

STATEMENT OF

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ON BEHALF OF

**THE ANTIMICROBIALS WORKING GROUP (AWG) AND THE BIOTECHNOLOGY
INNOVATION ORGANIZATION (BIO)**

BEFORE THE

**U.S. SENATE COMMITTEE ON HEALTH, EDUCATION, LABOR, AND PENSIONS
SUBCOMMITTEE ON PRIMARY HEALTH AND RETIREMENT SECURITY**

HEARING ENTITLED

**SUPERBUGS: THE IMPACT OF ANTIMICROBIAL RESISTANCE ON MODERN
MEDICINE**

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I – Opening Remarks

Chairman Markey, Ranking Member Marshall, and distinguished members of the Committee, thank you for the opportunity to speak with you today. My name is Christine Miller, and I am President and Chief Executive Officer (CEO) of Melinta Therapeutics. Melinta is a small, innovative biotechnology company providing life-saving therapies to patients impacted by acute and life-threatening illnesses. In addition to my role as CEO, I serve as Chair of the Antimicrobials Working Group – or AWG – a coalition of emerging antimicrobial companies committed to improving the commercial environment for drug development. Melinta is also a member of the Biotechnology Innovation Organization (BIO), the largest trade organization representing biotechnology companies, academic institutions, state biotechnology centers and related organizations in the US and 30+ countries.

My story begins in the New York, the product of two amazing parents who immigrated from Jamaica. I grew up in a family where the women were all in healthcare as either nurses or dietitians and dedicated their careers to helping patients. My mother, a Registered Dietitian, worked at Montefiore Hospital for 38 years. I remember visiting her at the hospital as a child and watched her solve patients' problems. I too have always been passionate about problem solving and applied that to degree in Chemical Engineering. I was inspired to pursue a career in pharmaceuticals when I realized I could use my education, like my mother and the women of my family to help patients. Everything that I have tried to do in my 20 plus year career is about creating access for patients so that they can get the medicines they need. That's why being here in front of you is so important to me. I want to help identify the unmet need of patients and providers and address the issue of how we can create the access needed to live-saving antimicrobials medicines.

Put simply, antimicrobial drugs are the cornerstone of modern medicine. These drugs are critical for the effective delivery of medical care more broadly for patients receiving chemotherapy, organ transplants, and even those undergoing routine surgical procedures like hip replacements and cesarean sections. However, bacteria and fungi adapt and evolve over time and become resistant to these treatments -- a phenomenon known as "antimicrobial resistance," or AMR for short. Overuse and misuse of current antibiotics accelerates AMR. For example, in the outpatient settings, the CDC estimates that one-third of antibiotics are used improperly.¹ This rise in AMR is rapidly rendering our antimicrobial arsenal ineffective and represents a problem in the here and now – it will also continue to get progressively worse over time. As AMR becomes more prevalent, many medical procedures that are commonplace today will become too risky to undertake, with catastrophic consequences to medical care, including death.

As I was drafting my testimony today, I was reminded of a story from one of our patients – Sue Paxton. Sue, who is a resident of Manakin Sabot, Virginia, was the recipient of a successful liver transplant, and while hospitalized, found out she had a severe fungal infection. After multiple rounds of antifungals and further deterioration of her condition, Sue and her infectious disease physician were able to gain early access to rezafungin, a novel anti-fungal developed by Cidara Therapeutics and that Melinta will launch later this month, and within a few days, Sue was on the path to recovery. When I asked Sue, a mother and grandmother about her experience, she was

¹ <https://www.cdc.gov/media/releases/2016/p0503-unnecessary-prescriptions.html>

extremely grateful to her medical team that they were knowledgeable about the latest in the field and could help her get access to the innovative medicine she needed. I was moved, when she said, “It was a live-saving drug for me, I wouldn’t be here without it”. New, innovative, and effective antimicrobials used in the hospital setting are critical to saving lives like Sue’s– and her story is a testament to the importance of today’s hearing.

Unfortunately, what happened to Sue happens all too often in hospitals. The only way to combat these life-threatening infections is to continually innovate newer, safer antibiotics, and to ensure their access and appropriate use. AMR is a “silent pandemic” in the American healthcare system. In my testimony today, I hope to convey how serious a threat AMR is to our nation, and why the challenges surrounding this issue have become so difficult for our health system to overcome.

