



March 28, 2023

Senator Bernard Sanders
Chairman
Senate HELP Committee
428 Dirksen Senate Office Building
Washington, D.C., 20510

Senator Bill Cassidy, M.D.
Ranking Member
Senate HELP Committee
428 Dirksen Senate Office Building
Washington, D.C., 20510

Robert P. Casey, Jr.
Member
Senate HELP Committee
428 Dirksen Senate Office Building
Washington, D.C., 20510

Mitt Romney
Member
Senate HELP Committee
428 Dirksen Senate Office Building
Washington, D.C., 20510

Dear Chairman Sanders, Ranking Member Cassidy, Senator Casey, and Senator Romney,

On behalf of the Cystic Fibrosis Foundation, we urge you to address the growing crisis of antimicrobial resistance (AMR) by including the PASTEUR Act in the upcoming reauthorization of the Pandemic and All-Hazards Preparedness Act (PAHPA). While several programs authorized through PAHPA aim to address AMR, they have struggled to sufficiently bolster a limited ecosystem of antimicrobial products. The PASTEUR Act would fill this gap and increase national resilience by strengthening the antimicrobial development pipeline, ensuring that our country has the tools it needs to combat AMR and the biological and health security threats associated with it.

AMR poses a dire threat to U.S. public health preparedness and significantly hampers our nation's ability to respond to a wide range of other threats, including pandemics, outbreaks, natural disasters, and bioterror attacks. In recognition of this, the Administration for Strategic Preparedness and Response (ASPR) has not only tasked the Biomedical Advanced Research and Development Agency (BARDA) with combatting AMR through its involvement with the National Action Plan for Combatting Antibiotic-Resistant Bacteria (CARB), the Combating Antibiotic-Resistant Bacteria Biopharmaceutical Accelerator (CARB-X), and Project Bioshield, but has also deemed emerging infectious diseases and AMR a priority health security threat in the 2023-2026 National Health Security Strategy (NHSS).

The reason for this is clear. Natural disasters, such as hurricanes, can 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 supplies may force individuals to turn to rivers or other *ad hoc* water sources. Consumption of untreated water, combined 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, TX area following Hurricane Harvey. Conditions in crowded shelters and severely damaged homes can significantly increase the spread of these infections, each of which may trigger sepsis among victims and emergency workers. Additionally, immunocompromised individuals may not only lose access to crucial

systems such as infusion or dialysis centers due to the loss of power during natural disasters, but are also even more vulnerable to these infections.

Combatting AMR is also critical to our nation's counter-bioterrorism efforts. The World Health Organization has estimated that if 50kg of *Y. pestis* were to be aerosolized and released over a city with a population of 5 million, 150,000 people might fall ill with pneumonic plague—36,000 of whom would die. Drug resistant strains of *Y. pestis* have already been reported; use of these naturally occurring strains, or similar biological agents genetically engineered to resist current therapeutic antimicrobials, would only magnify the devastation of such a bioterrorist attack. Further modeling estimates that deliberate release of aerosolized *F. tularensis* over London would result in 130,000 infections and 24,000 deaths. Natural resistance is already observed in tularemia, and the overuse of fluoroquinolones in the last two decades has led to treatment failure and relapses in tularemia patients.

However, we cannot afford to think about AMR as a potential threat to public health—it already is one. In 2019, AMR directly caused an estimated 1.27 million deaths worldwide and played a part in nearly 5 million deaths total, making AMR a leading cause of death globally. COVID-19 further exacerbated the AMR crisis; in 2020, U.S. hospitals experienced a 15 percent 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-pandemic levels without concerted action. It is now apparent that any emergency resulting in high levels of hospitalization, particularly high levels of ventilator use, creates a ripe opportunity for the spread of secondary drug resistant infections. This is particularly dangerous for people with cystic fibrosis, who are extremely vulnerable to pathogenic colonization due to the thick, sticky mucus in their airways, and often require frequent hospitalization and treatment with antimicrobials.

With this in mind, it has become clear that the current PAHPA framework is insufficient for incentivizing the development of novel antimicrobials. Since the inception of the BARDA Antibacterials program in 2010, the Advanced Research and Development (ARD) portfolio and Project Bioshield have resulted in a combined total of three approved antibacterial therapies. Furthermore, the global antimicrobial development pipeline is inadequate to address even current AMR threats, let alone those that will come in the future. As of late 2021, fewer than 50 traditional antibacterial products were in clinical development worldwide, only a handful of which target the most threatening gram-negative pathogens. This reinforces the urgent need to stimulate investment in novel antimicrobials and rapidly bolster the pipeline through alternative mechanisms.

We therefore urge you to address the growing crisis of AMR by including the PASTEUR Act in the upcoming PAHPA reauthorization. PASTEUR would increase national resilience by strengthening the antimicrobial pipeline to ensure that our country has the tools we need to be prepared to address public health threats. PASTEUR's subscription model is an innovative way to pay for novel antimicrobials that will revitalize the pipeline while, at the same time, supporting appropriate antimicrobial use. Under PASTEUR, the federal government can enter into contracts with developers of innovative antimicrobials to pay for a reliable supply of product. Payments are decoupled from the volume of antimicrobials used, thereby removing the incentive for companies to promote the widespread use that often results in the development of drug-resistant pathogens. Critically, PASTEUR contracts are awarded exclusively on the basis of innovation and success. PASTEUR will only fund antimicrobials that have been approved by the FDA and meet established criteria for novelty and fulfilling unmet AMR needs—in other words, products

with a significant impact on patients and public health. Furthermore, the subscription contract is all-inclusive, and the federal government only pays once.

Importantly, these antimicrobials must also be used judiciously to limit the development of resistance. To further address the widespread problem of antimicrobial overprescription, PASTEUR would also provide new funding for health facilities, including rural, critical access, and safety net hospitals to support antimicrobial stewardship. This ensures that antimicrobials are used appropriately to limit the development of resistance, which is particularly important for the vulnerable patients served by these hospitals. Stewardship teams also typically play critical roles in preparedness and response, including overseeing the administration of novel therapeutics during emergencies and managing antimicrobial drug shortages.

PASTEUR provides our nation the opportunity to remedy dangerous gaps in how the PAHPA framework addresses the ongoing threat of AMR. Delays in the development of novel antimicrobials for treating highly resistant, life-threatening infections erode our public health preparedness and put the entire country—particularly individuals susceptible to infections, such as patients with cystic fibrosis, cancer, or organ transplants—at risk. Every day we wait to address the crisis in the antimicrobial ecosystem is another year patients and providers must wait to have access to life-saving medicines. For these reasons, we once again urge you to include PASTEUR in the 2023 PAHPA reauthorization.

Sincerely,

A handwritten signature in black ink, appearing to read 'Mary B. Dwight', written in a cursive style.

Mary B. Dwight
Chief Policy & Advocacy Officer
Senior Vice President, Policy & Advocacy
Cystic Fibrosis Foundation