Pfizer's Policy Position on Combating Antimicrobial Resistance

As a leader in addressing infectious disease challenges, Pfizer recognizes our responsibility and is committed to the long-term effort to combat antimicrobial resistance (AMR), including its associated health disparities. Pfizer has set forth a **five–part strategy** to help address AMR: **1) antimicrobial stewardship** to enable more responsible prescribing; **2) surveillance** of resistance patterns to assess the nature and scope of the problem and the effectiveness of efforts to combat it; **3) vaccines** to help prevent infections and therefore decrease reliance on and need for antimicrobial drugs; **4) incentives and novel business models** to support development of new antimicrobials; and **5) responsible manufacturing and disposal** of antimicrobials to help mitigate potential adverse impacts on health and the environment. Given the scientific, economic, equity, and public health challenges presented by AMR, multiple strategies and collaboration between stakeholders are essential. To implement our strategy, Pfizer is working with national and global stakeholders, including public-private partnerships.

Background:

Antimicrobial resistance (AMR) is an urgent threat to global population health. According to the World Health Organization (WHO), AMR "occurs when bacteria, viruses, fungi and parasites change over time and no longer respond to medicines, making infections harder to treat and increasing the risk of disease spread, severe illness, and death."[i] Unlike almost every other class of drugs, antimicrobials, including antibiotics, antifungals, and antivirals, drive their own obsolescence because the more an antimicrobial is used, the more selection pressure pathogens face to develop resistance, survive, grow, and spread.[ii] AMR compromises many medical advances, such as surgical procedures, including organ transplantation, and chemotherapy, which rely upon our ability to prevent and treat infections. There were an estimated 4.95 million deaths associated with bacterial AMR in 2019 globally.[iii] Importantly, AMR is a global health equity issue, as the economic impact is expected to be larger for patients in low-income countries than in the rest of the world.[iv] In the U.S., a disproportionate number of antimicrobial-resistant infections occur among people who are at higher risk for health disparities and inequities.[v]

The current global COVID-19 pandemic has further highlighted the risk of AMR. A 2022 CDC report found that the COVID-19 pandemic led to increases in AMR, likely due to use of antibiotics to attempt to treat COVID-19 early in the pandemic, longer hospital stays for COVID-19 patients, and protective equipment shortages.[vi] Additionally, staff shortages and reassignment to treat COVID-19 patients led to weakened enforcement of hospitals' infection control programs and, in some cases, public health resources were shifted away from tracking AMR to tracking COVID-19 cases.[vii] Importantly, addressing both COVID-19 and AMR requires global partnerships and strong public health and prevention measures, including extensive surveillance to help curb spread. The pandemic also has reinforced a need to invest in development of medicines now to help protect patients from future global health crises, which is critical to combating AMR as the existing and current pipeline of antimicrobials are insufficient to address the ongoing and future threat of antimicrobial infections.[viii] However, while there are learnings from COVID-19, AMR requires tailored solutions.

Global collaboration regarding AMR has increased in recent years with several large-scale initiatives led by public sector stakeholders such as the WHO. AMR has also become a focus area for the Group of 7 (G7) and Group of 20 (G20), with G7 Health Ministers most recently committing to take several global steps to combat AMR in their May 2022 communiqué,[ix] while the Finance Ministers made a commitment in 2021.[x]

The private sector has increased its efforts as well. For instance, in January 2016, the Davos Declaration, signed by more than 100 companies and trade associations, including Pfizer, called for collective action to create a sustainable and predictable market for antimicrobials, vaccines, and diagnostics, and encouraged appropriate use of new and existing treatments. As a leader in addressing infectious disease challenges, Pfizer recognizes our responsibility and is committed to the long-term effort to combat AMR, including its associated health disparities. Given the scientific, economic, equity, and public health challenges of AMR, multiple strategies and close collaboration between stakeholders are essential.