The problem right now is that our nation’s physicians lack the access needed to prescribe these innovative products, and in turn, patients are not receiving the care that they need. This broken ecosystem for antimicrobials has created an unviable marketplace that renders innovative drugmakers unable to develop the products needed to catch up – and keep up – with the growing threat of resistance.

From an industry perspective, antimicrobial development is uniquely different than any other area of biotechnology. Unlike a disease area like oncology, it is very rare for a patient to know *exactly* what type of infection they have and *exactly* what drug they are being given.

Remember, also, that antibiotics are intended to be used sparingly and only until the infection has resolved to prevent further exacerbation of resistance. What this means for industry is that many companies have tended to focus on other novel product areas, such as chronic diseases, where there is a more stable and long-term market for therapies. It is not surprising then that the vast majority of research being done in the antimicrobial space today is led by small companies like ours, and not large pharmaceutical firms.

Many are familiar with the concept of the “valley of death” – the period between promising lab research and clinical trial launch when biotech companies run out of funding. It takes 10-15 years to develop one successful drug, and despite significant investments in time and money, 90% of drug candidates fail in clinical trials, never reaching regulatory approval.ⁱⁱⁱ The antimicrobials sector faces another unique obstacle, what many of my colleagues have termed the “***second valley of death***”, which occurs after FDA approval. In most areas of biotech, the period after FDA approval is a time for celebration for both providers and patients. Unfortunately, for the antimicrobials sector, it can take years for newly approved therapies to *actually* reach patients. This is due in part to the flawed reimbursement structure for antimicrobials, which disincentivizes hospitals from giving physicians access to the newest, safest, and most appropriate drug. This is also due to the unique way that innovative antimicrobials are held in reserve in the hospital setting to guard from exacerbating resistance.

Since antimicrobials companies are unable to recoup their investment under traditional volume-based payment structures for drugs alone, many are unable to remain commercially viable and end up failing shortly after launch. The loss of a company in the antimicrobials sector does not just represent an economic loss. In some cases, it represents the loss of intellectual property to

foreign adversaries and the outflow of talent and scientific expertise. This, in turn, results in industry specific skilled workforce challenges, commonly known as “brain drain.”

Most importantly, the loss of these companies poses an existential risk to patients. Without immediate solutions, the antimicrobial development industry will wither away, and we will face a daunting future without effective antibiotics, where commonplace procedures and infections can become fatal.

I am here today to characterize the unique problem facing the antimicrobial sector.

- We do **not** have an innovation problem. Recognizing the need for novel antimicrobials to address resistant infections, the U.S. government has taken action to support the critical research and development of these important therapies. U.S. Government programs like CARB-X have successfully funded over 90 early-stage clinical candidates and diagnostics.
- We do **not** have an approval problem. In 2012, Congress enacted a policy to streamline regulatory approval for antimicrobials to address serious and life-threatening infections. As I mentioned earlier, companies are getting innovative products approved, but are failing *after* launch. This has a ripple effect that has a chilling impact on the pipeline of drugs in development.
- What we **do have** is a commercial marketplace problem – driven by reimbursement and access challenges – that is fundamentally unique to antimicrobials. Without reforms on the post-approval side of the equation to increase access to new antibiotics – through reforms to antimicrobial reimbursement and novel payment mechanisms called “pull incentives” that decouple payment from the volume of antimicrobials used – hospitals will continue to be forced to rely on older medications. Without changes to this system, we will continue to see further deterioration of the innovation pipeline, and patients – grandmothers, children, fathers, mothers, our neighbors – will continue to die.

The good news is that Congress and the Federal Government are in a position to solve this problem. There are already policy solutions that could make a significant impact to correct the broken antimicrobial marketplace in both the short-term to sustain patient access and in the long run to “pull” other novel products across the finish line and ensure they reach patients.

My hope for today is that this committee views the collective expertise of this panel as a “call to action” to address AMR both as the threat it poses to our public health and to our nation’s preparedness in the event of future biosecurity threats such as pandemics, and as the silent killer in hospitals every day.

