

Addressing the Antimicrobial Resistance Crisis Through Pull Incentives for Novel Antimicrobials

Antimicrobial Resistance (AMR)

AMR is a growing global health crisis that threatens to undermine modern medicine. It occurs when microorganisms (e.g., bacteria, viruses, fungi, parasites) develop the ability to resist the drugs designed to kill them. Without effective antibiotics, routine medical procedures like surgery and cancer treatment will become high-risk, and common infections could once again become deadly.

In 2019, an estimated 5 million deaths occurred globally as a result of AMR¹. The OECD estimates that without intervention, AMR will lead to GDP losses of about 2.9 trillion USD by 2050 and will result in over 569 million extra hospital days annually². At EU level is one of the highest public health priorities, leading to approximately 35,000 deaths annually across Europe—a toll comparable to that of flu, tuberculosis, and HIV/AIDS combined. The economic burden is also significant, with healthcare costs and productivity losses attributed to AMR estimated at €1.5 billion each year³.

Greece faces the most severe epidemiological burden among EU countries. Based on the latest available data concerning infections from ECDC Greece has: a) the highest incidence of infections due to antibiotic-resistant bacteria (increased by 76% from 23,199 to 40,891 between 2016 and 2020) and b) the highest mortality due to antibiotic-resistant bacteria (2,013 attributable deaths per year)⁴. During the recent IFPMA/BCR meeting in Athens, Greek PM Kyriakos Mitsotakis presented AMR issue among the top public health priorities of the country.

The rise of AMR worldwide is driven by the overuse and misuse of antimicrobials, as well as a lack of investment in the development of new antimicrobial therapies. As existing antimicrobials become less effective, there is an urgent need for novel antimicrobials to treat drug-resistant infections. However, the current market model fails to provide adequate incentives for pharmaceutical companies to invest in this high-risk, low-return area.

The Unique Challenges of the Antimicrobial Market

Antimicrobials, particularly antibiotics, face unique challenges that make them a less attractive investment for pharmaceutical companies compared to other types of drugs. These challenges include:

- 1 Low returns on investment:** Antibiotics are typically used for short courses of treatment, and their use is often restricted to preserve their effectiveness. This limits the potential sales volume and revenue for pharmaceutical companies, making it difficult to recoup the significant upfront investment required for R&D.
- 2 Rapid resistance development:** As bacteria and other microbes evolve to resist existing antimicrobials, the useful lifespan of new antimicrobials is often limited. This further reduces the potential return on investment for pharmaceutical companies.
- 3 Regulatory and reimbursement barriers:** Regulatory pathways for antimicrobials are often more complex and time-consuming compared to other drug classes. Additionally, reimbursement policies often fail to adequately value the broader public health benefits of novel antimicrobials, making them less financially attractive for pharmaceutical companies.

These market challenges have led to a significant decline in antimicrobial R&D over the past few decades, with many large pharmaceutical companies scaling back or exiting the antimicrobial market altogether. As a result, the antimicrobial pipeline is drying up, leaving us increasingly vulnerable to the growing threat of AMR.

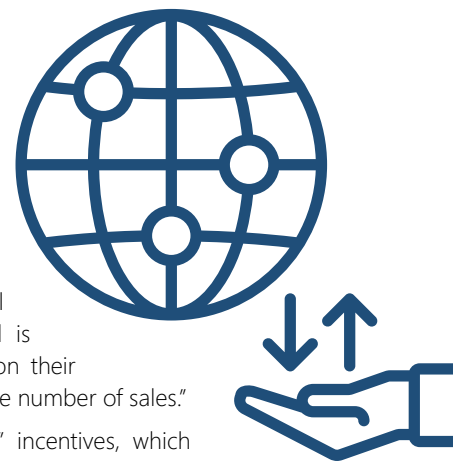
The Need for Pull Incentives for Novel Antimicrobials

To address the market failure & revitalize antimicrobial R&D, policymakers should implement “pull” incentives that delink a company’s revenue from the volume of antimicrobials sold. These incentives would reward successful innovation at a level sufficient to attract necessary investment and encourage companies to undertake the substantial risks associated with anti-microbial R&D. The goal is to assess the value of novel antimicrobials based on their contribution to public health, rather than simply by the number of sales.”

Pull incentives are a critical complement to “push” incentives, which provide upfront funding and support for early-stage antimicrobial R&D. By addressing the challenges in the later stages of development and commercialization, pull incentives can help create a more sustainable and robust antimicrobial pipeline. Innovation-promoting policies are essential, as they build the foundation for an active pipeline, a fundamental requirement for ensuring future access to and availability of novel antimicrobials.

