push incentive and pipeline coordinator in the early stages of antibacterial product development. CARB-X runs competitive funding calls to select the best science from around the world (more than 1,200 applications were submitted from 39 different countries), employing rigorous application standards (with a < 8% acceptance rate). The selected projects receive scientific, regulatory, and business support in addition to non-dilutive grants via a lean and efficient organization (95% of funding goes to product developers via direct awards or technical and in-kind support). In only six years CARB-X has already accelerated 92 R&D candidates (including new classes of antibiotics and

[23] https://carb-x.org/carb-x-news/gardp-and-carb-x-welcome-renewed-commitment-by-g7-leaders-to-address-antimicrobial-resistance/; https://carb-x.org/carb-x-news/carb-x-welcomes-g20-call-to-action-on-amr/.

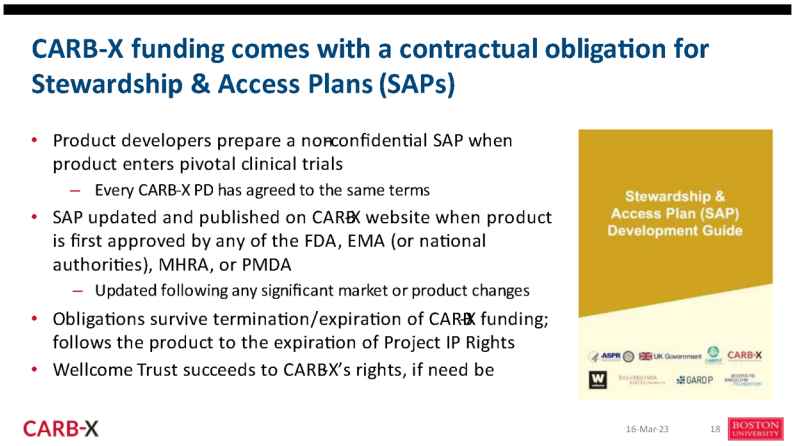
non-traditional agents, vaccines and other preventatives such as CRISPR-phage, microbiome-modifying agents and antibodies, and rapid diagnostics), 18 of which entered or completed first-in-human clinical trials. Among these 18 R&D candidates, 2 have already reached the market, 7 have advanced development partnerships and 12 remain in active clinical development.[24]

Product developers supported by CARB-X since 2017

- While CARB-X's primary focus is accelerating antibacterial innovation, its funders and staff also actively supports stewardship and access to ensure that products funded and supported by CARB-X are used responsibly and are made accessible to patients who need them. CARB-X-funded product developers are contractually obligated to develop a Stewardship and Access Plan for their funded product, outlining what strategies they will deploy to ensure responsible stewardship and appropriate access in low- and middle-

[24] https://carb-x.org/wp-content/uploads/2021/06/Carb-X_FactSheet_7-31-21.pdf.

income countries (LMICs). Many of the R&D projects accelerated by CARB-X target pathogens that cause the greatest health challenges in low- and middle-income countries.



- In addition to funding product development worldwide, CARB-X has been a driving force in preserving, solidifying and empowering the global antibacterial R&D community, creating and maintaining a network of expertise and support to help product developers and their projects succeed. This comprehensive support is a distinct strength of the CARB-X accelerator model. CARB-X's Research & Development Team works closely with more than 120 subject matter experts from around the world, and the CARB-X Global Accelerator Network consisting of several accelerator organizations, to provide scientific, technical and business support tailored to the needs of each project and product developer.[25]

[25] https://carb-x.org/partners/global-accelerator-network/.

Mr. GRIFFITH. I thank the gentleman. I now recognize Ms. Jezek for her 5-minute opening statement.

Ms. JEZEK. Chairs Griffith and McMorris Rodgers, Ranking Member [audio malfunction] inviting me to testify on behalf of the Infectious Diseases Society of America. IDSA represents over 12,000 infectious diseases physicians and other health professionals specializing in ID.

Our members are seeing more patients with resistance, sometimes impossible-to-treat infections——

Mr. GRIFFITH. Yes, is your mike functioning? Is the light on?

Ms. JEZEK. Yes, it's on.

Mr. GRIFFITH. Can you pull it up, get a little closer to it?

Ms. JEZEK. Sorry.

Mr. GRIFFITH. That is all right.

Ms. JEZEK. Our members are seeing more patients with——

Mr. GRIFFITH. Yes, I don't think it is working. Hang on.

Ms. JEZEK. It is lit up.

Mr. GRIFFITH. There you go, that worked.

Ms. JEZEK. Do you want me to start it again?

Mr. GRIFFITH. Yes, I think it is probably good if you start again, so we get it all recorded so that, when they replay it, people can hear at home.

Ms. JEZEK. That is a good idea.

[Pause.]

Ms. CASTOR. I think you need to switch.

Mr. GRIFFITH. Yes. Let's see if we can switch mikes for you. We will get you our highly skilled technical team down there.

[Laughter.]

Mr. GRIFFITH. Or just slide the other mike over. All right, go ahead.

Ms. JEZEK. OK, take three.

STATEMENT OF AMANDA JEZEK

Ms. JEZEK. Chairs Griffith and McMorris Rodgers, Ranking Members Castor and Pallone, distinguished subcommittee members, thank you for holding this hearing on antimicrobial resistance and for inviting me to testify on behalf of the Infectious Diseases Society of America.

IDSA represents over 12,000 infectious diseases physicians and other health professionals specializing in ID.

Our members are seeing more and more patients with resistant, sometimes impossible-to-treat infections, such as the report earlier this week of an ongoing outbreak of Klebsiella bacteria at a Washington State hospital that has impacted dozens and resulted in four deaths. Today I will describe AMR challenges and one health policy opportunity to ensure we have the tools to combat AMR, including novel antimicrobials, stewardship programs, and an expert workforce.

Antimicrobial resistance is pathogens' ability to resist to—to evolve to resist antimicrobial drugs. When resistant—while resistance does occur in nature, antimicrobial misuse speeds up resistance. Antimicrobials are unlike any other therapeutics, in that use in one individual can impact efficacy in the rest of the population.

In 2019 an estimated 1.27 million deaths worldwide were directly caused by AMR, and AMR played a part in nearly 5 million deaths.

Antimicrobials enable modern medicine, because so many of our medical advances—cancer chemotherapy, organ transplantation, hip and knee replacement, C-sections, wound and burn treatments—all carry a risk of infection.

The opioid epidemic is also fueling the spread of resistant infections. CDC estimates that individuals who inject drugs are 16 times more likely to develop a MRSA infection.

AMR is even impacting healthy individuals in the community. For example, an ongoing outbreak of drug-resistant eye infections due to contaminated eyedrops has caused blindness and even death in several patients.

AMR disproportionately impacts historically marginalized populations, exacerbating health inequities.

National healthcare costs linked to infections of just 6 of the biggest AMR threats are estimated to be more than $4.6 billion annually, with $1.9 billion of those costs estimated to be borne by Medicare.

AMR was further exacerbated by COVID–19. In 2020 U.S. hospitals experienced a 15 percent increase in AMR infections and deaths. Emergencies like outbreaks, pandemics, and even hurricanes and bioterror attacks all create ripe opportunities for the spread of secondary drug-resistant infections.

The current antimicrobial pipeline is insufficient. Antimicrobials must be used judiciously to limit the development of resistance, which thus limits the ability to earn a return on investment for antimicrobial R&D. This broken market has resulted in large companies leaving the market, has forced small companies who have developed new antimicrobials into bankruptcy, and has prevented promising drugs from getting to patients.

In addition, we must ensure the optimal use of antimicrobials. In 2020 about 80 percent of patients hospitalized with COVID received antibiotics, despite that COVID is caused by a virus. Even before the pandemic, about half of all hospitalized patients were prescribed antibiotics, with up to 50 percent of those prescriptions being estimated as inappropriate or unnecessary.

Antimicrobial stewardship programs aim to ensure that patients receive the right drug for the right bug. They improve patient outcomes, while also reducing inappropriate antibiotic use and lowering healthcare costs. While many hospitals can meet CMS stewardship requirements on paper, they often lack the resources and staff necessary to extend the benefits of stewardship to all patients.

The infectious diseases workforce that is needed to care for patients with resistant infections is in crisis. Nearly 80 percent of U.S. counties lack an ID physician. Only 56 percent of ID physician training programs filled in 2023. Financial barriers pose huge challenges to ID recruitment. ID physicians are among the lowest-paid medical specialists, and high levels of medical student debt often drive physicians to higher-paying specialties.

Congress must take steps to ensure the availability of an expert ID workforce to combat AMR by addressing medical student debt, improving ID physician reimbursement, and providing sufficient resources for training and early development.

Congress can also revitalize antimicrobial innovation by paying for the value of antimicrobial drugs instead of volume under a subscription model approach, like the bipartisan PASTEUR Act, which would also support antimicrobial stewardship programs.

Nontraditional therapies such as phages may also have a very useful role in treating resistant infections, and additional research should be pursued to inform optimal clinical use of phage therapy.

IDSA is deeply grateful for this committee's history of leadership on AMR, and we look forward to working with you to address persistent needs. Thank you.

[The prepared statement of Ms. Jezek follows:]

Antimicrobial Resistance: Examining an Emerging Public Health Threat
House of Representatives Energy & Commerce Committee, Oversight & Investigations Subcommittee
Testimony of Amanda Jezek, Senior Vice President, Public Policy & Government Relations
Infectious Diseases Society of America
April 28, 2023

Chairman Griffith, Ranking Member Castor and distinguished members of the Subcommittee, thank you for holding a hearing on the critical issue of antimicrobial resistance (AMR) and for inviting me to testify on behalf of the Infectious Diseases Society of America (IDSA). IDSA represents over 12,000 infectious diseases (ID) physicians, scientists and other health care and public health professionals specializing in infectious diseases. IDSA has been sounding the alarm about AMR since 2004 with the release of our "Bad Bugs, No Drugs" report. ID physicians are seeing more patients with resistant infections and increasing multi-drug-resistant strains, including those that are highly contagious and resistant to every available antimicrobial drug. While the federal government, with bipartisan action and leadership from the Energy & Commerce Committee, has made important strides to strengthen the federal response to AMR with a One Health approach that covers human health, animal health, agriculture and the environment, significant work remains to protect patient safety and national security and to safeguard modern medicine as we know it.

I will outline why AMR is one of the greatest public health crises of our time; the current state of AMR response efforts, including progress and gaps regarding the antimicrobial drug pipeline, stewardship, prevention, surveillance, data collection and the expert workforce needed to drive these activities; and finally, I will highlight urgently needed solutions, including the bipartisan *Pioneering Antimicrobial Subscriptions to End Upsurging Resistance (PASTEUR) Act* by Representatives Ferguson and Peters.

Antimicrobial Resistance: Undermining Modern Medicine

Antimicrobial resistance refers to pathogens' natural ability to evolve to resist the effects of antimicrobial drugs, ultimately making those drugs ineffective. While resistance occurs in nature, the

overuse and misuse of antimicrobials greatly increases the speed at which resistance develops, significantly shortening the time for which antimicrobial drugs remain effective and reducing the number of useful antimicrobials. **Antimicrobials are unlike any other therapeutic in that use in one individual can impact efficacy in the rest of the population.**

In 2019, an estimated 1.27 million deaths worldwide were directly caused by AMR, and AMR played a part in nearly 5 million deaths. This makes AMR a leading cause of death globally.[1] The post-antibiotic era is not just a looming threat — for many patients it is already here.

To fully understand the scale and scope of the AMR crisis, one must first recognize the fundamental role antimicrobials play in human health. **Antimicrobials enable and sustain modern medicine because so many of our modern medical advances carry a risk of infection and rely upon antimicrobials.** Consider procedures like cancer chemotherapy, organ transplants, hip and knee replacements, C sections and other surgeries and complex care. All of these procedures save and enhance human lives, and they all carry risk of infection. Clinicians are only able to provide this care because they have safe and effective antimicrobials to prevent and manage infectious complications. But as our antimicrobial arsenal diminishes, our modern medical gains are unraveling, and patients are facing devastating consequences. Consider a few examples:

- **Cancer**: Cancer and many cancer treatments can weaken the immune system. Infections are a primary or associated cause of death in 50% of patients with cancer, as AMR can make these infections difficult or impossible to treat.[2]
- **Maternal mortality**: Sepsis—the body's overwhelming and life-threatening response to untreated infections that can result in organ failure and death—is the second leading cause of pregnancy-related deaths. AMR exacerbates the risk of sepsis by making infections much more

[1] https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(21)02724-0/fulltext
[2] https://acsjournals.onlinelibrary.wiley.com/doi/full/10.3322/caac.21697

difficult to treat. Between 2014 and 2017, infection or sepsis caused 12.7% of pregnancy-related deaths in the United States. Pregnancy-related infections that can lead to sepsis can be related to miscarriages, C-sections, prolonged or obstructed labor, and mastitis (breast infection).[3]

- **Biologics**: Certain biologics that are used to treat a wide range of conditions weaken the immune system, making individuals more susceptible to infections.
- **Implantable medical devices**: Prosthetic joints, pacemakers, implantable defibrillators, ventricular assist devices for patients with serious heart disease, and other implantable devices can easily become infected. In many cases, removal of these devices may be impossible or impractical, and patients may face recurring or chronic infections that can become increasingly resistant.
- **Opioid use**: The opioid epidemic is also fueling the spread of resistant infections, including life-threatening heart valve infections, skin and soft tissue infections, bone and joint infections, and more. The Centers for Disease Control and Prevention (CDC) estimates that individuals who inject drugs are 16 times more likely to experience an invasive methicillin-resistant *S. aureus* (MRSA) infection.[4]
- **Fungal infections**: In March 2023, CDC warned that cases of *Candida auris*, a difficult-to-treat resistant fungal pathogen, have been increasing steadily since they were first reported in 2016. *C. auris* is resistant to multiple antifungal drugs, spreads easily in healthcare facilities, and has high mortality rates.[5]

[3] https://www.sepsis.org/sepsisand/pregnancy-childbirth/
[4] https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7045815/#:~:text=Data%20from%206%20sites%20of,develop%20invasive%20MRSA%20infections%20than
[5] https://www.cdc.gov/media/releases/2023/p0320-cauris.html

- **Organ transplants**: More than 42,000 organ transplants were performed in the US in 2022, a 3.7% increase over 2021 and a new annual record.[6] Unfortunately, AMR and the dwindling arsenal of antimicrobial drugs available to support these patients means many of them face death due to infection despite a successful transplant.
- **Cystic fibrosis**: People with cystic fibrosis (CF) face a heightened, life-long risk of infections because of the thick sticky mucus in their lungs. Routine use of antibiotics in CF care is medically necessary, however, too many people with cystic fibrosis find themselves battling difficult-to-treat infections for which existing antibiotics are not effective.

Increasing resistance is forcing ID physicians to turn to older, more toxic antibiotics like colistin—a drug that causes serious kidney damage. Patients are left with the unfathomable choice of dying from their infection or taking an antibiotic that could leave them in need of dialysis for the rest of their life or a kidney transplant. The rapid spread of the transferable gene, mcr-1, which confers colistin resistance, threatens the efficacy of even colistin—a last resort drug for the treatment of many drug-resistant bacterial infections.[7] We must do better.

