DRIVE AB
RE-INVESTMENT IN R&D AND RESPONSIBLE ANTIBIOTIC USE

Policy Brief

The Importance of Multinational Coordination and Increased Public Financing for 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

Stimulating antibiotic innovation for unmet public health needs requires substantial and sustained public financing.

Disease-causing bacteria are becoming resistant to antibiotics faster than new antibiotics are being developed to stop them.[1] Due to a combination of factors, discovering and developing antibiotics with novel mechanisms of action is a highly demanding scientific challenge.[2] There are 37 antibiotic candidates currently being tested through clinical trials.[3] Arguably, only a handful represent a truly novel class for an unmet public health need, i.e., where there are few or no treatment options available today.

As resistance spreads, the demand for effective antibiotics will continue to rise. Since discovery and development of a novel antibiotic takes at least 10-15 years[4], this important work needs to start long before hard-to-treat infections emerge. This would allow the antibiotics to be available before there is significant unmet need or just as demand is growing. However, there is little commercial incentive to invest in antibiotic research and development for a future unmet need when, at launch, there may be very low demand for the novel medicine. This is why several initiatives, including the United Kingdom's AMR Review and the European Union's DRIVE-AB project, are proposing several economic incentives to stimulate antibacterial discovery and development. These are targeted at the public, private, and non-profit sectors, with the goal of increasing antibacterial innovation that meets current and future unmet public health needs. Importantly these proposed incentives are linked to conditions that should prolong the utility of the resulting antibiotics as well as ensure equitable and appropriate global access.

Ideally, the numbers of patients with multi-drug resistant infections will be low when new forms of resistance are observed. For example, a group of bacteria have recently been found to share a gene (MCR-1) that makes them resistant to colistin, a "last resort", though not widely used, antibiotic. These bacteria have been found in China, United Kingdom, the United States, and other countries and recently identified in some patients with clinical infections.[5-7] This exemplifies the potential for resistant genes to spread to common, disease-causing bacteria creating either difficult or even impossible-to-treat infections. Although society should implement best practice infection control methods to prevent the spread of resistant bacteria, novel antibiotics are still needed. Bacterial evolution will inevitably create resistant strains, and outbreaks may occur despite good practice. It is not a question of "if" but "when". Unfortunately the onset of resistance is hastened through consumption.[8] This combination of low numbers of patients with multi-drug resistant infections and conservation efforts will lead to low volume use of novel antibiotics targeted for these infections. At these low volumes, sufficient revenues have not been generated to make antibiotics an attractive investment case.

To effectively incentivize the private sector to develop novel antibiotics for small patient groups, new economic incentives are needed with large reward values.[9,10] The UK Review on AMR, which has a wider remit than antibiotics including tuberculosis and antifungals, has estimated that globally USD 16 billion is needed over 10 years to promote the development of new antimicrobials including making better use of existing ones.[9] The Review also estimated that USD 2 billion is needed over five years to support basic and non-commercial discovery work. DRIVE-AB is currently working on estimates focused solely on antibiotics. However, the magnitude will likely be similar, in the billions of dollars, requiring significant new financing. While this is a sizeable investment, the cost of inaction is substantially more, threatening modern medicine's ability to treat infections, perform common surgeries and even treat cancer.[11] Effective antibiotics are also a prerequisite for achieving several of the Sustainable Development Goals, including those related to health (SDG 3), economic growth and development (SDG 8), and food security (SDG 2).

The consequences

Action to stimulate greater antibiotic innovation is occurring but without unified multinational commitments.

No single country or healthcare system can or should foot the antibiotic innovation bill. The sums are large and the resulting benefits are global. Significant financing is already occurring to bolster antibiotic innovation, including from a collaboration of 22 countries through the Joint Programming Initiative on Antimicrobial Resistance (JPIAMR); Europe through its Innovative Medicines Initiative (IMI); the United States through its Biomedical Advanced Research and Development Authority (BARDA); the combined UK and US initiative, Combating Antibiotic Resistant Bacteria Biopharmaceutical Accelerator (CARB-X); the United Kingdom's and China's Global Innovation Fund; and the independent, not-for-profit Global Antibiotic Research and Development Partnership (GARD).