II. AMR Is a Societal Issue of Mass Scale

The patients our novel antimicrobials can save have no bounds – children with cancer, a marathon runner post routine surgery, a new mother delivering a child via c-section. It does not take a lifetime of antibiotic exposure to fall victim to a resistant infection that can change your life, or a loved one’s life forever. In 2023 alone, a number of superbug outbreaks have gripped the attention of health experts, the media, and the public.ⁱⁱⁱ

- *Candida auris* is a fungus that can cause serious bloodstream, skin, and other infections and is often multi-drug resistant – and has caused recent outbreaks in healthcare settings. In 2021, there were nearly 1,500 clinical cases of *Candida auris* in the United States – more than a 300% increase since 2019.
- *Pseudomonas aeruginosa* is a strain of bacteria that can cause infections in the lung or blood or other parts of the body post-surgery and is often drug resistant. This year, contaminated eyedrops caused severe *Pseudomonas aeruginosa* infections in at least 68 patients in 16 states, including 8 who suffered permanent vision loss, 4 who needed surgical removal of their eyeball, and 3 deaths.
- *Shigella* are bacteria that cause the infection shigellosis, which often manifests itself as a stomach bug. Extensively drug-resistant strains of *shigella* are on the rise. 5% of *Shigella* cases in 2022 were extensively drug-resistant – up from 0% in 2015.

As mentioned previously, AMR threatens to undermine the major advances in medicine made over the last 90 years. Globally, AMR has become a leading cause of death having killed over 1.2 million people in 2019 and played a part in nearly 5 million deaths that year.^{iv} In the United States, AMR was associated with over 173,000 deaths in 2019 – the third leading cause of death, behind only heart disease and cancer.^{vii} By 2050, AMR infections will result in over 10 million deaths per year globally. The economic impact on the United States will also be substantial – a \$20 billion per year cost to the U.S. healthcare system and \$35 billion annual loss in productivity.^{vii}

The burden of AMR has become even more prominent since the start of the COVID-19 pandemic and threatens future responses to biosecurity threats. In 2020, hospital-onset drug-resistant infections and deaths jumped 15% as COVID-19 erased years of progress in the fight against superbugs. AMR also threatens to undermine other areas of medicine. One report cites that infections are a primary or associated cause of death in 50% of patients with cancer.^{viii}

Recognition of these alarming trends and a realization that safer and more novel products are needed have led Congress to take a series of actions over the years to address AMR.

In 2012, Congress passed the Generating Antimicrobial Incentives Now (GAIN) Act to promote the development of new antimicrobial products known as Qualified Infectious Disease Products, or QIDPs, intended to address “unmet medical need” for the “most serious and life-threatening infections.”^{ix} Passage of the GAIN Act was intended to spur antimicrobial innovation. However, it has fallen short in “pulling” novel drugs to approval, and even more importantly, ensuring patients have access to those drugs once they are approved.

The Federal government also implemented additional incentives to support the research and development of new drugs, such as the CARB-X program under the Biomedical Advanced Research and Development Authority (BARDA). These programs have been resoundingly successful in their mission and have become vitally important to antimicrobial development.

Subsequent to these important steps, and as stated earlier –

- We do **not** have an innovation problem
- We do **not** have an approval problem

What remains is a commercial marketplace problem underpinned by systemic post-approval and reimbursement challenges which must first be acknowledged, and then corrected for.

III. State of Innovation of the Antimicrobials Pipeline

Antimicrobial drug development is at an all-time low. Unlike other areas of biotechnology, where investors typically see high returns upon a drug's FDA approval, antimicrobial products are used sparingly and can take years to see appropriate uptake in a clinical setting. Oncology companies raised close to \$7 billion in 2020 (up 900% from 2011), whereas antibiotic companies raised just \$0.16 billion (less than what they raised 10 years prior).^x For drugs in human testing, there are about four dozen antibiotics currently undergoing trials compared to more than a thousand cancer drugs.^{xi}

Small biotech companies remain committed to bringing novel drugs across the finish line. More than 60 companies and non-profit research institutes are developing the 64 clinical-stage drug candidates to meet the growing need for differentiated antibacterials. In recent years, small companies accounted for 80% of novel antimicrobial drug discoveries, with 8% being discovered by non-profit institutes and universities, and only 12% originating from large companies.^{xii} In terms of characterizing the entire R&D engine, there remains a \$150 billion cumulative revenue gap since 2001 for on-patent global antibiotic sales, an unheard-of trend in any other area of biotechnological development.^{xiii}

IV. Innovation Without Implementation

The answer to fixing the commercial marketplace for these drugs is not as simple as inventing new therapies. Firstly, the principle of antimicrobial stewardship dictates that antibiotics should be used only when appropriate and should always be the foremost consideration in care.