Key Facts and Figures:

- A study in The Lancet showed there were an estimated 4.95 million deaths associated with bacterial AMR in 2019 globally, including 1.27 million deaths attributable to bacterial AMR.[xi]
- In the U.S., more than 2.8 million antibiotic-resistant infections occur each year. CDC estimates that more than 35,000 people die each year as a direct result of these infections. Many more people die from other conditions that are complicated by an antibiotic-resistant infection.[xii]
- A CDC report on the impact of COVID-19 on AMR in the U.S. found that deaths and infections from several antimicrobial resistant pathogens increased at least 15% during the first year of the pandemic.[xiii]
- By 2050, due to AMR, annual global GDP could fall by 3.8%, shortfalls in economic output could reach $6.1 trillion annually, and an additional 28.3 million people could fall into extreme poverty.[xiv] The poverty impact will be larger for low-income countries compared to the rest of the world.[xv]
- The CDC estimates that the cost of AMR is $55 billion every year in the U.S., including $20 billion for health care and $35 billion for loss of productivity due to extended hospital stays.[xvi]
- In Europe, AMR is responsible for an estimated 33,000 deaths per year and €1.5 billion per year in health care costs and productivity losses.[xvii]
- Although there have been 164 FDA-approved direct-acting antibacterial new chemical entities (NCEs) since the early 1900s, only one new molecular target NCE has been approved over the last 35 years. As of February 2022, according to the Biotechnology Innovation Organization (BIO), the biopharmaceutical sector's clinical pipeline for antibacterials contains 64 new antibacterial therapeutics, with 31 (48%) having novel targets.[xviii]
- Recent research found that for a fully delinked subscription program, the optimal size for a global antimicrobial R&D pull incentive over 10 years to create a functional antimicrobial market is $4.2 billion, with lower- and upper-bound estimates of $3.3 billion and $8.9 billion.[xix]
- In 2022, Pfizer entered into a partnership with Nigeria's National Health Insurance Authority to improve patient affordability and access to Pfizer antimicrobial agents through an innovative cost-sharing reimbursement mechanism.
- In 2020 alone, 28 million patients were treated with a Pfizer anti-infective therapy.[xx]

Pfizer AMR Policy Position:

Working with a broad group of health care stakeholders, Pfizer strives to overcome AMR challenges by using our expertise and capabilities to help develop solutions. Pfizer endorses a five–part strategy to help address AMR:

- **Antimicrobial stewardship** can help reduce AMR spread by enabling more responsible prescribing.
- **Regional and global surveillance** of antimicrobial resistance patterns are important tools to assess both the nature and scope of the problem as well as the effectiveness of efforts to combat it.

- **Vaccines** are an important tool to help prevent infections and therefore decrease the reliance on and need for antimicrobial drugs.
- **Incentives and novel business models** that support the development of additional antimicrobials, vaccines, antimicrobial alternatives, and diagnostics, and strengthen a sustainable marketplace, will be critical to broadening the tools available to address AMR.
- **Responsible manufacturing and disposal** of antimicrobials helps mitigate potential adverse impacts on human health and the environment.

Antimicrobial Stewardship

Responsible antimicrobial use requires an evidence-based, multi-disciplinary approach applied across health care settings to the individual patient's situation. Pfizer believes that multiple strategies to improve patient outcomes through appropriate use of antimicrobials should be employed across the health care system and endorses strategies that ensure patient access to and reliable supply of quality, prescription-only medicines that treat infections. Antimicrobial stewardship (AMS) should be tailored to the locale, including an understanding of the local epidemiology. The focus of AMS should be on appropriate use of all antimicrobials, regardless of time of market entry, exclusivity, and/or acquisition cost. Continuous evaluation of AMS is critical to confirm patient outcomes are being optimized, using metrics that include clinical outcomes, unintended consequences of antimicrobial use (e.g., toxicity, selection of pathogenic organisms, emergence of resistance), and process measures (e.g., adherence to clinical pathways/guidelines, time to appropriate therapy).

Pfizer believes that AMS that is focused on reducing antimicrobial expenditures/costs without assessing the impact on other metrics is not in the best interest of patients or population health. Accordingly, AMS efforts should consider the impact on population health, including the connection between humans and the environment, as well as health disparities related to AMR. Effective AMS should consider disparities in AMR awareness, incidence, and outcomes among racial and ethnic groups. Pfizer believes that surveillance, infection prevention, policy advocacy, education, research, health equity, and patient engagement are integral to successful AMS. Diagnostics that differentiate antimicrobial-resistant from antimicrobial-susceptible strains of bacteria are also important tools. Finally, appropriate patient access is a critical component of AMS; all patients must have access to appropriate and effective antibiotics as prescribed by their providers.