AMR is also impacting healthy individuals in the community. Rates of a type bacteria that cause resistant urinary tract infections or UTIs (extended-spectrum beta-lactamase (ESBL)-producing Enterobacteriaceae) increased by more than 50% from 2013 to 2019.[8] In fact, increasing numbers of patients with UTIs that were once easily treated with oral antibiotics now require intravenous (IV) antibiotics in the hospital — increasing our health care costs and creating serious disruptions to patients' lives. As another example, an ongoing outbreak of drug-resistant eye infections due to contaminated eye drops has caused blindness in several patients and the need for removal of the eye, a devastating

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[6] https://unos.org/news/2022-organ-transplants-again-set-annual-records/#:~:text=In%202022%2C%2042%2C887%20organ%20transplants,Transplantation%20Network%20under%20federal%20contract.
[7] https://www.nature.com/articles/s41429-023-00622-1
[8] https://www.cdc.gov/drugresistance/pdf/threats-report/2019-ar-threats-report-508.pdf

and disfiguring complication. This underscores that resistant infections are a threat to us all and that we must invest in the tools necessary to ensure we can manage such outbreaks with limited negative impacts.

Like so many health conditions, AMR disproportionately impacts historically marginalized populations, though more comprehensive data is needed to fully understand the inequitable impacts of AMR. A few examples:

- Community-associated MRSA rates are higher among Black populations when compared to White populations.[9]
- American Indian and Alaska Native persons have substantially higher population rates of all invasive Group A *streptococcus* disease.[10]
- In February 2023, CDC published a health alert on an increase in extensively drug resistant (XDR) *Shigella* infections. Historically, *Shigella* has largely impacted children under age 5. There is now an increase in *Shigella* infections among men who have sex with men, individuals experiencing homelessness, international travelers and people with HIV.[11]

National healthcare costs linked to infections from six of the biggest AMR threats are estimated to be more than $4.6 billion annually.[12] $1.9 billion of these costs are estimated to be borne by Medicare.[13]

Antimicrobial Resistance: A Threat to Readiness and National Security

The AMR crisis was further exacerbated by the COVID-19 pandemic. In 2020, U.S. hospitals experienced a 15% increase in AMR infections and deaths, though pandemic-related data gaps suggest that the total national burden of AMR may be much higher. Experts do not expect a return to pre-

[9] https://www.cdc.gov/drugresistance/pdf/health-equity-antibiotic-resistance-fs-508.pdf
[10] https://www.cdc.gov/drugresistance/pdf/health-equity-antibiotic-resistance-fs-508.pdf
[11] https://emergency.cdc.gov/han/2023/han00486.asp
[12] https://www.cdc.gov/drugresistance/solutions-initiative/stories/partnership-estimates-healthcare-cost.html
[13] https://academic.oup.com/cid/article/74/6/1070/6374434

pandemic levels without concerted action.[14] Any emergency resulting in high levels of hospitalization, particularly high levels of ventilator use and overwhelmed hospital staff, creates a ripe opportunity for the spread of secondary drug-resistant infections.

Hurricanes and other natural disasters can also increase the spread of infections, including drug-resistant infections. Loss of electricity increases the risk of food spoilage and foodborne illness. Interrupted access to safe water can lead individuals to turn to rivers or other ad hoc water sources. This approach, along with the presence of floodwaters, can increase the risk of illness caused by waterborne pathogens. Studies have found higher levels of pathogenic bacteria and antibiotic resistance genes in floodwaters and soil in the Houston area following Hurricane Harvey.[15][16] Conditions in crowded emergency shelters and severely damaged homes can significantly increase the spread of infection as well.

Addressing AMR is important for bioterror readiness and national security, as agents used by bioterrorists may be genetically engineered to resist current antimicrobials.[17] The World Health Organization (WHO) has estimated that if 50 kg of *Y. pestis* were to be released as an aerosol over a city with a population of 5 million, 150,000 people might fall ill with pneumonic plague, 36,000 of whom would die.[18] Drug-resistant strains of *Y. pestis* have been reported, which can increase mortality.[19] As another example, modeling suggests that deliberate release of aerosolized *F. tularensis* over London would result in an estimated 130,000 infections and 24,000 deaths.[20] Natural resistance is already

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[14] https://www.cdc.gov/drugresistance/pdf/covid19-impact-report-508.pdf
[15] https://pubs.acs.org/doi/10.1021/acs.estlett.8b00329
[16] https://pubmed.ncbi.nlm.nih.gov/33077230/
[17] https://books.google.com/books?hl=en&lr=&id=IiGEDwAAQBAJ&oi=fnd&pg=PR1&ots=ZXqKRYXnRH&sig=39-Vf6uaisjn-zSVfBI-1p_9TT4#v=onepage&q&f=false
[18] https://apps.who.int/iris/bitstream/handle/10665/39444/24039.pdf
[19] https://journals.asm.org/doi/full/10.1128/AAC.00306-06
[20] https://www.liebertpub.com/doi/abs/10.1089/bsp.2011.0004

observed in tularemia, and the overuse of fluoroquinolones, one of the main treatments for this infection, in the last two decades has led to treatment failure and relapses in tularemia patients.[21]

Military service people, who are often critical first responders in emergencies, can be at heightened risk for resistant infections, as combat wounds and burns can easily become infected. In the current conflict in Ukraine, patients are presenting with highly complex, multidrug-resistant musculoskeletal infections from gunshot and bomb wounds. Physicians identified multiple pathogens, including *Klebsiella pneumoniae, Pseudomonas aeruginosa, Acinetobacter baumannii, E. coli* and fungal pathogens. Infections showed high rates of resistance to some of our most powerful antibiotics: 72% were resistant to carbapenems and newer cephalosporins (ceftazidime-avibactam and ceftolozane-tazobactam), 39% were resistant to cefiderocol, 20% to colistin and 96% to ciprofloxacin.[22] International travel makes it very easy for drug resistant pathogens to spread across the globe.

Insufficient Antimicrobial Pipeline

Despite the urgent and increasing need for novel antimicrobials to treat resistant infections, the current pipeline has fewer than 50 antibacterial therapeutics in clinical development worldwide — only only a handful of which are for the most threatening gram-negative pathogens — a critical area of need.[23] Given that most drugs in development do not ultimately secure FDA approval, and that there is a wide array of drug-resistant bacteria and fungi for which new therapies are needed, the current pipeline is grossly inadequate. The last FDA approval of an antibiotic was in November 2019.

Novel antimicrobials must be used appropriately by prescribers with sufficient expertise to limit the development of resistance; this means ensuring that these precious medicines are not overused. This is essential from a clinical and public health perspective but creates a serious barrier to private

[21] https://ami-journals.onlinelibrary.wiley.com/doi/full/10.1111/j.1751-7915.2008.00063.x
[22] https://www.cidrap.umn.edu/antimicrobial-stewardship/clinicians-describe-challenge-treating-multidrug-resistant-war-wounds
[23] https://www.who.int/publications/i/item/9789240047655

sector investment in antimicrobial innovation. Currently, federal and commercial payers reimburse for antimicrobials when they are used, so judicious use to preserve effectiveness severely limits the ability of an antimicrobial developer to earn a return on their investment.

Between 2010 and 2019, 18 new antibiotics were approved by FDA, which is an improvement from the 11 new antibiotics approved from 2000-2009. However, only one of those 18 antibiotics had a new mechanism of action, and it was the first such antibiotic approved since the 1980s.[24] This underscores the need not only to strengthen antimicrobial research and development but more specifically to incentivize the development of truly novel antimicrobials.

Federal support from the Biomedical Advanced Research and Development Authority (BARDA) and the National Institute of Allergy and Infectious Disease (NIAID) has been critically important to the development of more recently approved antibiotics, and their funding for CARB-X has strengthened the pre-clinical antimicrobial pipeline. However, we see plain evidence of failures in the market for antimicrobials: There has been a disturbing number of instances in which small companies successfully bringing a new antibiotic to market are then pushed to file for bankruptcy due to the broken antimicrobials market that provides little to no opportunity to earn a return on investment. There is an urgent need for a novel solution that will revitalize and sustain antimicrobial innovation and availability.

Potential Role of Phage Therapy[25]

Non-traditional therapies, such as phage therapy, may also have a useful role in treating resistant infections, and additional research should be pursued to inform optimal clinical use of phage therapy. Experimental phage therapy can be considered for a variety of infections not responding to antibiotics, including respiratory tract infections, infections involving devices that cannot be removed, UTIs, gastrointestinal infections and more. Recent clinical data on phage therapy has been generated

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[24] https://www.bio.org/sites/default/files/2022-02/The-State-of-Innovation-in-Antibacterial-Therapeutics.pdf
[25] https://journals.asm.org/doi/10.1128/aac.02071-21#:~:text=In%20general%2C%20phage%20therapy%20should,not%20amenable%20to%20source%20control

primarily in compassionate use settings in conjunction with antibiotic therapy. Many cases were associated with apparent successful response of resistant infections that were not resolving with antibiotics alone, suggesting that in those cases, there may have been an additive effect of the phage-antibiotic combination. Much current phage data does not come from clinical trials with a control group, and failures of phage therapy are less likely to be reported, all of which limits our understanding of phage therapy. Phage therapy is currently limited to treatment of bacterial infections; however, data are emerging to indicate that fungal pathogens such as *Aspergillus* can be treated in the future.

Phages do not have reliable activity against all strains of any bacterial species, underscoring the potential importance of phage susceptibility testing (PST) to inform selection of phage therapy. Standardized PST methodologies should be developed to support this testing. Because of the potential for resistance to develop to phages during treatment, PST can confirm continued efficacy throughout treatment or identify the need for a new phage or phage cocktail.

Randomized controlled trials of phage therapy are needed to inform and understand treatment indications, route of administration, dosing, duration of therapy, optimal phage cocktail combinations and phage-antibiotic combinations, and development of resistance. In addition to clinical trials, a systematic approach to data collection from compassionate use cases and availability of such data to clinicians, including clinical failures, would be helpful for clinicians, and a common database to collect and access such data should be established.

Antimicrobial Stewardship

Overuse and misuse of antimicrobials in any setting—human medicine, animal health, agriculture, the environment—drives the development of resistance, and a One Health approach to combating AMR is critical. From March-October 2020, about 80% of patients hospitalized with COVID-19

received antibiotics.[26] COVID-19 is caused by a virus, and therefore does not respond to antibiotics, though antibiotics may be appropriate for the minority of patients with secondary bacterial infections. Even before the pandemic, about half of hospitalized patients were prescribed antibiotics, with 30%-50% of those prescriptions estimated to be inappropriate or unnecessary.[27]

Antimicrobial stewardship programs in hospitals aim to optimize antibiotic use to ensure that patients receive the right drug for the right bug with the right dosing and duration. These programs have been found to improve patient outcomes, reduce inappropriate antibiotic use, and lower health care costs.[28,29] Nationwide, 98% of hospitals report having implemented all seven of the core elements of antimicrobial stewardship recommended by CDC[30] and as required by the Joint Commission and the Centers for Medicare and Medicaid Services (CMS). Despite this important progress, there remain many important opportunities to improve antimicrobial therapy and reduce inappropriate antibiotic use in hospitals.

While many hospitals can meet stewardship requirements on paper, they often lack the resources and experienced staff necessary to fully implement medically recommended stewardship protocols and to extend the benefits of stewardship to all patients. Studies have found consistent gaps between necessary levels of physician and pharmacist staffing and existing staffing levels. A 2018 study found that each 0.50 increase in physician and pharmacist full-time employee (FTE) support for a stewardship program predicted a 1.48-fold increase in the odds of the program demonstrating effectiveness.[31]

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[26] https://www.cdc.gov/drugresistance/covid19.html#:~:text=Antibiotic%2FAntifungal%20Use%3A%20COVID%2D19%20Impact&text=Almost%2080%25%20of%20patients%20hospitalized,they%20can%20contribute%20to%20resistance.
[27] https://academic.oup.com/cid/article/63/12/1/2282817
[28] https://academic.oup.com/cid/article/66/7/995/4851152
[29] https://pubmed.ncbi.nlm.nih.gov/27246783/
[30] https://www.cdc.gov/antibiotic-use/stewardship-report/current.html
[31] https://doi.org/10.1093/cid/ciy255

The COVID-19 pandemic further stressed hospital budgets, diverting resources from stewardship programs despite the unprecedented need for stewardship to manage high levels of antibiotic use among hospitalized patients with COVID-19.[32] In many hospitals, stewardship teams led the complex administration of COVID-19 therapeutics, which was an appropriate use of limited human capital resources given their expertise. This work included evaluating treatments for COVID-19 in clinical trials, developing treatment guidelines and educating providers as data rapidly evolved, partnering with state and local health departments, assessing patient risk factors to prioritize limited quantities of therapeutics, and devising innovative strategies to reach rural and other underserved populations. These efforts were crucial to reducing COVID-19 hospitalizations and deaths, but came at the expense of traditional antimicrobial stewardship.

Outpatient antibiotic prescribing decreased overall during the COVID-19 pandemic, but prescribing rates still vary widely across the U.S., with some states in the South having prescribing rates more than double the rates in states in other regions.[33] However, antibiotics were frequently prescribed for COVID-19, despite the fact that antibiotics are not effective against viruses. A study published in the *Journal of the American Medical Association (JAMA)* reported that among Medicare beneficiaries who had an outpatient visit for COVID-19 in the first year of the pandemic, more than 30% received an antibiotic.[34] Prior to the pandemic, CDC estimated that at least 30% of antibiotic prescriptions in outpatient settings are unnecessary, and total inappropriate antibiotic use may be as much as 50% of all outpatient antibiotic use.[35] Additional resources are needed to support implementation of stewardship in outpatient settings.

AMR Surveillance and Data Collection

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[32] https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7375214/

[33] https://www.cdc.gov/antibiotic-use/stewardship-report/current.html
[34] https://jamanetwork.com/journals/jama/fullarticle/2791077
[35] https://www.cdc.gov/antibiotic-use/data/outpatient-prescribing/index.html

We need to understand where resistance is happening and how antimicrobials are being used to best target prevention and treatment strategies. The CDC National Healthcare Safety Network (NHSN) includes the Antibiotic Use and Resistance (AUR) module, which collects and provides actionable data to inform and evaluate efforts to optimize antibiotic use. More than 2,400 acute care hospitals across the United States had submitted at least one month of antibiotic use data as of August 2022. Of those hospitals, 2,283 reported in the past 12 months (July 2021 – June 2022). This represents a significant increase in reporting in the last several years, but gaps in data persist and more comprehensive reporting will better inform the current state of AMR in the U.S.

CMS included a requirement for antibiotic use and resistance reporting in their fiscal year 2023 Inpatient Prospective Payment System final rule. IDSA supports this requirement, which will help ensure that antibiotic stewards, clinicians and key decision-makers have access to more comprehensive antibiotic use data, enabling us to track antibiotic use and resistance over time, evaluate stewardship interventions, identify best practices and improve antibiotic use. It is critical that health care facilities not yet reporting antibiotic use and resistance data be provided resources necessary to begin reporting. It is also critical to provide CDC with resources necessary to support NHSN users, analyze and share data, and promote health professional education and appropriate antibiotic use.