Nevertheless, there are a combination of factors that lead to slow uptake and a lack of implementation in hospitals:

1. New AMR drugs when approved are most critical for inpatient care, especially for hospital-acquired infections.
2. Hospitals are currently incentivized to hold in reserve, or rely on cheaper, inferior generic antibiotics – a function of how reimbursement for inpatient care, which is currently capped by bundled payments set by CMS known as a diagnosis related group (DRG), is

designed. As a result, generic antibiotics are used as first line drugs, even when newer drugs may be more appropriate.

3. At the same time, companies see a weak demand for new antibiotics. Low revenues fail to offset the high costs of research and development, as well as costs to support production, commercialization, and post-approval regulatory requirements.
4. These market realities have led investors to flee antibiotic development. The combined market capitalization of all publicly traded antimicrobial companies is .01% of the top 10 global pharmaceutical companies.

As a result of these factors, numerous small biotech companies have ceased operations in recent years. One example is a company that, less than a year after approval, was forced to sell its assets to two principal buyers based in China and India.^{xiv} In the past two years alone, two other companies, both of which have drugs addressing CDC-identified AMR threats – have faced extreme financial difficulties.^{xv}

V. Solutions Are Needed to Right a Market in Free Fall

The federal government currently pays for antimicrobials in a way that fails to drive innovation or appropriate use. The unique way that innovative antimicrobial products are used requires fundamentally unique solutions to address the broken marketplace for antimicrobial innovation. Policy concepts that aim to achieve this goal include:

1. Fixing Reimbursement to Reflect the Market Dynamics Unique to Antimicrobials

Addressing antimicrobial reimbursement is two-fold. Companies, like mine– a clear and timely pathway to patient access and market uptake. Also, we need to address barriers to entry that are preventing biotechs from entering this space today. New, alternative payment models can create that signal needed to drive research and development back to this pipeline and catch-up in our battle against resistant infections.

First, we need to address hospital formularies head-on.

Currently, hospitals perceive that they lose money whenever a new antimicrobial is introduced to their formularies, which in turn blocks access to the therapy. However, numerous studies have demonstrated that better patient outcomes are strongly associated with the use of newer antimicrobial agents, meaning that patients who receive newer treatments spend less time in the hospital. Several studies indicate that the time to initiation of appropriate therapy is the key to improved patient outcomes and saves lives.

In the past few years, the Centers for Medicare and Medicaid Services (CMS) has introduced new tools to support antimicrobial innovation. However, structural issues remain with these reimbursement tools that continue to disincentivize hospitals from properly utilizing novel antibiotics. Difficulties with hospital formularies under the DRG payment structure in the inpatient system also represent a persistent challenge. In general, reviewing reimbursement

mechanisms for antimicrobials and further educating providers about novel products would help strengthen market uptake.

At the same time, we also need to implement novel antimicrobial payment mechanisms i.e., ‘Pull Incentives’. To promote necessary innovation in the antimicrobial industry, Congress should consider novel pull incentives such as subscription models that pay for a reliable supply of novel antimicrobials with payments that are decoupled from volume of the product used. This type of novel payment mechanism would incentivize the development of novel antimicrobials based upon the value they provide for public health, rather than the volume used. Such a model would directly support the appropriate use of the antimicrobials it supports while also providing support for antimicrobial stewardship programs (which improve patient outcomes, reduce AMR, and save money) in rural, safety net and critical access hospitals.

2. Reviewing Administrative Actions on AMR

In March of this year, the Presidential Advisory Council on Combating Antibiotic-Resistant Bacteria (PACCARB) released an updated report with clear recommendations to prepare for the next pandemic. Congress should review these recommendations for relevant areas of legislative action.