AMR Surveillance

Monitoring evolving resistance patterns enables health care providers to choose appropriate antimicrobial therapies for patients while also informing AMS strategies and highlighting R&D needs.[xxi] Pfizer supports improved surveillance data generation and use globally, including strengthening systems in low- and middle-income countries to help them mount data-driven AMR and broad infectious disease responses. We support transparency of and broad access to surveillance data as well as standardized methods to facilitate data collection across surveillance programs by making our raw data accessible through the Vivli global clinical trials data sharing platform. Pfizer also sponsors the Antimicrobial Testing Leadership and Surveillance (ATLAS) database, a global antimicrobial surveillance program that monitors resistance patterns across more than 70 countries and enables real-time public access to these data. In April 2020, Pfizer evolved ATLAS from an industry-recognized antibacterial surveillance platform to a much broader antimicrobial surveillance program with the inclusion of data from the SENTRY antifungal surveillance program—making Pfizer the first company to provide open access to both antifungal and antibiotic resistance data through a single platform.

In 2020, Pfizer and Wellcome Trust launched the Surveillance Partnership to Improve Data for Action on Antimicrobial Resistance (SPIDAAR), a public-private research collaboration with the governments of Ghana, Kenya, Malawi, and Uganda to track resistance patterns and better understand the burden of AMR on patients in low- and middle-income countries. The program leverages ATLAS data to support implementation of the countries' National Action Plans for AMR. In addition to ATLAS and SPIDAAR, Pfizer has provided support for several independent surveillance programs, two China-based antibiotic resistance surveillance programs, and a global antifungal surveillance program.

Vaccines

In addition to the need for the development of new antibiotics and rational use of antimicrobial drugs, experts, including at WHO, agree that vaccines play a vital role in the arsenal to address AMR.[xxii] Vaccines are typically administered to help prevent infections from happening in the first place, which naturally leads to reducing the use — and misuse — of antibiotics. Vaccines not only help protect the vaccinated individual by direct immunization but also can help protect others through indirect immunization (assuming the overall vaccination rate is high enough). Pfizer remains committed to R&D supporting the development of vaccines to help prevent infections caused by resistant pathogens across the life course. We continue to advance new vaccines against pneumococcal and meningococcal diseases to help address the burden of disease, and to explore the potential of vaccines to help prevent other infectious diseases.

Pfizer also supports the use of vaccines in routine national immunization programs which, along with the rational use of antimicrobials, can produce gains in public health. National immunization plans should ensure access to vaccinations for citizens of all ages. Additionally, national and global AMR strategies should include increased focus on the role of vaccination in preventing AMR to support patient access to and uptake of available vaccines. By reducing the incidence of infections, vaccines can extend the clinical utility of antimicrobials. Fewer infections translate to fewer prescriptions for these drugs, and thus reduce the risk of antimicrobial resistance. Pfizer is committed to helping to increase global recognition of the value of vaccines in addressing AMR.

Incentives and New Business Models to Support R&D

Pfizer is committed to antimicrobial R&D and is one of the few large research-based pharmaceutical companies still active in this area. Pfizer recognizes the urgent need for new and novel antimicrobials to address AMR and its associated health equity implications, as well as the challenges that limit the market potential for these products. Particularly for antibiotics, with the steep costs of development, high risk of failure, and long lead times, there are few incentives for pharmaceutical companies or venture capital to invest in R&D due to the difficulty of realizing a return even if a novel antibiotic gains marketing authorization. Additionally, traditional health technology assessment (HTA) techniques tend to undervalue new antibiotics. Specifically, current HTA techniques fail to consider the wider public health benefits of new antibiotics and the impact these new treatments will have on AMR. They also often do not account for antibiotics' role in making routine medical procedures, such as surgeries and chemotherapy, safe by preventing and treating infection. Without new effective antibiotics, procedures and treatments could become highly risky due to AMR. Pfizer believes that collaboration with industry, health care providers, and governments to implement a mix of complementary "push" and "pull" incentives and new business models is needed to encourage increased antimicrobial development.