Workforce Needed to Combat Antimicrobial Resistance

The ID workforce that is needed to respond to AMR is in crisis. ID physicians and other ID health care and public health professionals are needed to care for patients with resistant infections, lead antimicrobial stewardship and infection prevention and control activities, and conduct surveillance and research, including clinical trials. For patients with serious infections, including those caused by

resistant pathogens, ID physician care improves outcomes, decreases mortality, shortens hospital stays, and lowers health care costs.[36,37]

Workforce shortages coupled with lower pay and a lack of financial incentives for recruitment and retention persist among ID health care professionals, including ID physicians, clinical microbiologists, nurses, pharmacists, physician assistants and infection preventionists. In 2022, nearly 80% of U.S. counties lacked an ID physician,[38] and only 56% of ID physician training programs filled their positions for the 2023 appointment year, compared to most other physician specialties for which nearly all of their programs filled their positions.[39] A quarter of health care facilities have reported a vacant infection preventionist position and a 2019 survey showed a vacancy rate for clinical microbiologists of more than 10%. Communities without ID health care professionals are less equipped to respond to AMR.

IDSA has conducted extensive outreach and mentoring to medical students and residents, and we routinely find high levels of interest in the field of ID, but financial challenges consistently pose barriers to recruitment. ID physicians are among the lowest paid medical specialists, earning even less than general internal medicine physicians who lack the additional years of training that an ID physician undergoes.[40] High levels of student debt often understandably drive physicians to higher paying specialties, leaving our nation without enough experts to combat AMR. Without action to recruit, train and retain the next generation of ID specialists, we can expect to see an increase in mortality due to infectious diseases for years to come.

Solutions

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[36] https://academic.oup.com/jid/article/216/suppl_5/S588/4160394
[37] https://academic.oup.com/cid/article/58/1/22/372657
[38] https://www.acpjournals.org/doi/10.7326/m20-2684
[39] https://www.nrmp.org/wp-content/uploads/2023/04/2023-SMS-Results-and-Data-Book.pdf
[40] https://www.medscape.com/slideshow/2022-compensation-overview-6015043?icd=login_success_email_match_norm

IDSA is grateful for the Energy & Commerce Committee's long history of leadership on AMR, including passage of the *Generating Antibiotic Incentives Now (GAIN) Act* in 2012 and enactment of the Limited Population Antibacterial Drug (LPAD) review mechanism in 2016 as part of the *21st Century Cures Act*, which helped improve the regulatory environment for the study and evaluation of new antibiotics and antifungals to address unmet needs in limited patient populations.

The National Action Plan for Combating Antibiotic-Resistant Bacteria (CARB) was launched in 2015 and provided an important framework for a coordinated, comprehensive federal response to AMR. The second iteration of the plan was released in 2020 and largely aims to build upon the progress made since 2015. The five goals of the plan, which IDSA supports, are: 1) slow the emergence of resistance and prevent resistant infections; 2) improve One Health surveillance; 3) advance development and use of diagnostics; 4) advance research and development of antibiotics, other therapeutics and vaccines; and 5) improve international collaboration. We greatly appreciate the leadership of Representatives Buddy Carter and Chellie Pingree in leading an annual letter urging Congress to provide sufficient funding to BARDA, CDC and NIAID to advance critical AMR efforts. These resources have supported improved surveillance, clinician education about AMR, research and innovation, and it is critical that funding for these efforts continues. In addition, the Presidential Advisory Council on Combating Antibiotic-Resistant Bacteria (PACCARB) convenes key experts to provide a diverse array of perspectives, including frontline clinicians, to help inform federal AMR response activities. The PACCARB's recommendations have allowed federal efforts to benefit from a wide range of expertise, and the PACCARB should be reauthorized so this important work may continue.

It is also critical that we address gaps in existing efforts, specifically with regard to antimicrobial innovation, stewardship and the AMR workforce. The PACCARB released a March 2023 report, "Preparing for the Next Pandemic in the Era of Antimicrobial Resistance," and recommended urgently

needed efforts to strengthen antimicrobial stewardship, infection prevention and control, the ID workforce, data sharing, and medical countermeasure innovation.[41]

PASTEUR Act

The bipartisan *PASTEUR Act* would have a transformative impact on antimicrobial innovation, revitalizing the discovery and development of truly novel antimicrobials by providing a predictable, reasonable return on investment for novel antimicrobials. The federal government already pays for antimicrobials through various health programs including Medicare, Medicaid, Tricare and Veterans Affairs (VA), but it pays in a way that fails to incentivize innovation and appropriate use. Conversely, *PASTEUR* is smart spending. **Under *PASTEUR*, the federal government would pay for the value rather than volume.** *PASTEUR* would allow the federal government to enter into contracts with antimicrobial developers to pay set fees for a steady supply of a novel antimicrobial.

Importantly, *PASTEUR* is designed to deliver truly novel antimicrobials that provide important clinical benefits for patients. To receive a contract under *PASTEUR*, antimicrobials must meet certain characteristics, including "improving clinical outcomes for patients with multi-drug-resistant infections." Additional characteristics include treating an infection for which there is unmet need, being a new class of antibiotic, having a novel target or novel mechanism of action, or having an improved route of administration, such as oral. The more characteristics the drug meets, the higher the value its contract can be. An interagency committee, advised by non-government experts, will develop a list of infections for which new antimicrobial drugs are needed and regulations regarding the drug characteristics and how the characteristics will adjust the monetary value of a subscription contract.

PASTEUR would also support appropriate use of antimicrobials by providing urgently needed funds to hospitals and long-term care facilities to support their antimicrobial stewardship programs. Priority for these funds would be given to rural, critical access and safety net hospitals.

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[41] https://www.hhs.gov/sites/default/files/paccarb-pandemic-preparedness-report.pdf

More than 200 organizations have called upon Congress to enact *PASTEUR* this year on any moving legislative vehicle, including reauthorization of the *Pandemic and All Hazards Preparedness Act (PAHPA)*.[42]

AMR Workforce Investments & Physician Reimbursement

In addition, Congress must take steps to ensure the availability of the expert ID workforce needed to combat AMR, including ID physicians, ID physician-scientists, clinical microbiologists, infection preventionists, pharmacists and nurses. We must make ID a financially feasible choice for health care professionals by addressing student debt, improving reimbursement, and providing sufficient resources for training and early career development. Specific recommendations include:

- Fund implementation of the Public Health Loan Repayment Program and the Bio-Preparedness Workforce Pilot Program to incentivize individuals to pursue careers in public health and ID in shortage areas. IDSA greatly appreciates that Representatives Crow, Burgess, Trahan, Miller-Meeks and Fitzpatrick led a letter urging the Appropriations Committee to provide these needed resources.[43]
- Enhance Medicare reimbursement for ID physicians, through one or more of the following approaches: Increase the value of the codes most frequently billed by ID physicians (i.e., inpatient evaluation and management codes); provide a Medicare payment bonus for ID physicians (e.g., similar to the Medicare payment bonus for primary care physicians and general surgeons); and create new mechanisms to pay for critical population health activities to combat AMR that benefit the general patient population, but are not necessarily directly tied to the care

[42] https://www.pewtrusts.org/-/media/assets/2023/03/pasteur-stakeholder-support-letter-2023-committee-on-energy-and-commerce.pdf
[43] https://www.idsociety.org/globalassets/idsa/policy--advocacy/federal-funding/fy24-public-health-loan-repayment-and-bio-preparedness-pilot-program-house-appropriations-letter.pdf

of an individual patient (e.g., leading stewardship programs, infection prevention and control programs and outpatient parenteral antimicrobial therapy or OPAT programs).

- Increase NIAID funding to support training and early career ID and AMR researchers.

Once again, on behalf of IDSA, thank you very much for your attention to the critical issue of antimicrobial resistance and for inviting me to testify. We look forward to working with you and your colleagues to advance the solutions necessary to confront the AMR crisis, protect modern medical gains and save lives.

Mr. GRIFFITH. I thank you very much. We are going to take a brief timeout to change mikes for you, so that maybe yours will work next time. Apparently, we had an infected cable.

[Laughter.]

Ms. JEZEK. It is OK. ID people are used to dealing with the unexpected.

[Pause.]

Mr. GRIFFITH. All right, stand by, guys. Make sure that Dr. Mathers' mike works. Oh, yes, sounds good.

[Pause.]

Mr. GRIFFITH. All right, let's go ahead and finish our opening statements. If you all need more time to work on that, then we can do that after.

All right, thank you.

Dr. Mathers, you are now recognized for your 5-minute opening statement.

STATEMENT OF AMY J. MATHERS, M.D.

Dr. MATHERS. Chairman Griffith, Ranking Member Castor, and distinguished members of the subcommittee, thank you for holding a hearing on AMR and inviting me to testify. I am the clinical director of antimicrobial stewardship and associate director of clinical microbiology at the University of Virginia.

I am here today representing the American Society of Microbiology, ASM. With 30,000 members, it is one of the largest life science societies. Addressing antimicrobial resistance through science, clinical practice, global health programs, and policy is a top priority for ASM as well as myself.

As an infectious disease physician who sees hospitalized patients with serious infections, I am motivated by the harm AMR has had on many of the patients I care for. This hearing is very timely, as I am seeing firsthand several types of AMR bacteria and fungi that are emerging and reemerging in the wake of the public health emergency. In my clinical practice, through antimicrobial stewardship, I work with other physicians, pharmacists, and hospital leadership to minimize the selection pressure from antimicrobial overuse.

I am also a scientist. My expertise is in detecting and tracking AMR, and my research works to understand where AMR pathogens originate and how they spread in even the most sterile places like hospitals. My colleagues and I do this through collaborating on the following areas: developing novel interventions for the hospital environment to prevent transmission; developing genomic technologies to better detect and understand AMR emergence; utilizing diagnostic tools to treat infections and curtail antimicrobial overuse.

Given AMR is one of the most daunting public health challenges facing the U.S. and the world, I believe there are four elements that are crucial to addressing AMR.

First, investments in basic and translational research is foundational to addressing AMR, as there are large knowledge gaps in our understanding of the emergence and transmission. Unlike SARS–CoV–2 sequencing, where variants emerge from a single spe-

cies, AMR genes can move between bacteria and species strains, which adds a great deal of complexity.

AMR develops across a variety of pathogens, as already pointed out, and resistance may be exchanged between pathogenic and nonpathogenic bacteria. Resistant fungal infections have also emerged more recently and pose a serious threat. Perhaps the most prominent example of this is the rapid spread of Candida auris in healthcare facilities, which is now considered an urgent threat, according to CDC.

Second, improved antimicrobial resistance monitoring and reporting, especially with a focus on pathogens in hospitalized patients, both in the U.S. and globally, will be critical in addressing some of these gaps. Recent congressional funding of the Public Health Academic Partnership to adopt novel genomic technologies and improved data use through the CDC Pathogen Genomics Centers of Excellence Network will be hugely helpful if this funding is sustained.

As an academic partner in the network for Virginia, many of our projects focus on developing cutting-edge genomic tools for monitoring emerging AMR pathogens in hospitals, as well as exploring wastewater potential as a surveillance tool for AMR.

Third, improved diagnostics is critical in both preventing the continued use of antimicrobials—overuse of antimicrobials as well as maximizing the treatment of patients with AMR infections. For example, I recently had two unique patients come to UVA, both with severe bacterial infections requiring ICU care. Both were initially prescribed powerful antimicrobials while we had to guess at the type of infections that each one of them had while waiting for test results. One patient was exposed to broad-spectrum antibiotics for almost three days before testing showed a more targeted antibiotic would have worked. The other patient had a bacteria which was highly resistant and did not get effective antimicrobials for almost two days. We need investment in research and rapid diagnostics and approaches to more quickly reduce antimicrobial overuse and target AMR pathogens when needed to treat infections.

Last, another ongoing issue with diagnostics is personnel shortages in clinical microbiology laboratories. We need to recognize and incentivize people to pursue medical microbiology as a career. Adequate personnel will allow for the increased adoption of current improved laboratory practices, including the use of current susceptibility breakpoints to optimize prescribing and detect AMR, testing of newly developed antimicrobials, as well as the adoption of newer technologies which can streamline prescribing. We need more people postpandemic in the clinical micro lab.

In closing, ASM, I want to thank—in closing, ASM and I want to thank you for inviting me to testify at this really important hearing on a topic that affects every one of us. ASM and its members look forward to working with you and your colleagues to advance policies that will enable us to address the daunting challenge of AMR head on for the benefit of all humankind. Thank you very much.

[The prepared statement of Dr. Mathers follows:]

Overview of Written Testimony: American Society of Microbiology

"Antimicrobial Resistance: Examining an Emerging Public Health Threat"

Energy & Commerce Committee, Oversight and Investigations Subcommittee April 28, 2023

American Society for Microbiology (ASM), one of the largest life science societies with more than 30,000 members in the U.S. and around the globe focused on advancing the microbial sciences. We are here today because antimicrobial resistance (AMR) is one of the most daunting public health challenges facing the United States and the world and ASM has been focused on understanding the needs to address this issue.

Basic and translational research is foundational to addressing AMR as there are large knowledge gaps in our understanding of the emergence and transmission of AMR. Resources devoted to understanding the contributors and locations of antimicrobial resistance are needed to target interventions and slow or even reverse the emergence of antimicrobial resistance bacteria and fungi. Improved antimicrobial resistance surveillance both in the US and globally will be critical in addressing some of these gaps. Recent funding of public health-academic partnerships to adopt novel genomic technologies and improved use of the data through the Centers for Disease Control and Prevention Pathogen Genomic Centers of Excellence Network will be hugely helpful if funding is sustained. Funding in this area will also allow the research and public health community to explore the utility of wastewater surveillance for understanding and addressing AMR emergence and impact.

Improved diagnostics will be critical in both preventing the continued overuse of antimicrobials as well as the need to be able to maximize the treatment of patients infected with antimicrobial resistant infections. We need investment in research in novel diagnostic approaches. In addition, with ongoing personnel shortages in clinical microbiology laboratories we need to recognize and incentivize people to pursue medical microbiology as a career. This will allow for the increased adoption of current improved laboratory practices to optimize prescribing and for testing and therefore use of newly developed antimicrobials as well as adoption of newer technologies which streamline prescribing.

Written Testimony of
Amy J. Mathers, MD, D(ABMM)
Associate Director of Clinical Microbiology and
Associate Professor of Medicine and Pathology
University of Virginia School of Medicine

Submitted to the
House Committee on Energy and Commerce
Subcommittee on Oversight and Investigations

"Antimicrobial Resistance: Examining an Emerging Public Health Threat"
April 28, 2023

Chairman Griffith, Vice Chair Lesko, Ranking Member Castor and distinguished members of the subcommittee, thank you for holding a hearing on antimicrobial resistance (AMR) and inviting me to testify here today and share my expertise and perspective.

I am Dr. Amy Mathers, MD, clinical director of antimicrobial stewardship, associate director of clinical microbiology and associate professor in the school of medicine at the University of Virginia (UVA). I am here today representing the American Society for Microbiology (ASM), one of the largest life science societies with more than 30,000 members in the U.S. and around the globe focused on advancing the microbial sciences. I serve in multiple volunteer leadership roles through ASM, including as an elected leader of the Council on Microbial Sciences for the Antimicrobial Agents and Resistance community. Addressing antimicrobial resistance (AMR) through science, clinical practice, global health programs and policy is a top priority for ASM. I am also a fellow of the Infectious Diseases Society of America.