3. Strengthening Procurement and Late-Stage R&D for Novel Antimicrobials

As mentioned previously, during any public health emergency – a pandemic, terrorist attack, or natural disaster – secondary and opportunistic AMR infections are likely to increase morbidity and mortality in hospitalized patients. This is particularly important for pandemic preparedness, where bacterial infections secondary to viral pneumonia can be the primary driver of death, as was seen in the 1918-19 Spanish Flu Pandemic.^{xvi}

Project BioShield, or PBS, was created in 2004 to accelerate the availability of medical countermeasures (MCMs) to protect against recognized threat agents. Administered by BARDA, PBS contracts fund both late-stage development activities and drug procurement for the Strategic National Stockpile (SNS). To date, BARDA has awarded two PBS contracts to develop/procure small molecule antimicrobials to counter bacterial biowarfare agents.^{xvii} These contracts provide a near-term stabilizing effect to the recipient companies through procurement sales and support for mandatory post-approval studies. It is important to maintain and increase funding for PBS to align with current public health needs, specifically for procuring antimicrobials as outlined in BARDA’s current Strategic Plan.

VI - Conclusions

Thank you for this opportunity to testify and allowing me to share the positions of small, innovative biotechnology professionals. Every year we wait to address the crisis in the antimicrobial ecosystem is another year patients like Sue Paxton and our dedicated healthcare providers must wait to have access to life saving medicines. Strengthening investments in our Nation's public health preparedness, ensuring readily available stock of innovative antimicrobials in all hospitals and transforming the way we pay for innovation of antimicrobials is paramount to the health and security of our country's patients. AWG, BIO, and our member companies are committed to serving a resource to the HELP as it works to address AMR and strengthen American innovation.

ⁱ <https://www.nature.com/articles/d41573-021-00190-9>

ⁱⁱ <https://www.nature.com/articles/nrd.2016.136>

ⁱⁱⁱ Superbugs Are Here. The Time to Act Is Now. *BIO*. Infographic.

^{iv} Global burden of bacterial antimicrobial resistance in 2019: a systematic analysis. Murray, Christopher J L et al. *The Lancet*, Volume 399, Issue 10325, 629 – 655.

^v

<https://vizhub.healthdata.org/microbe/?settings=eylxljoia2V5X2ZpbmRpbmdzliwiMil6ImJhcilsljMiOiJzZXBzaXMiLCI0lJoyMiwilNSi6MSwiNil6MywiNyl6MywiOCi6MTAyLCi5ljoXLCiXMiil6MywiMTMiOjEsljE0ljoXLCiXNSi6MSwiMTYiOjEsljE3ljozLCiXOCi6MjAxOSwiMTkiOmZhbHNiLCiYMcI6dHJ1ZSwiMjliOjF9>

^{vi} <https://www.cdc.gov/nchs/data/nvsr/nvsr70/nvsr70-09-508.pdf>

^{vii} O'Neill, J. "Tackling Drug-Resistant Infections Globally: Final Report and Recommendations," 2016.

^{viii} Nanayakkara, AK, Boucher, HW, Fowler, VG, Jezek, A, Outterson, K, Greenberg, DE. Antibiotic resistance in the patient with cancer: Escalating challenges and paths forward. *CA Cancer J Clin*. 2021: 71: 488- 504.

<https://doi.org/10.3322/caac.21697>

^{ix} Jonathan J Darrow , Aaron S Kesselheim, Incentivizing Antibiotic Development: Why Isn't the Generating Antibiotic Incentives Now (GAIN) Act Working?, *Open Forum Infectious Diseases*, Volume 7, Issue 1, January 2020, ofaa001, <https://doi.org/10.1093/ofid/ofaa001>

^x The State of Innovation in Antibacterial Therapeutics. *BIO Industry Analysis*. February 2022.

^{xi} Kevin Outterson Testimony to House Energy & Commerce Committee. 28 April 2023.

^{xii} The State of Innovation in Antibacterial Therapeutics. *BIO Industry Analysis*. February 2022.

^{xiii} Outterson, K. "Trends in the Global Antibiotics Market. *Nature Reviews Drug Discovery* 22, 174 (2023).

^{xiv} Crisis Looms in Antibiotics as Drug Makers Go Bankrupt. *New York Times*. 25 December 2019.

^{xv} An Antibiotics Biotech Begins Wind Down, Lays Off Nearly All Works. *Endpoints News*. 6 January 2023.

^{xvi} Fauci, et. al "Predominant Role of Bacterial Pneumonia as a Cause of Death in Pandemic Influenza: Implications for Pandemic Influenza Preparedness".

^{xvii} Venatorx Pharmaceuticals Awarded BARDA Project BioShield Contract. 3 October 2022.