Policy Brief

The Necessity for Greater Antibiotic Innovation

DRIVE-AB: Transforming the way policymakers stimulate innovation, responsible use and global access of novel antibiotics to meet public health needs

The problem:

Dangerous bacteria are becoming resistant to antibiotics faster than new antibiotics are being developed to stop them.

Resistance to antibiotics increase with their use.[1] This is a natural evolutionary process whereby bacteria adjust so that the antibiotic is no longer effective. When such resistant bacteria cause health problems, another antibiotic will be needed to treat the infection. Antibiotic resistance becomes a problem when bacteria become resistant to all drugs so that there are no effective antibiotics to treat an infection. The development of resistance is accelerated by the use of antibiotics in health care, food production, and by pollution of the environment due to release of antibiotic manufacturing waste.[1]

Since the late 1980s there has been a lack of antibiotic innovation. Only two new classes of antibiotics meeting unmet needs reached the market in the last 20 years.[2,3] This is due to a combination of factors. Firstly, new antibiotics have proven to be very hard to discover. Secondly, generating the data required for regulatory approval of a new antibiotic is difficult and expensive. Finally, antibiotics offer an unattractive return on investment to the private sector: revenues from antibiotics sales tend to be low, and higher revenues are often possible in other disease areas (see box to right). In 1980, there were more than 25 large, pharmaceutical companies with active antibacterial drug discovery programs; today only four remain.[4]

> **Barriers to antibiotic investment**
> A company's return on investment for developing a novel antibiotic is significantly lower than other competing therapeutic areas due to:
> - Many older and inexpensive antibiotics are still highly effective for most patients. Therefore, hospitals and primary care rationally prescribe proven, inexpensive antibiotics.
> - The desire to preserve the use of novel antibiotics leads to slow initial uptake.
> - Although the overall antibiotic market is large, it is fragmented into multiple markets by hospital specialty and resistance patterns. Thus, the markets for each of the different drugs can be comparatively small.

The consequences:

Life-threatening, untreatable infections are emerging which also jeopardize modern medicine's ability to safely perform routine surgeries and cancer treatment.

Everyone has a role to play in reducing inappropriate use of antibiotics. Individuals can help by taking antibiotics only when prescribed and when medically necessary. However, responsible use needs to be adopted globally in order to significantly slow the emergence of antibiotic-resistant bacteria.

Anyone, however careful a steward, can carry antibiotic-resistant bacteria if he or she comes in contact with one. Bacteria travel from one person to another and from one country to the next.

In hospitals infections caused by antibiotic-resistant bacteria may prolong hospital stays or even kill patients. The European Union estimates that 25,000 patients die every year from infections by antibiotic-resistant bacteria.[5] Infections sometimes occur during health care interventions such as intra-abdominal surgery, and hip replacements, which have become 'routine' procedures. The availability of effective antibiotics makes performing these medical procedures less risky. A study examining the potential consequences of increases in antibiotic resistance on common surgical procedures and chemotherapy found that a 30% reduction in the efficacy of antibiotics used to prevent infections after these procedures would result in 120,000 additional infections per year in the USA alone.[6]

The interdependencies:

Stimulating antibiotic innovation alone will not solve the problem. Promoting sustainable use and greater access are also key.

Antibiotic resistance is a global problem, but far more people die today from a lack of access to antibiotics than from resistant infections. More than one million children die every year from pneumonia and sepsis, both of which are often treatable with inexpensive, older antibiotics.[7] Increasing access to effective antibiotics is a global priority. However, if these antibiotics are used inappropriately, higher numbers of drug-resistant bacteria will occur, increasing the need for innovation.

Pharmaceutical innovation is time-consuming (at least 10-15 years from discovery to market), risky (approximately 80% of drugs in development fail) and expensive (from USD 250 million to more than one billion).[8-12] Developing completely new antibiotics is scientifically complex. It is much more cost-effective to maintain the effectiveness of the world's existing antibiotics than trying to continually replace them. Innovation will always be necessary, but the pressure to find entirely new antibiotics can be reduced by working in parallel to prolong the efficacy of existing antibiotics. Yet even a slow pace of innovation is not being achieved today.

The opportunity:

New incentives, coupled with provisions for sustainable use and equitable access, are needed to stimulate antibiotic innovation.

The research project, DRIVE–AB (i.e., Driving reinvestment in research and development for antibiotics and advocating their responsible use, www.drive-ab.eu), is a consortium of 16 public sector partners and seven pharmaceutical companies supported by the European Innovative Medicines Initiative (IMI). DRIVE-AB is tasked with defining responsible use of antibiotics, identifying the antibiotic-related public health priorities, calculating the societal value of having new antibiotics available for these priorities, developing and costing new economic models to promote the desired antibiotic innovation, and sustainable use of the resulting, novel antibiotics. The purpose of the project is to transform the way policymakers stimulate antibiotic innovation and to ensure that these new antibiotics are used sustainably and available equitably.

DRIVE-AB is not the only project evaluating incentives for stimulating greater antibiotic innovation. Most notably the UK Review on Antimicrobial Resistance, Chaired by Lord Jim O'Neill, has delivered a series of reports recommending a set of high-level actions needed not only to stimulate antibiotic innovation but also about to increase infection prevention and surveillance, examine alternative antibacterial technologies and improve rapid diagnostics.[13] Its final report and recommendations will be issued May 2016. DRIVE-AB will further develop this work by providing specific recommendations regarding governance and financing models as well as the necessary provisions to ensure sustainable use and equitable access of novel antibiotics. DRIVE-AB's recommendations will be vetted by a broad range of stakeholders including policymakers, healthcare insurers (both national and private), medicines regulatory authorities, small and medium-sized pharmaceutical companies, national research funding agencies, academic research institutions, and more. Although principally European in focus, DRIVE-AB will actively engage globally to ensure that its recommendations can integrate in the broader context of ensuring access to effective antibiotics and combatting resistance.

DRIVE-AB will present its preliminary findings on June 2, 2016 in Amsterdam, and the final report and recommendations will be delivered in September 2017. Results will also be continuously published in peer-reviewed journals.

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