As an infectious disease physician who sees hospitalized patients with serious infections, I am motivated by the negative impact that antimicrobial resistance has had on many patients I have cared for. This hearing is very timely as I have been seeing first-hand several types of antimicrobial resistant bacteria and fungi that are emerging and re-emerging in the wake of the public health emergency. In fact, even within the last week one of our transplant patients succumbed to an untreatable infection. I bring a "bench to bedside" perspective when it comes to AMR. I conduct research at the bench, in the hospital and in the community. I also work at the interface of public health and medical research. My expertise is in detecting and tracking antibiotic-resistant bacteria and my research works to advance the understanding of where antibiotic-resistant pathogens originate and how they spread in even the most sterile places like hospitals. My colleagues and I do this by conducting research on the following areas: development of novel interventions for the hospital built environment to prevent transmission; development of technologies to better detect antimicrobial resistance and emergence; the utilization of diagnostic tools which help in the treatment and how to curtail antimicrobial overuse. Finally, we work at a basic level to understand how antimicrobial resistance evolves especially at the interface between patients and the environment. We have worked to develop genomic tools to understand transmission and emergence of AMR resistant pathogens with one of the only clinical labs in the country that utilizes next generation sequencing to track AMR pathogens. More recently in collaboration with UVA's Biocomplexity Institute (Drs. Madhave Marathe and Christian Reidy) we are working to use large data sets to build models to understand emergence of antimicrobial resistance. In my clinical practice through antimicrobial stewardship, I work with other physicians and hospital leadership to minimize the impact that antimicrobial overuse can have on selecting for resistant bacteria. In this role, I work with pharmacists and laboratorians to pair cutting edge diagnostics in the clinical lab to maximize appropriate use of antimicrobial in patients. We are here today because antimicrobial resistance (AMR) is one of the most daunting public health challenges facing the United States and the world.

Recent estimates demonstrated AMR associated deaths of almost 5 million and over 1 million directly attributable to AMR. The complexity and the urgency of the problem means it must be tackled with a

multi-faceted approach and with multiple stakeholders—from health care and clinical laboratory settings to agricultural and environmental microbial research perspectives, in the United States and around the world. It requires an understanding of the connection between the health of people, animals, and the environment – what we refer to as a "One Health" model. ASM supports policy solutions that, in the spirit of One Health, comprehensively address AMR from multiple angles and, when possible, with integrated strategies. With past support from Congress, we have made progress against AMR, but more work can and should be done to address this crisis.

My testimony today will focus on several components of the One Health aspects of AMR that I have been engaged as a scientist and clinician, and also on which ASM focuses its advocacy work. Specifically, I will discuss the importance of basic and translational research and development, including on diagnostics; the important role diagnostics play and need for antimicrobial stewardship; the role of public health surveillance and use of genomic sequencing technology to track, prevent and predict resistance; and the need to address medical microbiology workforce shortages.

Basic and Translational Research is Foundational to Addressing AMR

To address AMR's pressing challenge, our nation must continue to invest in basic and translational research on microbes through the National Institutes of Health and other federal science agencies including how they interact and persist in the environment, how they develop resistance, and how we can prevent, detect, and treat antimicrobial resistant infections. It is critical that this research focuses across the spectrum of microbial pathogens including bacteria and fungi. For example, tracking specific genes that drive AMR and which can be exchanged by unique bacterial species and not just confined to a single pathogen adds a great deal of complexity to the issue. We need to understand resistance as it emerges across pathogens and between non-pathogenic and pathogenic bacteria. Research in the area of resistance gene exchange between bacteria will be crucial for understanding the drivers of emerging antibiotic resistance. Research and development of novel diagnostic tools and approaches is an extremely important investment to prevent resistance emergence and utilization of new therapeutics. While optimizing current

diagnostics is extremely critical, developing the next generation of diagnostics that can provide rapid point of care analysis on resistance remains elusive. In addition, diagnostic testing which more conclusively demonstrated who had an infection warranting antimicrobials and those who do not would also limit unnecessary antimicrobials.

Antifungal resistance in particular is a serious emerging threat that requires more research to understand and address effectively. Resistant fungal infections have emerged more recently and pose a serious threat to plant, animal and human health in the U.S. and around the world. Perhaps the most prominent example is the rapid spread of *Candida auris (C. auris)* in U.S. healthcare facilities, which is now considered an urgent threat according to the CDC. We have large knowledge gaps surrounding emergent resistant fungi and we have fewer therapies to combat fungal infections and those we have are often highly toxic. It is especially important that we devote resources to this particular facet of AMR. Without sustained funding for research at all levels, we will not be able to make progress against AMR.

The Role of Diagnostics in AMR

Diagnostics play a central role in preventing, detecting and combatting AMR and in practicing antimicrobial stewardship in healthcare settings. The lack of rapid and affordable diagnostic tools to detect microbial pathogens is a major, often overlooked contributor to AMR. The state of diagnostics is directly connected to the long-term effectiveness of antibiotics already in the marketplace. Poor diagnostics can lead to incorrect prescribing of antibiotics and their overuse. Congress has an opportunity to expand investments in the Biomedical Advanced Research and Development Authority (BARDA) to focus on innovative diagnostics in the upcoming Pandemics and All-Hazards Preparedness Act reauthorization later this year. The newly established Advanced Research Projects Agency for Health (ARPA-H) also offers a new model for the development of novel diagnostics and therapeutics to address AMR.

An effective antibiotic marketplace requires effective use of diagnostics in addition to investments in research and development on novel diagnostics. The appropriate use of laboratory testing to guide patient

management, including treatment, is important to optimize clinical outcomes and limit the spread of antimicrobial resistance. During the pandemic it became very clear how essential clinical testing was to preventing COVID-19 transmission by detection of infected persons who could then go into isolation to prevent transmission. Some of the same principles also apply to AMR as knowing who is carrying or infected with highly resistant bacterial and fungal infection can aid in isolating and preventing transmission. Supporting clinical laboratories in though workforce development to adopt diagnostics for improved AMR detection as well as supporting research to develop novel and improved diagnostics are both critical in combatting toe spread as well as managing patients impacted by AMR.

Prescribing appropriate and timely therapy is critical to the proper management of infectious diseases. For example, when a patient is in the hospital for an infection, the first line of therapy is usually a broad-spectrum antibiotic while we wait for the results of the test to come back. Because current diagnostics take time to inform the practitioner of the type of infection, the consequence is that while we wait, we could be inadvertently using the wrong antibiotic or the wrong dose of antibiotic. This delay results in worse patient outcomes with antimicrobial resistant infections but also contributes to resistance emergence, increases hospital stays and as a result, increases health care costs. Rapid diagnostics can promote the prevention of unnecessary antimicrobials as well as by allowing the targeting of antimicrobials earlier. In addition, for patients with antimicrobial resistant infections novel diagnostics can be used to detect resistance sooner and employ novel antimicrobials which are reserved largely for the treatment of patients with AMR infections.

Another aspect of diagnostics is critical to the practice and treatment of antimicrobial resistant infections is through up-to-date susceptibility testing. Research and development in the area of pharmacology, clinical infectious diseases and microbiology all work together to make sure that susceptibility testing and reporting of resistance is accurate and using the most current research to inform clinicians how to treat infections. This is done though a consensus process and sometimes results in changes suggested in antimicrobial susceptibility testing and interpretation. It is critical that clinical laboratories are supported in making changes to use the most current and clinically informed susceptibility testing and reporting

standards to detect, report and give information to clinicians for how to treat antimicrobial resistant bacteria. We know that there has been a lag between the updating of testing recommendations and updates made by the Food and Drug Administration. This in turn often slows the adoption of new and updated breakpoints by clinical microbiology laboratories, leading to an underestimation of emerging resistance as well as the potential for worse outcomes for patients with serious infections. The 21st Century Cures bill championed by this Committee made strides to improve this process, but there is still work to be done.

The Role of Public Health Monitoring and Genomic Sequencing in Addressing AMR

Historically antimicrobial resistance is detected in clinical laboratories, but this has not necessarily been publicly reported or coordinated with state or regional epidemiology. Monitoring emergence of resistant organisms plays a unique and important role in combating antimicrobial resistance. As we will not have endless antimicrobials to count on in the future, prevention of antimicrobial resistance transmission will be critical. Using detection of resistance and reporting to understand where and how resistance is emerging can prevent the spread of resistant infections generally, allowing for fewer cases of drug resistant infections and elongating the effectiveness of current therapies. Deploying systems in the health care setting such as improved reporting and data sharing between clinical facilities, clinical laboratories and public health where antibiotic resistant infections are endemic and emerging is paramount to developing and targeting interventions. The current challenge lies in setting up systems and coordinating their data to drive a larger understanding of the problem and allowing targeted solutions to be deployed.

Leveraging next generation sequencing technologies both in research and in public health is an important way to detect and track resistance in both healthcare and environmental settings. We thank Congress for making important investments in this space and authorizing expanded partnerships and programs, but we need robust and sustained funding for programs funded through the Centers for Disease Control and Prevention's (CDC) National Center for Emerging and Zoonotic Infectious Diseases, which are critical to addressing AMR and complement the research and development taking place in academic centers and in the private sector. The CDC Advanced Molecular Detection (AMD) program supports technologies that help public health laboratories detect existing and emerging antibiotic-resistant organisms, including some of the biggest threats we face such as *Clostridioides difficile* (*C. diff*), "nightmare bacteria" carbapenem-resistant Enterobacteriaceae (CRE), the fungus *Candida auris*, *Mycobacterium tuberculosis*, and *Neisseria gonorrhoeae*. By adding AMD technologies to antibiotic resistance surveillance, scientists can look more deeply at these pathogens to understand their emergence and prevent transmission. Ultimately this type of data can also assist healthcare providers select the most effective medications to treat infections.

Thanks to recent, supplemental investments made by Congress in the AMD program, the CDC has established innovative public health-academic partnerships to advance the technology and capitalize on the potential synergistic strengths of public health and research entities. Last September, the Centers of Disease Control announced 5-year awards to five public health departments to establish the Pathogen Genomics Centers of Excellence (PGCoE) network. The PGCoE network is meant to foster and improve innovation and technical capacity in pathogen genomics, molecular epidemiology, and bioinformatics to better prevent, control, and respond to microbial threats of public health importance. Using many of the lessons from the COVID-19 pandemic, the network also represents an unprecedented opportunity to expand and deepen collaboration between U.S. public health agencies and academic institutions to form a national resource to better prevent, control, and respond to microbial threats of public health importance.

Each center of excellence consists of a health department and one or more academic institutions. I am proud to be an academic partner from one of these centers with a large portion of the research devoted to the emergence of AMR. Our partnership is between the Virginia Division of Consolidated Laboratory Services, the Virginia Department of Health, Virginia Commonwealth University, and my institution, the University of Virginia. UVA's role as part of the Center focuses on how "superbugs" which often do not respond to existing antibiotics, can emerge and be tracked by public health using next generation sequencing. We propose to develop genomic tools for improved use of data to understand AMR emergence including tools to better track AMR gene sharing between bacteria. In addition, we will perform the further refinement of wastewater surveillance to detect antibiotic resistance, as well as other infectious diseases. We hope to develop more accurate models and analyses of both future infectious disease outbreaks as well as the effects of antibiotic resistance through the data and information we collect.

This program has enormous potential, but it will not be sustainable without a strong commitment from Congress moving forward.

Another novel approach has been in wastewater surveillance. This method has already been shown during the COVID-19 pandemic to be an extremely useful metric for measuring the disease and guiding response to outbreaks and was significantly expanded during the public health pandemic. That said, the applications for AMR are still a new surveillance technique, and there is a lot of research needed to hone this into a fully operational and routine tool in our arsenal. Given viruses only live in humans or host animals, the signal we are receiving from wastewater likely reflects active shedding from hosts. Some bacteria however can live in persist in the environmental waste stream and may end up being too far divorced from what is going on in humans to replicate the same use as viral surveillance. However, wastewater AMR surveillance research is ongoing and our ability to understand emerging pathogens including the possibility that the environment is an ideal location for AMR gene exchange will be critical. No doubt, wastewater surveillance is on the cutting edge or frontier of surveillance and time will tell the extent of its effectiveness in identifying AMR pathogen emergence and impacts on human health.

We very much appreciate that Congress is funding this work and Centers as part of the supplemental funding provided in 2021, and I hope Congress will continue to fund this and other such initiatives as they have enormous value and future potential.

The Role of Medical Microbiologists in Fighting AMR

ASM appreciates the Committee's attention to the needs of the healthcare workforce and the threat that shortages have on patient care and the broader medical ecosystem. Clinical laboratories, including microbiology laboratories, have experienced personnel shortages for many years now, and the COVID-19 pandemic shone a spotlight on the critical need to bolster this workforce. Without medical microbiologists to validate, develop and conduct antimicrobial susceptibility testing and infectious disease diagnostics, we cannot make progress against AMR. Shortages not only compromise diagnostic and antimicrobial stewardship efforts, but also prevent laboratories from updating susceptibility testing methods, bringing new testing platforms online and also lead to unacceptable delays due to the need to "outsource" the tests.

The pandemic only exacerbated an existing shortage in medical laboratory scientists and infectious disease laboratory professionals. In 2016, several years prior to the pandemic, the Bureau of Labor Statistics predicted we needed 12,000 new clinical laboratory professionals annually to meet rising demand. At that time the vacancy rate for medical laboratory scientists working in clinical microbiology laboratories was 6.25% and the vacancies for supervisory positions was nearly 4%. By 2018-19, the vacancy rates had grown to 10.56% and nearly 7%, respectively. These facts, coupled with the anticipated retirement of 20% of staff in microbiology departments over the coming years, set the stage for what has now become a full-blown crisis.

We must address these shortages and plan for the future. While the challenges facing the profession are myriad, the federal government can provide incentives and support. These include the establishment of loan forgiveness programs that include medical microbiologists and other medical laboratory scientists, both in and outside of public health settings and the establishment of federal training grants for medical microbiologists and other medical laboratory scientists and professionals. Diagnostic tests in infectious disease also are reimbursed at lower rates than other types of tests; sometimes not fully covering the cost of the test. This has the downstream effect of devaluing the work of the laboratory and subsequently the profession, depressing salaries and in some cases, leading to substandard care.

AMR is a Global Threat

Lastly, we must think globally when considering strategies to address AMR. AMR is not only a public health threat but a national security threat, and rising resistance anywhere is a threat everywhere. As a global scientific society, ASM urges Congress to consider how federal support here in the U.S. can also extend to addressing research, surveillance, stewardship efforts in countries around the world. Aligning US domestic AMR policy with the global policy infrastructure is critical to tackling the problem, and U.S. policy must reflect the global challenges while also reflecting specific domestic concerns. One area

where the US experience can be instructive is laboratory capacity. Globally, laboratory availability and capacity can be limited, particularly in lower-middle income countries. And the labs that do exist often do not have access to the necessary infrastructure to perform the basic surveillance and testing required to assess AMR. Congress must continue to support the U.S. Antimicrobial Resistance (AR) Laboratory Network funded through CDC and which is now authorized to focus on global laboratory capacity to provide technical assistance to countries around the world to address AMR.

In closing, on behalf of ASM and myself I want to thank the Chairman, Ranking Member and the Subcommittee for inviting me to testify at this important hearing on a topic that affects each and every one of us. ASM and its members look forward to working with you and your colleagues to advance policies that will enable us to address the daunting challenge of AMR head on for the benefit of all humankind.