One leading innovative model that global stakeholders are currently exploring is **subscription payment models**, through which in exchange for developing a new antimicrobial, payers agree to provide companies upfront and/or annual negotiated payments at a fixed price or preset fee. This ensures product availability and enables improved stewardship of the antibiotic while improving financial predictability for payers and

manufacturers. In the UK, Pfizer has engaged the National Institute for Health and Care Excellence (NICE) on a pilot program to test the feasibility of a subscription-type model which would pay companies for antimicrobials based on a HTA of their broader value to society given the rise of AMR, as opposed to the volume used. While the UK model requires further work to quantify this broader value, it is an important step. Pfizer supports further development of this and other models that could become a new standard for reimbursing antimicrobials based upon their societal value.

In the U.S., Pfizer supports the bipartisan **PASTEUR Act**, which was first introduced in Congress in 2020, and would establish a subscription reimbursement program to encourage development of innovative antimicrobial drugs targeting the most threatening infections. [xxiii] The proposed program is a "delinked" model with revenues from patients covered by federal insurance subtracted from payments. Importantly, there is no "one-size-fits-all" model to spur antimicrobial innovation; different solutions may be needed for different countries or regions.

Additional potential incentives and business models include:

- **Transferable exclusivity extension (TEE):** In the E.U., the European Commission is exploring pull incentives for novel antimicrobials as part of a broader pharmaceutical legislation revision. In partnership with the European Federation of Pharmaceutical Industries and Associations (EFPIA), Pfizer is advocating for a pan-European pull incentive in the form of a TEE which would reward companies for a product for a resistant pathogen with a voucher to extend the market exclusivity of another product. With appropriate stewardship and access provisions, such a policy could support R&D and a sustainable marketplace because it does not require upfront government funding and is sustainable. Other advantages are that it generates manufacturer revenue through the transferable IP exclusivity, rather than volume sold, and places R&D risk on companies with rewards only for success. The Duke-Margolis Center for Health Policy has proposed such a TEE voucher program in the U.S.[xxiv]
- **Regulatory incentives:** Increased eligibility of new antimicrobials and vaccines for accelerated regulatory review pathways globally are important incremental changes that would reduce R&D timelines and costs and increase access, while more transformational changes would be needed to drive significant increases in R&D.

Responsible Antimicrobial Manufacturing & Disposal

Pfizer is committed to responsible manufacturing practices across our supply chain to minimize the potential environmental impact related to the production of antimicrobials.

Pfizer's strategy for responsible manufacturing practices focuses on applying the Common Manufacturing Framework, developed by the Antimicrobial Resistance Industry Alliance (AMRIA) manufacturing group, of which Pfizer has been a member since its formation in 2017, as a framework for managing antimicrobial discharge. Our efforts to apply the Framework include: 1) Risk assessments against science-based discharge targets (known as Predicted No Effect Concentrations (PNEC)) at Pfizer and supplier manufacturing facilities, and 2) Evaluation of our manufacturing supply chain to assess practices in controlling releases of antimicrobials into the environment. Pfizer is also engaged in programs focused on appropriate disposal of unwanted medicines, including the Pharmaceutical Product Stewardship Work Group (PPSWG) in the U.S., and MEDSdisposal in Europe. AMRIA releases a biannual report demonstrating progress by the Alliance.[xxv] Pfizer's progress against its responsible manufacturing strategy, including risk assessments against published science-based discharge targets (PNEC), was also recognized through the 2020 and 2021 Access to Medicine AMR Benchmark reports.[xxvi]

In June 2022, AMRIA published an Industry-leading Antibiotic Manufacturing Standard: *Minimizing risk of developing antibiotic resistance and aquatic ecotoxicity in the environment resulting from the manufacturing of human antibiotics.*[xxvii] This standard, which Pfizer is committed to meeting, provides guidance to manufacturers in the global antibiotic supply chain to support the responsible production of antibiotics, helping to minimize the risk of AMR in the environment. The standard marks the formalization of the Alliance's Common Manufacturing Framework, which describes a risk-based approach to assessing and controlling antibiotic manufacturing waste streams. It also provides the basis for an industry certification scheme that will enable antibiotic manufacturers to demonstrate that the requirements of the standard have been satisfied, through independent third-party evaluation. The certification scheme aims to launch in the first half of 2023.

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