To effectively implement pull incentives, policymakers should consider the following recommendations:

- 1 Establish Transferable Exclusivity Vouchers (TEVs):** Establishing a framework that would allow companies to extend the exclusivity period of another product in their portfolio in exchange for developing a new antibiotic. Goal: Provide substantial financial reward and offset the high R&D costs and risks associated with new antibiotics.
- 2 Implement subscription-style payment models:** Develop a subscription-style payment model that provides a fixed annual payment to companies in exchange for maintaining a supply of their novel antimicrobials. Goal: Decouple revenue



The role of vaccines in reducing AMR

The World Health Organization issued in October 2024 a Technical Report entitled: “Estimating the impact of vaccines in reducing antimicrobial resistance and antibiotic use”⁵. The report provides an in-depth evaluation of the potential role vaccines can play in reducing antimicrobial resistance, outlining the importance of vaccines as a crucial tool in reducing reliance on antibiotics, by preventing infections and curbing the spread of resistant strains of pathogens.

The report found that Vaccines have the potential to avert an estimated 510,000 of AMR related deaths each year. Vaccines targeting 24 pathogens could reduce the number of antibiotics needed by 22%, equating to 2.5 billion defined daily doses globally every year.

- Existing vaccines could avert up to 106,000 deaths, save US \$861 million in hospital costs, and US \$5.9 billion in productivity losses globally each year, all associated with AMR.
- Vaccines in late-stage clinical development could prevent up to 135,000 deaths per year, save US \$1.2 billion in hospital costs and US \$2.2 billion in productivity losses, all associated with AMR
- Vaccines in early clinical development could have the greatest impact, with 408,000 deaths averted annually, US \$30 billion in hospital costs saved and US \$17.7 billion saved in productivity losses, all associated with AMR.

Based on all the above, we propose the following topics for the agenda of SFEE multi-stakeholder workshop on AMR:

from sales **volume, ensuring stable access to critical antimicrobials.**

- Enhance regulatory pathways and incentives:** Streamline regulatory approval processes for novel antimicrobials, provide accelerated review pathways, and offer additional regulatory incentives (e.g., extended exclusivity periods) to encourage antimicrobial development. Goal: Reduce the time to market for antimicrobials and improve their financial attractiveness for pharmaceutical companies.
- Enhance access pathways:** Streamline reimbursement processes for novel antimicrobials, provide accelerated pathways, and offer additional incentives (e.g., differentiated payback status). Goal: Greece to become a competitive market for novel antimicrobials, promoting access and availability.
- Ensure sustainable funding sources:** Establish dedicated AMR research funds to support the implementation and long-term sustainability of pull incentive programs. Goal: Secure stable funding, promoting continuous innovation and investment in AMR research.”
- Engage with stakeholders:** Conduct regular consultations with pharmaceutical companies, healthcare providers, patient associations, and other key stakeholders to ensure that pull incentive policies are effectively designed and implemented. Goal: Create a collaborative framework that reflects the perspectives and needs of all stakeholders.

Proposed actions for Greece



- Establishment of a National Committee for Combating AMR: The goal is to develop a National Action Plan** with specific goals/KPIs, with commitments and actions for the State and other stakeholders (MoH, EODY, ODIPY, Infectiologists, Pharmacists, Pharma Industry). The Recent report by the University of Peloponnese on a 3-year Action Plan for AMR in Greece could be assessed and utilized. The Plan consists of 32 actions on the following priority domains: Awareness, Infection Prevention & Control, Stewardship, Research & Development, and Access to Antimicrobials⁶.
- Support the establishment of TEV (Transferable Exclusivity Voucher):** Promotion by the Greek government of the establishment of the TEV in the upcoming revision of the European Pharmaceutical Legislation. The estimated average cost per voucher for Greece is just 7.3 million euros, while the estimated annual cost of antimicrobial resistance for the country is 42.6 million euros.⁷
- Scale vaccine use:** Integrating vaccines as a tool to combat antimicrobial resistance into national action plans by accelerating their introduction and increasing their coverage, especially in children and older age groups.
- Secure a sustainable market environment** for novel hospital products by significantly reducing the payback levels.
- Abolishment of reimbursement barriers** such as the “5/11” external criterion, ensuring an accelerated HTA assessment and access to innovative medicines
- Integrate novel antimicrobials among eligible products of the upcoming Innovation Fund with the** aim of accelerating access to specific breakthrough medicines
- Secure the launch and sustainability of novel antimicrobials in the Greek market through the establishment of additional funding.
- Explore EU funding** for the implementation of the AMR Plan including the pull incentives for novel antimicrobials

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