These initiatives are all vital sources of antibacterial innovation support. Yet none have protected, long-term financing, and the financing in total falls short of the estimated global need [i]. Additionally while their efforts are complementary in nature, more could be done to present unified positions on priorities and financing.

From a priorities perspective, a clear global message is needed regarding which pathogens and antibiotic profiles represent unmet public health needs. The United States has already documented its priorities for public health activities through a threat assessment report.[12] Priorities for research and development of new antibiotics on a global level are still needed. Agreement regarding priority pathogens will present a clear message to innovators about the preferred profiles of novel antibiotics. Yet this consensus must be combined with a sustained willingness to pay for novel antibiotics, accounting for the long lead times from discovery to market launch for these critical medicines.

The opportunity

Multinational agreement is needed on principles and financing commitments.

A global fund could be one way of gathering the necessary finance to support antibacterial innovation. In order for governments to contribute with such large sums of financing to an independent, global fund, significant negotiations and legal agreements are needed.

While countries are considering global commitments, a multi-country political agreement is needed to agree to common principles, including: (1) the amount of total funding to be made available over a set time period, (2) a percentage breakdown of each country's financial commitments, (3) and antibiotic innovation priorities, i.e., lists of priority pathogens and antibiotic profiles, as well as to resource a coordinating secretariat to facilitate joint processes and monitor implementation.

Each government, of course, would determine the best way to satisfy this financial commitment. The strongest options would be those that also support antibiotic

[i] IMI's New Drugs for Bad Bugs programme has financed seven projects with IMI funding totaling to € 314 million (with projects running from 3 to 7 years). JPIAMR has performing four financing rounds with a total of € 54 million available. Kelly et al (Lancet ID 2015) determined that JPIAMR and EU countries financed in total € 1.3 billion for antibacterial research projects from 2007 to 2013. NIH/NIAID has awarded USD 978 million in "antimicrobial resistance" grants from 2012 to 2014. BARDA has awarded between USD 175 - 600 million to perform antibiotic clinical trials from 2011 to 2015. The United States government (including BARDA), Wellcome Trust, and AMR Centre have invested more than USD 350 million over 5 years in antibacterial discovery through CARB-X. The United Kingdom and China are in the process of launching The Global Antimicrobial Resistance Innovation Fund aiming to attract GBP one billion targeting R&D of novel vaccines, drugs, and diagnostics. The Global Antibiotic Research and Development Partnership (GARD) was launched in May 2016 with seed funding of over € 2 million.

conservation. Regardless of which method is chosen, funds should be sustainable.

All countries may not be able to contribute financially, but all could commit to sustainable use measures of the resulting new antibiotics.

DRIVE-AB continues to detail and explore economic incentives for antibiotic innovation, including specific recommendations regarding multinational principles for financing and coordination of antibiotic innovation. Our final recommendations will be issued in September 2017.

We commend the recent commitment made by G20 members to support antibacterial innovation in an inclusive manner, and we look forward to working with the Organization for Economic Co-Operation and Development (OECD) on options for new economic models to stimulate antibacterial innovation in collaboration with the World Health Organization (WHO), the Food and Agriculture Organization (FAO) and World Organization for Animal Health (OIE).

About DRIVE-AB

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 7 pharmaceutical companies supported by the Innovative Medicines Initiative (IMI) Joint Undertaking (www.imi.europa.eu), resources of which are composed of financial contribution from the European Union's Seventh Framework Programme (FP7/2007-2013) and EFPIA (European Federation of Pharmaceutical Industries and Associations) companies' in kind contribution.

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.

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