Mr. GRIFFITH. Thank you. Let me apologize on behalf of the committee that, you know, we had our team down there working in front of you while you were giving your statement, and at one point they actually popped up in front of you. The fact that you kept your composure is remarkable, so we appreciate your patience.

That being said, I do appreciate all of your testimony, and thank you for being here today and for that testimony. We will now move into the question-and-answer section of our hearing, and I will begin the questioning by recognizing myself for 5 minutes.

Now, you all are the experts. You are probably wondering why we finally paid attention to this. And it is not just me, but there were others who were interested in this. But I got hooked a few years ago when I read "The Perfect Predator."

For those at home that may not understand this, this is a great romance story with a medical mystery wrapped all around it. It is good stuff.

[Laughter.]

Mr. GRIFFITH. Ms. Jezek, in—for those who don't have time to read the book or figure it out on their own, could you please share with the committee and with those at home what phage therapy is and how it could be an effective tool to combat AMR, or be an alternative to antibiotics in those cases where needed?

Ms. JEZEK. Absolutely. So we think phage therapy actually has a great deal of progress—or a great deal of promise, but there is not enough known about it.

So most of the information that we have now about phage comes from reports collected through compassionate-use cases. And in many of those cases, phage was actually used in addition to and in concert with antibiotics for infections that were not responding to antibiotics on its own, suggesting that phage therapy has sort of an additive effect.

But what clinicians really want are more robust studies to help them understand all the different kinds of indications where we could use phage to help us better understand how phage resistance can develop, because that happens, as well, and to help us understand the optimal dosing and duration of phage therapy, so that we can really make sure patients get the greatest benefit. It is really an area where more research could yield tremendous benefits.

Mr. GRIFFITH. Well, and in the book that I just referenced, Thomas Patterson's life was saved. His wife was a virologist who had all kinds of medical folks, and they did use a cocktail of antibiotics. In the end, what did it was they found—I think it was a Maryland sewage treatment plant—they found a virus that attacked the shell of the bacteria that was causing all of his health problems—and he was in a coma—and they found a bacteria that cracked the shell, but they still needed the antibiotic to kill the bacteria off. So you are exactly right.

So that being said, let me ask you this, because this is one of the problems that we have, and I am glad the FDA granted them compassionate use in that case. But we are so used to having the clinical trials, but so many of these AMRs are one-offs or very rare. Some of them aren't. We have heard about the case in Washington. But clinical trials aren't going to work, are they, for a lot of these fixes?

Ms. JEZEK. Well, I think we can get more creative with our approaches to clinical trials.

Mr. GRIFFITH. All right.

Ms. JEZEK. I think for phage, in addition to clinical trials, simply having one central database, where anyone who is using phage in a compassionate-use setting or any other setting can report that data, and making sure that we are reporting not only the cases where phage worked, but also the cases——

Mr. GRIFFITH. Where it didn't work.

Ms. JEZEK [continuing]. Where phage didn't work, because sometimes we learn as much from our failures as we do from our successes.

There—I believe there actually is a clinical trial for phage therapy that is starting to get up and running. So we are hopeful that we will have more information soon.

On the antibiotic side, yes, clinical trials are difficult, there are a lot of enrollment challenges, but they are absolutely possible. And in fact, the 21st Century Cures legislation included some provisions to streamline and improve clinical trial processes. It is really the economic challenges that several of us talked about that are the biggest barrier right now for antimicrobial R&D.

Mr. GRIFFITH. And this committee as a whole is very proud of the work we did on 21st Century Cures.

Professor Outterson, you have been wanting to jump in on these issues. Jump on in.

Mr. OUTTERSON. I also wanted to be polite to Amanda Jezek.

CARB–X supports three phage companies. I think it is the most concentrated support anywhere in the world for phage.

I would say that they are moving into clinical trials, and it will be interesting how they interact with the FDA and the agencies to make sure that they are well supported in that endeavor.

I would say I know Tom and Stephanie, the authors of this book, well. I would encourage you to—maybe to have a hearing in which you just hear from patients, because the stories that they tell—and people like them—are remarkable.

Mr. GRIFFITH. We are certainly working to maybe have that happen, but this is step one. And obviously, there is more than just phage. That is what I am interested in, because of the book, but there's a whole lot of things that each of you all have touched on.

Dr. Mathers, did you want to jump in on this? And I apologize——

Dr. MATHERS. Sure.

Mr. GRIFFITH [continuing]. I am not probably going to have time to get to you, but somebody will.

Dr. MATHERS. Very, very quickly, I just—I think with your question about clinical trials, they are really important. But I think the days of, you know, penicillin, finding another penicillin or finding another fluoroquinolone, or, you know, a kind of magic bullet, if you will, that antibiotics were coming from the 1950s through—into the early 1980s, and coming to market, those days may not exist. And so we may have to cobble together in a different way than our historic clinical trials to treat antibiotic resistance and to actually get drugs to market.

Mr. GRIFFITH. And it is important, and I will just make this note before I yield back. It is important that we get these things to market quickly, particularly when we don't have anything else that might work.

I note that George Orwell died of tuberculosis with probably about 6 to 8 months before antibiotics were available for him to use.

But anyway, I yield back and now recognize Ms. Castor for her 5 minutes for questioning.

Ms. CASTOR. Well, thank you, Mr. Chairman, and thank you for providing me a copy of the book. I am going to dig into it really soon, and thanks to our witnesses.

I want to focus on two important factors identified by our—the experts here today as being essential parts of the approach to AMR diagnostics and surveillance. Arming doctors with better diagnostic tools can allow them to provide more targeted care to their patients.

Dr. Mathers, in your testimony you say that diagnostics have, quote, "a central role in preventing, detecting, and combating AMR and in practicing antimicrobial stewardship." What improvements in diagnostic tests are most needed, and how would those advancements help doctors provide better care to patients with infections?

Dr. MATHERS. Thank you so much for the question. I—you know, diagnostics are so critical to preserving antimicrobials. And as more antibiotic resistance emerges, we are going to need diagnostics to make sure that we target. With these sort of niche antibiotics, you don't know what somebody is infected with. Current state, when somebody comes in with a serious bacterial infection, you do not know what they are infected with. We do not have immediate antibiotics. Things that would tell us whether or not somebody has a bacterial versus a viral infection would be very helpful for doctors in prescribing.

And then once, you know, you take the blood, let's say they have got blood—or a bacteria in their blood, we take their blood. Right now sometimes it takes 3 to 4 days before we know which bacteria, and what that bacteria is susceptible to so that we can really target antibiotics. In that timeframe sometimes we have to use multiple antibiotics that the patient really doesn't need, when we could be using more targeted antibiotics. So the collateral damage of resistance selection and overuse is occurring during that time.

So if we had—if we could move the clock back and have more rapid diagnostics, that would be helpful.

Ms. CASTOR. So what is your recommendation to Congress to move ahead on that?

Dr. MATHERS. So I think there's a couple of different things. I think investments—and CARB–X, I know does—also looks at diagnostics, but investing in diagnostic technologies, and research and development in how we could move the clock backwards for diagnostics. Some of this will probably be molecular and genomic, and some of it may be taking advantage of the fact that the bugs grow so well and cheaply, because we want them to be affordable and not break the bank, as well.

Ms. CASTOR. Great. And, you know, one of the lessons we learned from the fight against COVID–19 was the importance of data gath-

ering and surveillance, high-quality data, to understand and respond to a public health threat.

Dr. Denigan-Macauley, GAO found in its 2020 report that CDC faces challenges in conducting disease surveillance for antibiotic resistance. And they made—you made recommendations to improve the collection of public health data from various stakeholders. You noted, though, that CDC has made some progress on addressing these recommendations, but you are—they remain open. How can improving the quality of reporting critical information to the CDC improve the U.S. response to AMR?

Dr. DENIGAN-MACAULEY. Yes, we reported that the data is neither comprehensive or complete, and this is particularly the case if you have data that is voluntary. So a lot of the data that is coming in is required only for certain organizations—for example, the VA or DoD—because of the tie, obviously, with the Federal Government. So if you have something that is optional and you have hospitals that already are taxed and short on resources, being able to get that data, even if they could do it, to the Federal Government is very challenging.

And there is some promise out there. It is our understanding that there is some legislation that is going to come into effect in 2024 with some strings for hospitals to improve their data collection, which will definitely help with our surveillance activities.

Ms. CASTOR. Because I understand across the data-reporting enterprise from local communities, States, hospitals, it is just so outdated. And we—the Congress provided significant funds to help modernize reporting. Not having to do it by fax machine would—that is so costly.

So what is your recommendation for us to continue focusing on this, and providing public health interest the ability to report in a modern fashion, efficient fashion?

Dr. DENIGAN-MACAULEY. Well, as I mentioned in my oral statement, I mean, there are a lot of parallels with what we see with antibiotic resistance as we saw with COVID. And so not losing the gains that we have—we already lost some of the developments that we had with antimicrobial resistance with the pandemic, seeing the number of resistant infections going up any time you have more people in a hospital, and the strains have an opportunity to be able to spread and infections rise—so making sure that we don't lose the gains that we already have.

Many of our recommendations also went to HHS. They have to get a better understanding on how much information is enough to know what the magnitude of the problem is and to be able to track the progress. And for example, if COVID were to come back, it would be disheartening if we weren't able to know when are we done, when are we out of this problem. And so we have recommendations to HHS, and we urge Congress to not lose the gains that we made during COVID.

Ms. CASTOR. Thank you.

Mr. GRIFFITH. The gentlelady yields back. I now recognize the chairwoman of the full committee, Mrs. McMorris Rodgers, for 5 minutes of questioning.

Mrs. RODGERS. Thank you, Mr. Chairman. According to the Congressional Research Service, there are over 10 task force commit-

tees and programs across the U.S. Government, including 5 separate interagency programs that are specific to or include antimicrobial resistance and—oh, OK, so that is that. And then eight different offices and agencies within Health and Human Services: AHRQ, ASPE, ASPR, CDC, CMS, FDA, NIH, and the Office of Global Affairs. So each one of these have individual, ongoing work on AMR, and this is in addition to the numerous multilateral efforts the U.S. is a part of, and internationally.

So I wanted to start with Ms. Denigan-Macauley. Has GAO examined to the extent there is coordination and collaboration among all these efforts, or at least the sharing of lessons learned?

Dr. DENIGAN-MACAULEY. We have. And we are happy to report that, because there is a presidential task force and there is a coordinating body, there is the task force among the Federal Government—and within HHS they are currently leading that—there is a task force right now that has a rotational leadership capacity between USDA, DoD, and HHS, and HHS has the lead. Within that they have ASPE, that is helping to coordinate.

So from GAO's standpoint, we always look at leadership. Leadership is absolutely paramount, and those coordination—understanding roles and responsibilities is key, as well. So we have looked at that. We did make a recommendation about how to better coordinate. In one particular aspect we were talking about diagnostic tools and resistant infections and making sure that there is not a lot of finger-pointing of who is going to take the lead to ensure that we have the studies that are needed to show that using diagnostic tests have outcomes—have positive health outcomes so that we have judicious use of antibiotics.

Mrs. RODGERS. Thank you. And you referenced this, because I was focusing on Health and Human Services and the programs there, and then there's seven different USDA offices that have AMR programs, and other departments such as DoD, State Department, EPA, USAID, VA, and Department of the Interior each have their AMR efforts. Would you speak to how well the Federal Government is doing with a problem like this, when it is assigned to so many departments and agencies?

Who is responsible for the strategy—which I think you were talking to a little bit—who can be held accountable, and how can any progress, lessons learned, or successes be shared appropriately?

Dr. DENIGAN-MACAULEY. Yes. So as I mentioned before, we do have a task force. We do have leadership, which is extremely important.

This is a very complex issue, and we are pleased to see also that we are taking a One Health approach. This is not just a human problem. This is a problem of agriculture. We give drugs to our food animals in a preventative measure. We also give drugs to our pets. It happens in the environment, and resistance occurs naturally. So that coordination across the Government is absolutely key, and the fact that we have task forces that are able to do that coordination across the Government is very good.

You had mentioned lessons learned. One of the recommendations that we did make was you not only need to report on their progress—which, I want to say, they do report yearly on the progress to the President that they are making—but you need to,

I think as Dr. Mathers had said, you need to also talk about your failures. What can't you do?

That is where we are having the problems. That is why we don't make the progress that we need. We need to own up to that and to say, "Here is what we need." And we do see in the budgets this year at least there is mention of antimicrobial resistance and some need for direction there.

Mrs. RODGERS. OK. Well, as a followup to that, you—in your testimony you discuss how HHS and CDC haven't taken significant steps to address information on uncertainties around estimates of resistant infections and creating timely, comprehensive reports on antibiotic resistance. Would you tell us any—you want to elaborate any more on the efforts to achieve those recommendations and the consequences of not achieving them?

Dr. DENIGAN-MACAULEY. Yes. So the agencies did agree with the recommendations. They are working on them. They understand the importance of this. As I mentioned, it is a complex issue. It is not only one that impacts the United States, but we are global, right? We travel. The COVID showed us that, the COVID–19 pandemic.

More is needed, though. As I mentioned, the CMS rule is promising. Having hospitals require reporting is quite important, but we also don't have a good understanding of what is happening in our community. And we had mentioned the fact that we had problems—COVID complicated the number of resistant infections. But if you recall, a lot of people weren't even going to the doctor.

Mrs. RODGERS. OK.

Dr. DENIGAN-MACAULEY. We don't know that——

Mrs. RODGERS. I am out—I appreciate that. There is more.

I just want to highlight that there's always fiscal concerns, and programs always request more funding. The 2020 report outlines certain funding provided. BARDA has awarded 959 million in grants, agreements, contracts to developers of antibiotic drugs since 2010. CARB–X funded 47 programs, costing up to 133 million. I recently sent a letter to NIH regarding the $1 billion they have spent on public relations and communications—$1 billion. Perhaps NIH could do a better job of allotting funding that is already—should be put towards fighting this AMR program—or problem.

Yes, I yield back.

Mrs. LESKO [presiding]. Thank you. And now I recognize the ranking member of the full committee, Mr. Pallone.

Mr. PALLONE. Thank you. Democrats on this committee have long prioritized a holistic approach to public health preparedness and response. And over the past 2 years in particular, we have taken steps to foster a resilient public health workforce, protect disproportionately impacted communities, and empower researchers to understand how infectious diseases begin and spread. And public health preparedness requires that Congress and the American people encourage rather than stifle beneficial research, and build trust in our public health institutions rather than tearing them down.

So let me start with Dr. Mathers. As we emerge from the COVID–19 public health emergency, what are some of the lessons that we can take away from the pandemic to better tackle challenges like antimicrobial resistance?

Dr. MATHERS. Thank you so much for the question. I think there's a couple of things that I take away from it.

First off, we are seeing emerging antibiotic resistance postpandemic. The CDC has incomplete data, as already was highlighted. But from the data that we do have, there is emerging resistance in some of the most significant pathogens, especially those affecting hospitalized patients, which to me says what we were doing and how we were able to dedicate the same resources that then had to be somewhat diverted to manage the public health emergency in hospitals and clinical micro labs and in infectious disease writ large, it was working to prevent the emergence of antibiotic resistance.

There were several areas where we were making progress and seeing decreased. And now that we sort of took the eye off the ball, we are seeing in our hospitals—like, in my hospital I am seeing antibiotic resistance I haven't seen in years, and in a way that it is affecting patients—now sort of postpandemic, but maybe postpublic health emergency.

