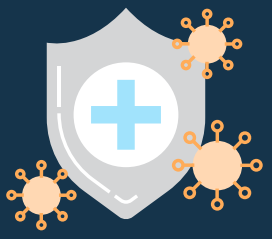
ANTIMICROBIAL RESISTANCE:

A Growing Public Health Threat



Antimicrobial Resistance (AMR) is a natural process that occurs when microorganisms such as bacteria, viruses, fungi and parasites develop the ability to survive against the drugs designed to kill them. AMR is driven by the very use of the medicines needed to combat these organisms. The only way to slow down resistance is to preserve the effectiveness of existing antibiotics by using them under careful stewardship programs – however, even these measures can't stop resistance completely. A growing list of infections – including pneumonia, tuberculosis, blood poisoning, gonorrhea and foodborne diseases – are becoming harder and sometimes impossible to treat, as our current arsenal of medicines is not effective against resistant strains of the microorganisms that cause these infections.

Research published in *The Lancet* on the global impact of AMR found antibiotic-resistant infections are directly associated with at least 1.27 million deaths per year, making drug-resistant bacteria a leading cause of death globally, higher than HIV/AIDS and malaria.[i] In the U.S. alone, the Centers for Disease Control and Prevention (CDC) estimates resistant infections affect at least three million Americans and result in 48,000 U.S. deaths annually.[ii]

Unfortunately, a growing body of evidence indicates the COVID-19 pandemic has been exacerbating this growing crisis. As more patients are hospitalized due to severe COVID-19 infections, often due to worsening respiratory symptoms requiring ventilation, an increasing number of patients have been acquiring secondary bacterial infections that require treatment with antibiotics – thereby worsening current levels of resistance.[iii] A recent analysis found about quarter of hospitalized COVID-19 patients had a secondary infection. Among these patients, greater than 25% were co-infected with staph and more than half of those staph infections were antibiotic-resistant infections known as MRSA.[iv] CDC research also confirms that cases of resistant, hospital-acquired secondary infections are greater than pre-pandemic levels.[v] To make matters worse, not only have resistant infections become more common, but also they have become more deadly. Another study of hospitalized COVID-19 patients with secondary infections found these patients were associated with a higher risk of death.[vi]

Challenges in Researching, Developing and Commercializing New Medicines to Address AMR

Developing new medicines is a long, complex and risky process. Among antibiotics, this process is fraught by significant risk and can take anywhere from 10 to 20.5 years to develop a single new medicine. In fact, in existing classes of antibiotics in preclinical development, just one in 15 will ultimately be approved and reach patients. And among new classes of antibiotics, these odds are even slimmer, with just one in 30 ultimately obtaining FDA approval.[vii] In order to manage the growing threat that AMR presents, we need a robust and diverse pipeline of treatments. Experts believe it will be necessary to generate new chemical substances, as well as a better understanding of how to overcome the most difficult-to-treat infections in order to make progress on new research and development.

Unlike most other medicines, the market for antimicrobials is inherently limited by design. To slow and control continued antimicrobial resistance, public health experts have recommended stewardship programs to ensure that newer medicines are used

responsibly, only in a limited set of circumstances and in only the most necessary cases. This makes it challenging for biopharmaceutical research companies to recoup research and development costs in subsequent sales. Owing to these challenges, many biopharmaceutical research companies have declared bankruptcy in recent years or exited the field.

While policies such as the GAIN Act have enhanced the research ecosystem and have provided support and incentives for researchers to develop new antimicrobial medicines, additional policy reforms are still needed to create a more sustainable environment for antimicrobial R&D and commercialization and ensure a robust pipeline for future treatments.

Addressing AMR is Key to America's Future Preparedness

PhRMA and our members are committed to bolstering pandemic preparedness and health care resiliency to make sure our country and American patients are stronger, healthier and better prepared for the next public health emergency. Having a robust pipeline of medicines to address AMR is a key part of that preparedness. If we fail to address this growing crisis, many modern medical advances that depend on antibiotics – such as routine surgery, cancer therapy and treatment of chronic disease – may be jeopardized. Along with our government's commitment to addressing the COVID-19 pandemic, we can be prepared for the next public health emergency if we all work together to ensure a sustainable pipeline for new antimicrobials for this crisis and those in years to come.

A Path Forward

In the past decade, health policy experts have advanced new policy ideas aimed at incentivizing companies to continue to invest in, or return to, antimicrobial product development. One measure policymakers should consider is the Pioneering Antimicrobial Subscriptions to End Upsurging Resistance (PASTEUR) Act, which would offer "subscription" contracts to manufacturers to provide full access to antimicrobial products for patients covered under federal programs. The subscription would de-link payment from volume for all U.S. government payers, with contracts offered ranging from $750 million to $3 billion based on the clinical characteristics of the drug. The intent of the policy is to incentivize companies to develop antimicrobial medicines for organisms, sites of infection and type of infections for which there is unmet medical need. Importantly, the PASTEUR Act also includes provisions to ensure appropriate stewardship by requiring companies to develop communications strategies for appropriate use of their drug, as well as submitting a plan for registering the drug in countries where unmet medical need exists and ensuring a reliable supply chain.

Payment reforms addressing misaligned incentives in the inpatient bundled payment system that encourage use of low-cost generics over antibiotics that might be more appropriate for patients in Medicare would also make a meaningful difference.

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iii. Doctors Heavily Overprescribed Antibiotics early in Pandemic, New York Times, 6/4/2020.

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v. Weiner-Lastinger, L., Pattabiraman, V., Konnor, R., Patel, P., Wong, E., Xu, S., . . . Dudeck, M. (2022). The impact of coronavirus disease 2019 (COVID-19) on healthcare-associated infections in 2020: A summary of data reported to the National Healthcare Safety Network. Infection Control & Hospital Epidemiology, 43(1), 12-25. doi:10.1017/ice.2021.362

vi. Shafran, N., Shafran, I., Ben-Zvi, H. *et al.* Secondary bacterial infection in COVID-19 patients is a stronger predictor for death compared to influenza patients. *Sci Rep* 11, 12703 (2021). https://doi.org/10.1038/s41598-021-92220-0

vii. Wellcome Trust, Q&A, https://wellcome.org/news/why-is-it-so-hard-develop-new-antibiotics