And so what we were doing was probably working. I think that—yes, I guess the main answer to my question.

I think that, you know, the other things that we need is we need to—you know, it has kind of come across here—we need to both preserve the antibiotics we have with efforts in antimicrobial stewardship and diagnostics that we talked about, but also to come up with new antibiotics so I have agents to give patients. I have—I mean, it was within the last month that I just had a patient that expired from an untreatable antibiotic infection.

I mean, this is happening in hospitals right now. And I need new antibiotics, or maybe, like I am alluding to, it may not be that we have another super antibiotic or magic bullet because the bacteria have really developed armor for the antibiotics we have. And so we probably need multipronged approaches between all the different technologies to treat antibiotic resistance.

And lastly, I will say that surveillance would be hugely helpful. Patients transferred from other hospitals, I don't know what their resistance looks like at that hospital because we don't have a central repository to really communicate about antibiotic resistance emergence, even at a State level, let alone Federal Government level. I mean, it is all voluntary right now. So there's just huge gaps in where are the problems. And as a researcher trying to understand where should we put our efforts, I don't really know or have resolution on what the biggest issues are.

Mr. PALLONE. Let me just ask you one more question, because we are out—almost out of time. But one of my concerns coming out of the pandemic is that the public has lost trust in some of our public health institutions and in doctors, generally. So do you have—can you talk about the importance of patients' trust in their doctors and medical institutions when dealing with these—you know, this issue?

Dr. MATHERS. Yes, I am not an expert in this, but I can tell you personally I feel it. I feel mistrust from patients, and it feels like somebody else is at the bedside. I don't know if it is social media or who is—but it—there is just a lot of misinformation that has

been out there that has impacted trust that is making it harder to take good care of patients, and rightfully so.

You know, I think there were a lot of—you know, we had a novel virus that a lot of people didn't know what to do with, including myself or—and so we had to change course many times, and I think that caused mistrust because maybe we overpromised and underdelivered in some areas, as a medical community, not as a society. So I think it is a big issue.

And I think antimicrobial resistance is such a complicated issue, it doesn't fit in a sound byte. And so it is going to be really hard to communicate why this is so important and how it is affecting individuals—maybe until it is too late.

Mr. PALLONE. Yes, I mean, I worry because, as we said earlier, you know, you have these challenges as to, you know, basically telling people when they should take things, when they should not. And if they don't trust the doctors or the health institutions, they are not going to listen. So thank you so much, really.

Dr. MATHERS. Thank you.

Mr. PALLONE. Thank you, Madam Chair.

Mrs. LESKO. Thank you. And now I recognize Representative Guthrie for his 5 minutes of questioning.

Mr. GUTHRIE. Thanks, Madam Chair. I appreciate the recognition.

And Ms. Denigan-Macauley, we are currently 2½ years into our national plan for combating antibiotic resistance bacteria. Could you give us an update on this plan, and focus on—you know, the first national plan released in 2015 indicated there were 6 milestones in progress, and 5 not achieved. And would you address where we are in the plan and how we are going to ensure we effectively address the milestones that weren't achieved?

Dr. DENIGAN-MACAULEY. Yes. The new plan came out after we last reported. So we have not done a deep analysis on that plan. However, it is our understanding that they are behind in doing their progress reports. And so we will be reviewing those as part of our recommendation followup when they do come out.

Mr. GUTHRIE. We want to make sure we meet the new milestones, or—that weren't achieved. So just—would you commit to working with us, the committee——

Dr. DENIGAN-MACAULEY. Absolutely.

Mr. GUTHRIE [continuing]. To ensure that we get to those—thank you very much.

And Mr. Outterson, how does CARB–X decide which products to invest in, and why?

And since 2016, how many of these products that have been funded have reached the market, and what are some of the specific products on the market?

Mr. OUTTERSON. Thank you, Mr. Guthrie, for the question.

CARB–X makes its decisions based on using an external scientific review committee. We always pick based on what we think is the best science. We then evaluate across our portfolio using a portfolio risk and value tool to try to—because we want to take many shots, we are quite early, we do translational work that is just barely out of the university into a small start-up company.

And our deliverable is to result in products that are—have completed their first in-human clinical trials.

At that point, the follow-on funders are groups like BARDA as well as the AMR Action Fund and other private investors. To date we have had 12 products, therapeutic products, that have gone into clinical—human clinical trials, first in-human trials. And of those, the—none of the therapeutics are anywhere near FDA approval. That is probably another 5 to 8 years away, just—it takes time. But two of our diagnostic products that we have supported are actually on the market. They have CE marks in Europe that are not yet approved here in the United States.

Mr. GUTHRIE. Yes, you mentioned BARDA. So CARB–X has also been supported by NIH—infectious diseases at NIH, as well as BARDA. Can you outline specifically how this money has been used and what successes there are to show for it?

And I know you had always—and areas that—anything. I was a quality engineer, you always look at needs for improvement and room for improvement. And what are those, and what are your plans for improvement?

Mr. OUTTERSON. Certainly. The money that we receive from BARDA right now is 40 million USD per year. We have leveraged that by attracting other governments and other charitable foundations to support CARB–X. Our total spend is—BARDA is a little bit less than half of our total expenditures. The NIH provides preclinical services to CARB–X-supported companies but doesn't fund us directly. But they collaborate with us in the governance, together with BARDA.

The program—you know, the goal here is to radically enhance the pipeline, the quality of the pipeline. And as we have heard from many witnesses, the clinical pipeline today, the things that we have seen recently, are not very innovative, and not new classes, as the witnesses have said.

In the therapeutics and CARB–X, almost everything that we have supported is an entirely novel class—would be the first in my lifetime, really, to make it—or an entirely new mechanism of action, or something that is so new that there is not even an established FDA path. We call these nontraditionals, things like phage. Many of the products that we support are two out of those three, and more than a dozen or three out of those three.

And so we are taking high-risk, high-reward shots. And our goal is to deliver, again, you know, through first in-human testing so that others like BARDA behind us, downstream from us, can take those forward.

Mr. GUTHRIE. Thanks. And also, getting back to BARDA, in the Consolidated Appropriations Act of 2023 there was $950 million provided to BARDA, and 820 million for the Project BioShield Reserve Fund. And how does CARB–X interact or benefit from the—particularly, the BioShield Reserve Fund? You had—you mentioned BARDA already, but the BioShield Reserve Fund.

Mr. OUTTERSON. Yes, I don't think the—CARB–X doesn't receive any money from the Project BioShield Reserve Fund. We receive $40 million per year. And so all of that other money goes to other antimicrobial programs at BARDA, including their phase two, phase three, broad-spectrum antimicrobial program.

The BioShield program, they have funded two antibiotics companies with that program, and that has been publicized, but that is completely separate from CARB–X, and much further downstream, these are companies that are either on the market or almost on the market, typically.

Mr. GUTHRIE. OK, thank—perfect timing. My time is expired, and I will yield back. Thank you.

Mr. GRIFFITH [presiding]. I thank the gentleman for yielding back. I now recognize the gentleman from New York, Mr. Tonko, for his 5 minutes of questioning.

Mr. TONKO. Thank you, Mr. Chair, and thank you and the ranking member for bringing attention to what is a very important topic.

I would be remiss if I didn't mention that this was a topic close to the heart of my good friend, the late Congresswoman Louise Slaughter. As the only microbiologist in Congress, Louise raised the alarm on antibiotic resistance. And in her honor, I hope that as a Congress we can continue to work on this issue and build on her legacy.

Each of you here today has talked about how the situation is only getting more dire, and that is why federally funded research is so important as we move forward. I recently heard from a family in my district who knows how urgent the situation is. They have a 6-year-old named Kellen, who was diagnosed with cystic fibrosis when he was a newborn, just 9 days old.

Kellen is a funny, athletic, and vibrant kindergartner. Kellen plays baseball, hockey, and football. He adores his older brother and is the heart and, as they say, funny bone of their family. Kellen's family feels fortunate for the breakthroughs in the CF medical world. Kellen has, unfortunately, had two bouts with Pseudomonas, along with other respiratory and lung infections that required Kellen to take antibiotics to fight off the infections.

Antimicrobial resistance is a fear for Kellen's family, along with others who live with CF, because they know that this is a likely issue they may face somewhere down the road if he becomes resistant to the few antibiotics that can indeed fight these infections.

Recognizing the magnitude of the threat, President Biden's budget for fiscal year '24 includes increased funding for CDC's antimicrobial resistance and public health data modernization efforts, increased funding for Project BioShield, and steady funding for NIH's National Institute of Allergy and Infectious Diseases, which funds research into diagnostics and novel treatments for antimicrobial resistant infections.

So, Mr. Outterson, what do we need to do to more efficiently translate this research into new treatments for those who need it most, like my constituent Kellen?

Mr. OUTTERSON. Thank you for the question, and thank you also for remembering Louise Slaughter.

The CF community is remarkable. I have spent a lot of time talking to these individuals, and it is shocking that the new drugs are—they are not dying from cystic fibrosis anymore. They are dying from resistant lung infections. And this is a tragedy. And I have met and talked with many of these people that are struggling with that.

What we have to have, then, are entirely new classes, entirely new approaches to restock the pipeline. I mean, penicillin was a wonderful drug. We would love to have a drug that good again. And it is just hard to do it without taking radically difficult scientific approaches.

For the companies, given how little money is to be made, they have typically stayed within known classes and focused on things that are small, incremental improvements. And so at CARB–X we take the 40 million a year from BARDA and match it with other governments, and we invest in things that are completely, radically novel so that 5 or 10 years from now we will actually have options for patients like this young man.

Mr. TONKO. Thank you, sir.

And Dr. Mathers, what benefits have Federal investments, including partnerships between the Federal Government and academic institutions like the University of Virginia, brought about in addressing antimicrobial resistance?

Dr. MATHERS. Thank you for the question. Just in my own experience, CDC has funded us to understand transmission of highly resistant bacteria within the hospital environment and funded research and successfully developed interventions through that funding to prevent the spread of antimicrobial resistant organisms from the hospital environment to patients. And so that has been one successful funding effort.

I would say also there has been some really important developments in the way that we do susceptibility testing, and partnership between the—you know, the way that we test bacteria for susceptibilities through standard development organizations like CLSI and FDA, with the 21st Century Cures Act. That was quite helpful in making sure that we are updating and adopting current breakpoints based on available new science so that those can be used readily in micro labs across the country. And so that has been incredibly important partnership and recognition and funding that has come.

I would say most recently, with the Pathogen Genomics Centers of Excellence, like I have already alluded to, the complexity around antibiotic resistance tracking and genomics and even the way that the bacteria exchanged the resistance genes is really complicated. And so that effort is getting going, and that partnership, I think, will bear fruit.

Mr. TONKO. Well, I certainly hope there is hope on the horizon in terms of battling antibiotic resistance and provide that kind of inspiration for Kellen and his family and many of those individuals that are waiting on that kind of progress.

So thank you, one and all, for your exchange here. It is important to get updated. So thank you so much.

And I yield back, Mr. Chair.

Mr. GRIFFITH. I thank the gentleman. I now recognize the gentlelady from Florida, Mrs. Cammack, for her 5 minutes of questioning.

Mrs. CAMMACK. Thank you, Mr. Chairman, and thank you to our witnesses for appearing before us today. We will just jump right into it.

And I hope I pronounce this right. Ms. "Jezz-ick"?

Ms. JEZEK. Yes.

Mrs. CAMMACK. Ah, yes. All right.

[Laughter.]

Mrs. CAMMACK. It is a good win on a Friday.

As you know, in my home State of Florida, hurricane readiness, preparedness, response, these are significant issues that we all face. In your testimony you noted how resistant infections can impact our response and response time to national disasters like hurricanes. Can you tell us a little bit more about the connection between antimicrobial resistance and natural disasters, how we can be better prepared on the front end?

Ms. JEZEK. Absolutely. Thank you for the question. So with hurricanes, there are a couple of different things that can happen that can trigger an increase in infections. When we see widespread loss of activity, we see increased food spoilage and more foodborne infections. When we see decreases in access to safe water, and when we see interactions with floodwater, we start to see more infections from waterborne pathogens. When people need to leave their homes and have to go to emergency shelters, those shelters can be very crowded. That is a very easy area for infections to spread.

Many of those infections can be resistant. Even when those infections are not resistant, if individuals are given antibiotics, that can help fuel future resistance.

As we think about other types of natural disasters, wildfires, serious burns can very easily become infected with pathogens that are very difficult to treat.

So as we think about preparedness for natural disasters, we need tools in the toolbox to deal with these infections, so we need those novel antimicrobial therapies and we need experts who know how to use them, who can figure out quickly—because hours matter in infectious disease——

Mrs. CAMMACK. Yes.

Ms. JEZEK [continuing]. Who can really figure out quickly what does this patient have, and what is going to be the most effective treatment.

Mrs. CAMMACK. Thank you. And just to build on that, so taking it from a natural disaster to maybe a national security threat, a natural—a national or even global incident, you talk about all the different ways in which antimicrobial resistance could lead to a national security crisis.

And I know certainly we are alarmed of some of the things that we are hearing today, but when you think of it on a massive scale and how it could potentially lead to the proliferation of an antimicrobial resistance, can you share with the committee how it is a threat, this issue that we are discussing today is a threat to national security, and what we need to do to be better prepared on a national and global scale?

Ms. JEZEK. Absolutely. Well, as terrifying as it is to think about, pathogens can easily be weaponized, and the pathogens can be engineered to become more resistant and weaponized. And if they—if some bad actor were to weaponize an antibiotic-resistant pathogen and spread it across the United States, we are not prepared. We don't have the therapeutics that we need. We don't have the

diagnostics that we need. We don't have as many infectious diseases experts as we need.

Even getting away from bioterror specifically, any mass casualty event where you have a lot of people in a hospital, that can be—any kind of terrorist attack, it can be another pandemic—if our hospitals get overwhelmed, we start to see these infections really flourish, and we need more tools in the toolbox.

Mrs. CAMMACK. Thank you for that. This is getting scarier as we go through this, so——

Ms. JEZEK. I am sorry.

[Laughter.]

Mrs. CAMMACK. My apologies to everyone on a Friday, but it is important. And you know, you hit on this, so I am going to shift to Ms.—I am going to—I hope I get it right—"Den-eh-gen-Ma-call-ee"? OK.

So your report discusses four areas for addressing this issue, AMR: surveillance, testing, treatment, and stewardship. Of these, which is the most important, and what should this committee be prioritizing?

Dr. DENIGAN-MACAULEY. Yes, unfortunately, I can't tell you which is the most important because they all go hand in hand. As we had mentioned, this is a One Health approach. It is very complex.

So, for example, if you create a new antibiotic, if you don't have judicious use of that antibiotic, you are just going to end up with resistance again. So really, they all go hand in hand. You have to understand the magnitude, you have to be able to track the spread for all the different things that we have talked about today.

Mrs. CAMMACK. Thank you. And the GAO, based your work—based on your work, what has the Federal Government done to combat AMR, and how successful have those efforts been?

And I fear that I know the answer to this question, but for the record.

Dr. DENIGAN-MACAULEY. Well, I do want to give credit. There has been a lot of work. And as we have talked about before, there have been tasks force. Having leadership and sustained attention is absolutely critical. It is something the GAO feels very strongly in, and having hearings like we are having today and continuing this attention. Our report came out in 2020—unfortunately, in the midst of the pandemic. And so being able to continue and bring this to light—this is a pandemic. It is a public health threat.

And so they do have many efforts underway. But as I had mentioned in my opening statement, there are more things that need to be done. We need better diagnostic tools. We need those tools to be able—we need doctors to use those tools. Even if we have them, you know, when the—when someone walks in with a screaming baby and they are, like, "I have an ear infection," and the doctor only has a few minutes with them, are they going to take the time to decide whether or not, you know, they are giving the right antibiotic to treat the right bug, as has been mentioned before.

So it is quite complicated, and there's a lot of things, but more is definitely needed, and GAO continues to track this as we go forward.

Mrs. CAMMACK. Thank you. My time has expired.

With that, Mr. Chairman, I yield back.

Mr. GRIFFITH. The gentlelady yields back. I now recognize the gentlelady from Illinois, Ms. Schakowsky, for her 5 minutes of questioning.

Ms. SCHAKOWSKY. Thank you so much, Mr. Chairman. I want to thank our witnesses so much. This is so very, very important. This has been somewhat of a difficult morning with votes, et cetera, but I am so happy that you are here with your expert testimony.

So I have really, throughout my life and career, really focused on older Americans. So it really was no surprise to me when the CDC pointed out that Medicare patients were most likely to actually die from drug-resistant infections than—in American hospitals than any other—than any other group. So I wanted to ask Dr. Mathers or any of you who would like to comment on this, are there any precautions, protocols that should be in place in hospitals right now that would be particularly more protective of older patients that are in hospitals?

Dr. MATHERS. Thank you so much for the question. And the geriatric population is of particular interest to me, and I think they are particularly vulnerable to antimicrobial-resistant infections.

So for me, it is critically important in antimicrobial stewardship—so just sort of day to day—they are one of the groups I worry about the most in the hospital, especially because of an infection called C. diff, which is related to antimicrobial overuse and is one of the recognized threats by the AR reports from CDC. And so unnecessary antibiotic exposure can disrupt the gut flora and then allow persons to become vulnerable to this bacterial infection that can cause death, in fact, but often causes a severe diarrhea. Elderly patients are more vulnerable to that infection. And so I am—I mean, just my day-to-day work is trying to make sure that we are not overusing antibiotics in geriatric populations.

Also, again, back to the importance of diagnostics: If we had better diagnostics, is it really a urinary tract infection or is it some other infection that may be mimicking other symptoms in the geriatric population? More research—and research has been coming out.

And again, I think it gets back to Amanda Jezek's—you know, we need experts to be able to diagnose, work with new diagnostics to make sure that we are diagnosing and using antibiotics properly in our geriatric populations so that we don't overuse antibiotics and put them—and select for more resistant infections, as well as put them at risk for infections that they wouldn't otherwise have following antibiotics.

So I really appreciate the question, and——

Ms. SCHAKOWSKY. Did you want to answer, someone else? I mean, anyone. This is a real——

Ms. JEZEK. Thank you. I would just expand. The protocols that are needed, infection prevention programs, antimicrobial stewardship programs, they are in place. In fact, they are typically required, but they aren't staffed appropriately.

Even before the pandemic, we saw studies showing enormous gaps between recommended staffing levels for stewardship programs of infectious diseases physicians and pharmacists and the staffing levels that we actually had. And that is even at big, major

academic medical centers. It is worse when you get into more rural hospitals. And they can't hire people. We consistently hear open positions, positions staying open for months, months at a time for ID physicians, for infection preventionists, for clinical lab personnel. We need to incentivize people to go into these careers.

Ms. SCHAKOWSKY. Thank you.

Yes, go ahead.

Mr. OUTTERSON. If I may.

Ms. SCHAKOWSKY. Sure.

Mr. OUTTERSON. There was a milestone yesterday in that the first microbiome therapy for recurrent C. diff was approved by the FDA, and it kind of got lost in the news. It is a remarkable first-in-class approach. And that company has been working on that for more than a decade. CARB–X actually supports a more advanced version of their product, which is—we have been working with them for 5 years now—and it is a—you know, it takes time to get these things done, and—finally got across the line, first FDA approval ever. It is great.

Second thing is data. Many people who die in hospital with a resistant infection, the death certificate does not say AMR. It says something else. And until we collect the data to know how many people are dying, we won't respond appropriately.

Ms. SCHAKOWSKY. OK. In the few seconds, I just want to say that, overall, aren't we using too many antibiotics, and ultimately, especially for seniors, because through their lifetime—that this is a problem? Is this a yes?

Dr. MATHERS. Unfortunately, yes.

Ms. JEZEK. Yes.

Ms. SCHAKOWSKY. OK.

Dr. DENIGAN-MACAULEY. I will add, though, that we need better data on use.

Ms. JEZEK. Yes.

Ms. SCHAKOWSKY. OK. Thank you so much.

I yield back.

Mr. GRIFFITH. The gentlelady yields back. I now recognize the gentleman from Texas, Dr. Burgess, for his 5 minutes of questioning.

Mr. BURGESS. Thank you, Mr. Chairman, and just following up on that last question, let me just ask: Is anyone on the panel an M.D. and treats patients?

OK. So you know when you are treating a patient, you are treating that patient, you are not treating a population. And the expectation of that patient and their family is you are going to get them better, and you are going to use every tool at your disposal to get them better.

Dr. MATHERS. Absolutely.

Mr. BURGESS. And the argument that, well, you know, we are holding this back so it might benefit someone else later on, that really doesn't fly in the clinics, does it?

Dr. MATHERS. I appreciate the question, and I agree. My day-to-day job is antibiotic stewardship, so talking to physicians about these difficult discussions, and then also talking to patients about these difficult discussions, and you have to be a really good doctor to know when you can, you know, hold back antibiotics.

Diagnostics would help, if we could tell viral from bacterial infections sooner.

Mr. BURGESS. Sure.

Dr. MATHERS. As well as working with patients to talk through, "I don't think an antibiotic is going to be helpful. I recognize you are very sick," and then also talking through and educating doctors. That is part of my bread and butter.

You know, pancreatitis, maybe we don't need—even though it looks like an infection, it is actually an inflammatory response that doesn't require antibiotics often. And so working with my ICU doctors or my surgeons, I go on surgical rounds trying to help and educate other doctors. But there's not enough people trained like me, or maybe even that want to have these discussions.

So I think it is a really good point, though. And I always want doctors to treat the patient in front of them.

Mr. BURGESS. Sure.

Dr. MATHERS. And I support that, and then I need to support them.

Mr. BURGESS. We have had hearings on this subject multiple times over the years. They are always important, and I always learn a lot when we do these. But I also have to remember the father of our country died from what began as a pharyngitis and turned into a peritonsillar abscess. They didn't have antibiotics back then, but it would have been a lifesaving intervention had it been available.

Dr. MATHERS. Yes, there is nothing more exciting when you save somebody's life with antibiotics in my ilk, as a physician.

Mr. BURGESS. Yes.

Dr. MATHERS. And so I want to preserve those so that the next generation of physicians and patients can benefit from that.

Mr. BURGESS. Well, I do thank each of you for being here, and I thank you for your insightful testimony that you have provided.

Professor Outterson, if I could just ask you, I represent a part of Texas that is kind of outside the area where you normally think of San Joaquin Valley fever, but you are finding it outside of its normal distribution. So are there things that are going on now in your world that are working on fungal infections broadly, because there—that is emerging as a new threat, and then in particular the San Joaquin Valley fever problem?

Mr. OUTTERSON. So I actually grew up in Texas, spent 18 years there in Clear Lake and, no, had never heard of valley fever at that time in Texas. But valley fever and other fungal infections are rising in importance and focus. People understand now, and it is—for example, fungal infections are on the CDC threat list, and people are taking it seriously.

For CARB–X specifically, if that was your question——

Mr. BURGESS. Yes.

Mr. OUTTERSON. Our authorities from BARDA limits us at the moment to bacteria. And so that is a decision that is made by BARDA.

Mr. BURGESS. OK. Well, are there lessons learned from other countries that could help us in these decisions?

Mr. OUTTERSON. I think the key lesson is that, if you want a new drug to treat an infection today, you needed to have started 10 years ago. And so we need serious research efforts today.

I was talking to a—Rob Purdy who is a, you know, a patient advocate on valley fever, he suffered from it personally himself, was talking this week. It is a much more serious condition than I think the average people in the public understand. We need to respond to it with the same level of seriousness.

Mr. BURGESS. Well, in fairness to this committee, we were talking about this 10 years ago. Unfortunately, we haven't done the follow-on that is necessary, and maybe this hearing and this year will be different.

Dr. Mathers, you mentioned diagnostic tests, and everyone is now more familiar with diagnostic tests, one of the positive sides to coming through the COVID pandemic. But how can we encourage the greater use of diagnostic tests before prescribing an antibiotic?

Dr. MATHERS. Yes, I think that good diagnostic tests need to be available, and I think making sure that we have got the workforce to run good diagnostic tests—we do not. We have shortages and gaps. And I am just at University of Virginia. We have had openings in our clinical micro lab for—since 2020. And so we need people going into a career in medical microbiology——

Mr. BURGESS. Yes.

Dr. MATHERS [continuing]. So that we can give the result, we can run the tests, and give timely results so that it can help patients.

In addition, I think, you know, research and development in diagnostic tests is also needed. Thank you.

Mr. BURGESS. Thank you, Mr. Chairman. You have been very indulgent. I will yield back.

Mr. GRIFFITH. I thank the gentleman for yielding back. I will say one of the concerns about having this hearing was that folks were afraid that everybody would want to blame the doctors, and the doctors are just trying to cure patients' problems.

That being said, I now recognize another doctor on the committee, Dr. Ruiz, for his 5 minutes of questioning.

[Laughter.]

Mr. RUIZ. Thank you, and thank you for that statement.

Antimicrobial resistance is a problem here at home and around the world. Resistant pathogens do not care about geographical borders, so we must make sure that we address this issue not just in the United States but globally.

The World Health Organization reported in 2014 that, quote, "a postantibiotic era in which common infections and minor injuries can kill is a very real possibility for the 21st century," and declared antimicrobial resistance one of the top 10 global public health threats facing humanity.

So, Mr. Outterson, how does global collaboration improve our ability to tackle this problem?

Mr. OUTTERSON. Thank you for that question. You know, more than half of the funding from CARB–X comes from outside the U.S. Government. It is the U.S. Government, together with the governments of the United Kingdom and Germany—so three G7 mem-

bers—with charitable foundation support from Wellcome Trust and the Gates Foundation. This is a global problem.

We always make our decisions at CARB–X looking not just at any one country but everywhere, because the best way to know what might threaten a U.S. hospital today or in 5 or 10 years is to visit a hospital in India or Pakistan or some other place. And you will see the sort of things that we will be seeing in a short period of time, or we could see today from somebody coming home on an airplane.

You know, what Tom Patterson almost died from he contracted in Egypt——

Mr. RUIZ. Yes.

Mr. OUTTERSON [continuing]. And then was flown back in emergency, you know, settings. So it has to be a global response——

Mr. RUIZ. Thank you.

Mr. OUTTERSON [continuing]. You have to work together with other countries.

Mr. RUIZ. Thank you.

Dr. Denigan-Macauley, has the GAO identified any areas where the U.S. Government could better engage with international partners to address the increased spread of AMR?

Dr. DENIGAN-MACAULEY. We have. And we do believe strongly—and part of our methodology was to go over and to speak to how that better engagement could occur. We met with the WHO and with members over in the United Kingdom, as well. So we do believe that global engagement is very important, and we continue to track that.

And honestly, they turn to us as leaders. So if the U.S. doesn't take action, then other countries do get worried. And that was a common message that we heard.

Mr. RUIZ. This is very interesting. I was just thinking, I know we have infectious disease doctors on the panel, and my—one of my medical school professors and mentor was Dr. Paul Farmer. And so I am thinking of the central plateau of Haiti, and how very few people have access to even the most basic antibiotics, period. And so here we are, trying to increase the access to lifesaving basic antibiotics for common infections, and at the same time we are trying to limit its use, its improper use in these areas, which pose a big challenge, especially in the most underserved, resource-poor settings.

As in many other areas in healthcare space, there are workforce challenges at play. So, Ms. Jezek, your testimony says that there is a shortage of infectious disease physicians. And are there certain regions of our Nation or specialties that are most in need of infectious disease doctors or consultations?

Ms. JEZEK. Thank you for that question. So we know that nearly 80 percent of counties in the United States do not have a single infectious diseases physician, and the shortages are worse in more rural areas.

I think what is even more disconcerting is looking at the future. We are not training enough infectious diseases physicians. So the most recent match where residents get placed into their specialty fellowship programs, only 56 percent of ID training programs filled their positions.

Mr. RUIZ. Wow.

Ms. JEZEK. And that is not true across other medical specialties. Most specialties are filling all or nearly all of their programs, and this really has to do with a lot of the financial challenges. Infectious diseases doctors actually earn less money——

Mr. RUIZ. Yes.

Ms. JEZEK [continuing]. Than general internal medicine physicians despite getting that additional training——

Mr. RUIZ. Yes.

Ms. JEZEK [continuing]. Because of the way that we reimburse for physician care.

Mr. RUIZ. Yes. Dr. Mathers, how do investments in building a skilled healthcare workforce contribute to better prevention, diagnosis, and treatment for AMR?

Dr. MATHERS. I think that the question is very timely. I think we need not just infectious disease physicians, but we need infection prevention personnel, epidemiologists, and we also need clinical microbiologists, and——

Mr. RUIZ. You know, I think, you know, we have two problems with the physician shortage crisis that I have been working on. And I exist and live in communities where I did research before I ran for Congress, where we had one-time—full-time equivalent physician, 1 per over 9,000 residents. So we have an absolute physician shortage crisis.

But we also have a—on top of that, a crisis of its distribution of our physicians. And we don't have a strategic plan or an idea or objectives to help create the incentives for where we need the doctors and where they are needed the most to be able to really increase access for the—our—the American people who need it the most.

So it is something that I would like to work with the committee on establishing, so that we can take a bird's-eye strategic plan to help address critical areas in the provider workforce that would make the biggest difference to create a healthy population and keep our health safe.

Thank you, yield back.

Mr. GRIFFITH. I thank the gentleman for yielding back. I now recognize the gentleman from Alabama, Mr. Palmer, for his 5 minutes of questioning.

Mr. PALMER. I thank the chairman.

Director Denigan-Macaulay, what can we do to improve communication between healthcare facilities and to prevent the overuse or overprescription or misuse of antibiotics?

Dr. DENIGAN-MACAULEY. So the Federal Government has taken a variety of steps to try and what we call stewardship and judicious use of the antibiotics. But there are barriers. There is only—the data is not sufficient that is coming in. We have to be able to say—we have to be able to understand the question earlier about the use.

We have to be able to understand how much is being used, where the infections are occurring so that we can tailor the communication to those areas specifically. Agriculture doesn't want the finger pointed at them. Human Health doesn't want the finger pointed at them. So getting better data will help us to say with certainty

where judicious use is needed, and to communicate and to make better communication.

Mr. PALMER. Well, how rigorous is the reporting when you have—whether it is a rural hospital or a major metropolitan hospital or veterinarian, when they discovered the antibiotics are not working as they should, that the—because of resistance? Do we have a rigorous reporting requirement that would allow you to accumulate the data that you need?

Dr. DENIGAN-MACAULEY. So we do not. As of right now, really, the rigorous reporting requirements are for the VA and DoD hospitals, for example. We—there is new legislation out there that hopefully we are going to get better reporting coming from the hospitals because of the CMS angle, the Medicare-Medicaid angle that we can get there. We don't have rigorous reporting coming in from the general community.

And there can be silent infections, and we just don't have that reporting at the doctor level, either. So there is much work to be done.

Mr. PALMER. Mr. Chairman, that is an area where I think we need to engage more vigorously on our side to try to get to a point where we are getting this data.

One of the things, Ms.—I believe it was you, Ms. Jezek, on the third or fourth time you tried to give your testimony, you mentioned the—one of you mentioned the fact that these drug development companies are not able to recover their investment, their stranded cost. What suggestions do you have for that?

Was that you? I believe it was you.

Ms. JEZEK. I think both Mr. Outterson and I both did, but I can start.

So we pay for antibiotics based on the volume that is used, and we want to try to keep that volume as limited as possible, particularly for the really new, novel antibiotics for these multidrug-resistant infections, so that preserves their effectiveness. So we need a different way to pay for antibiotics. We need a way that will allow us to pay for the value that they provide to society rather than just paying per use.

And I know it is not a legislative hearing, but I would be remiss if I didn't say the bipartisan PASTEUR Act that Representatives Ferguson and Peters just reintroduced yesterday would set up exactly that kind of subscription model that would allow the Federal Government to enter into contracts with antimicrobial developers to really pay for the value that these antimicrobial drugs provide, delinked from how much or how little of the drugs are actually used.

Mr. PALMER. OK, I am going to—go ahead, if you would like to add to that.

Mr. OUTTERSON. I completely agree and would say that other G7 governments are taking the same approach. The UK has had their subscription model in place now for a couple of years, and they are about to revamp it and improve it. Japan announced that they are intending to do it on April 1st. They will say more about it at G7. Europe this week made their proposal public. And so everyone is hoping that the U.S. will also lead on this issue.

Mr. PALMER. And one of my concerns, too, is the exposure this creates for our armed services. And I see this is a huge healthcare issue, but I also see it as potentially a national security issue and that we could be exposing our troops to things that we don't have the antibacterials to treat. I could see it with the number of immigrants that are coming into our country as well, that we could have a major healthcare crisis, but we could also turn it into a serious crisis dealing with our military. Have you looked at that, as well?

Ms. JEZEK. Absolutely. And combat wounds and combat burns are two of the easiest things that can become infected. There was a new study that came out a couple of weeks ago looking at infections in individuals in the current conflict in Ukraine and found some of these infections were enormously resistant to even some of our very new, novel antibiotics. And it is very frightening because, once we see these in a small population, they can spread very quickly.

Mr. PALMER. Mr. Chairman, we have made remarkable progress in treating our wounded on the battlefield, particularly in that golden hour. And it would just—it is shocking to think that we could have someone survive a battlefield wound and then die from an infection.

So I thank you for holding this hearing. I think it is extremely important. I look forward to what we are going to do going forward, and I yield back.

Mr. GRIFFITH. It is interesting that you mention that, because my understanding is that penicillin was considered a state secret when it first came out because of its advantages on the battlefield.

Having said that, I now recognize—and thank you for yielding back—I now recognize the gentlelady from Arizona, the vice chair of this subcommittee—thank you for filling in when I went to vote—Mrs. Lesko.

Mrs. LESKO. Thank you, Mr. Chair.

Ms. Mathers, how long do University of Virginia medical students study antimicrobial resistance and how to combat it?

Dr. MATHERS. So that is a great question. I think that we actually need improved education in antimicrobial effectiveness and management.

And so we have started at UVA giving stewardship lectures. Between myself and my partner, Heather Cox, who is a pharmacist, we give a joint stewardship lecture once they learn the basics of how antibiotics work and how we test them, and then we come back and talk through how to not overuse them, how to make sure that you understand your role as sort of the keeper of this precious resource.

And so——

Mrs. LESKO. So is it about an hour?

Dr. MATHERS. Yes.

[Laughter.]

Dr. MATHERS. So later on it is about an hour.

Mrs. LESKO. OK, all right. Thank you.

Ms. Jezek, can you go into more detail about the efforts that your society, the Infectious Disease Society of America, is making to increase awareness of AMR and to educate physicians on AMR?

Ms. JEZEK. Absolutely. So we have developed a couple of different curricula at different levels, beginning with medical students and then on for physicians that are a little more advanced in their training, to learn about appropriate antibiotic use.

For physicians that are becoming infectious diseases physicians, we have curricula to teach them about how to run an effective antimicrobial stewardship program, which is really, again, focused on making sure patients get the optimal treatment. We certainly don't want to, you know, deny antimicrobial drugs to people who need them, but we want to make sure they get the right drug.

We also—our members do an enormous amount of communications through media briefings, through social media, through every communication channel that we can find. And they do this both through the Society and on their own, as individuals, to educate the public, to educate their communities about AMR. And we have actually found that oftentimes those individual physicians are some of the most effective messengers, because there has been an erosion of trust in some of the more maybe government-associated messengers on this. And so having those ID physicians in the communities as those messengers is so important.

Mrs. LESKO. Yes, that is important.

Mr. Outterson, I want to give you the opportunity to highlight the major accomplishments that CARB–X has done since its inception.

Mr. OUTTERSON. I think the key way to measure success at CARB–X is whether highly innovative products make it into human clinical testing. And I am happy to say that it was not prearranged, but our annual report came out yesterday, and we show exactly that sort of progress with the, you know, more than a dozen in the—outside of the diagnostics coming directly into human clinical testing. And then, for the diagnostics, a couple of them actually are now on the market in Europe.

Mrs. LESKO. I—that is my last question, so I yield back.

Mr. GRIFFITH. I thank the gentlelady for yielding back. I now recognize the gentleman from North Dakota, Mr. Armstrong.

Mr. ARMSTRONG. Thank you, Mr. Chairman.

According to the American Veterinary Medical Association, of the 118,000 veterinarians in the United States, only about 5.3 percent, or around 6,000, are in the food animal space. There is a shortage of large-animal veterinarians throughout North Dakota, especially in rural areas where producers often need veterinarians to drive hours to inspect cattle and livestock.

I understand that antimicrobial resistance is a global health and development threat that requires a multilateral approach to ensure we promote their appropriate use. And while the responsible usage of antibiotics is crucial, I am also concerned about the effects of the recently issued FDA rule on ranchers and farmers who do not overmedicate their animals. Ranchers are already under extreme economic pressure, and we have to balance the effect of antimicrobial—I have a really hard time saying that word——

[Laughter.]

Mr. ARMSTRONG [continuing]. Policies with unintended consequences on the food supply. Medication of livestock by producers is expensive and takes up significant amount of producers' time.

However, groups on both sides of this issue recognize that overmedication is something that can and should be prevented.

Ms. Jezek, how do we ensure that the FDA's regulatory action in this space balances concerns with antimicrobial resistance with potential—potentially unintended consequences on the food supply?

Ms. JEZEK. Thank you for the question. I will say the animal health space is not my area of expertise, but I think that, as we have seen in human health, having good surveillance and data collection to understand where and how antimicrobials are being used and to understand how resistance patterns are tracking is critical to inform those efforts. And I think making sure we have that complementary data collection and surveillance on the animal and agricultural side is critical.

And I think Dr. Mathers may have more.

Dr. MATHERS. I would just—you know, at clinical—as the CLSI are coming up with standards and testing and susceptibility—actually, as I understand it, working with veterinarians there—the ability to diagnose and understand what animals have resistant organisms by susceptibility testing is also a really important area to focus on, I think, and having more veterinarians in the space.

So the vets that I work—at—in that space, trying to come up with standards because cows metabolize penicillin different than humans do, and that is different than chickens do. So we need research in each one of those so that we make sure that, when we are giving an antibiotic effectively to an animal, it is one that is going to work.

Mr. OUTTERSON. Mr. Armstrong, I think you can't just tell a rancher or a farmer no and not give them a good option. That is going to bankrupt them. So I think we also need to be researching vaccines in other ways so that there is—animals don't get sick.

In Norway, the farmed salmon 20 years ago required 1 pound of antibiotic for every pound of salmon produced until they came up with a vaccine, and now Norwegian salmon has almost no antibiotics use. So I would strongly support giving farmers excellent tools so that they don't—aren't forced with this choice that you are describing.

Mr. ARMSTRONG. We—I am—it is interesting we brought Norway into this conversation. My father-in-law was a microbiologist and an oncologist in Oslo, Norway.

But—and I think, like, you know, there's opportunities for educational campaigns, responsible stewardship, and all of those different issues. And I appreciate the research. And we do need more large-animal vets. We need them in places like North Dakota. We need them all over the country.

I just get concerned we recognize we need all of those things, but far too often in this space what ends up happening is we pass a regulation and then try and figure it out later. And, I mean, between drought and travel and the lack of availability of real veterinary services in all of these places is—I appreciate the answers, I just—we have to do them both at once. We can't pass a regulation and then come back to this 3 years later, 5 years later and say, "Well, we don't have the resources to actually do this," because the rancher in western North Dakota is going to have to follow the regulation, regardless if the actual resources exist.

Dr. DENIGAN-MACAULEY. Yes, I just wanted to mention the GAO does have a body of work looking at the veterinarian workforce. We agree that there is a crisis there. And we had asked OPM to step in and to help because one of the things we found, too, is that you are pulling the veterinarians from a very limited pool to, you know, to more lucrative jobs, for example, in the private sector, and they don't want to work in the food animal sector.

And we also have a body of work looking at the animal side and surveillance that is needed on the farm and the diagnostic tools.

Mr. ARMSTRONG. I know two large-animal veterinarians in North Dakota that retired a decade ago. They are busier today than they were when they retired.

And with that, I yield back.

Mr. GRIFFITH. Maybe these folks can work with the veterinarians in my district. I have the only district with two schools of veterinary medicine, although one is licensed to Harrogate. Virginia Tech always tells me that. They are not licensed in Virginia.

[Laughter.]

Mr. GRIFFITH. And I say, yes, but I have been there, and it is in my district.

That being said, I now recognize Mr. Carter of Georgia for 5 minutes of questioning.

Mr. CARTER. Thank you, Mr. Chairman, and thank you for allowing me to waive on to this subcommittee, and thank you all for being here. This is extremely important.

Professionally, I am a pharmacist, and I have witnessed over the years the excessive use of antibiotics that has led to a lot of this, and it has been a concern for many years.

I am always in awe of the advanced—advancements that we have made in research and development. You know, I started practicing pharmacy when I—in 1980, when I was 10 years old, by the way.

[Laughter.]

Mr. CARTER. But anyway, I have seen nothing short of miracles, and I mean that sincerely, nothing short of miracles as a result of research and development. And so I am a big fan of the pharmaceutical manufacturers from that aspect of it. But I am very, very concerned about the antimicrobial resistance and about the overuse of antibiotics.

I get it. I know the pressure that physicians are under when you got a mother who has just been struggling with a child's ear infection and is just demanding that they—and no one was as demanding as my wife whenever she took our sons in. And so I get it, and I understand that. But this is something—so I am glad we are—and I am glad that this subcommittee is looking at that, and that our full committee is looking at it, because it needs to be addressed.

We had an example just 6 months ago where we had some contaminated eyedrops that were causing highly resistant eye infections, and this is—this was a never-before-seen strain of bacteria that left patients blind and in need of a corneal transplant. You know, that is the kind of thing we need to avoid in this country. That is why the time is now to invest in the pipeline.

And I get it. I—look, I know we live in a capitalist society, and I know that—and pharmaceutical manufacturers are going to invest in the drugs that are going to give them and their investors—their stockholders, if you will—the biggest returns. I understand that, and I have a healthy respect for that. But that is where we in Congress need to be assisting and need to be making sure that we have got a pipeline out there of these antibiotics and, in particular, because they are not as profitable as maybe the cancer drugs are, or some of the other drugs. And that is why I was a cosponsor of the bipartisan PASTEUR Act legislation last Congress, and why I am again this year, in this session.

Mr. Outterson, I wanted to ask you. In your testimony you said that pull incentives like subscriptions are now needed. Can you dumb that down for me, and tell me what pull incentives and subscriptions are?

Mr. OUTTERSON. Thank you for making the effort to be at this committee today and waiving on.

Certainly, you know, the language sometimes is too professorial, and I apologize for that. But for antibiotics, we don't really want the drug that sells to a million people or 10 million people, because that would represent a public health disaster. The best case is that infection control does a great job and everything else works perfectly, and we only need these new drugs for a small number of patients.

Now, in some disease areas, that—they would then charge $1 million for that drug for a small number of patients, and that is how the company makes money. In antibiotics, we really don't want the million-dollar drug. The PASTEUR Act or subscriptions tries to pay for the value to society for this drug, even if the volume, especially in early years, is quite low. And so the company goes away not bankrupt, we don't have any incentive to overuse it, but it is there when we need it for the patients who need it.

And the last thing I will say is that, for CARB–X, the companies we support, the companies that are doing all the innovation in this space, the average size—about 20 full-time employees. Big Pharma has generally left. It is tiny startup companies that are doing a lot of the innovative——

Mr. CARTER. Right, and you articulated that well. Thank you for that. That is important for people to understand, and thank you for that explanation.

Ms. Jezek, in your testimony you described the overuse of antibiotics. Through your research have you uncovered any reason for the overuse of antibiotics, besides what I mentioned in my experiences as a pharmacist?

Ms. JEZEK. I think there are a lot of reasons, and I think oftentimes when a patient presents and they are very, very ill, you don't know right away what is infecting them. But because hours can matter in treating an infectious disease, you need to treat them right away, empirically, while you wait for the test results from diagnostics to come back.

I think we also don't have enough experts who really understand the best ways to use our antibiotics. So a lot of inappropriate antibiotic use is giving someone the wrong antibiotic or keeping them

on it for the wrong duration. And so making sure that we have more people who are trained in how to use antibiotics is critical.

Mr. CARTER. So giving them a standing prescription so the mother won't be calling every 15 minutes.

Ms. JEZEK. I was that mom too. I get it.

Mr. CARTER. Been there and done that. Listen, I know.

So thank you all. This is this is extremely, extremely important, and I want to compliment you and applaud you for what you are doing. I know this firsthand.

And Mr. Chairman, again, I want to thank you for this hearing, and it is vitally important.

So thank you all, and I yield back.

Mr. GRIFFITH. The gentleman yields back, and I appreciate it.

And let me say to the witnesses, we appreciate you being here. This has been a great panel. Everybody has been engaged and passionate. And even with our technical difficulties and the vote series taking place, it says a lot when you have Members coming back, and the vote has been over for 45 minutes or more on a Friday. That tells you that folks are really interested in this issue, and we greatly appreciate it.

Seeing no further Members wishing to ask questions, I would thank our witnesses again for being here.

And pursuant to committee rules, I remind Members they have 10 business days to submit additional questions for the record, and I ask the witnesses that they submit answers 10 days following the receipt of the questions from the Members who may have additional questions for you.

Again, thank you all so very much for being here.

That being said, meeting adjourned.

[Whereupon, at 11:01 a.m., the subcommittee was adjourned.]