Towards New Antibiotics:

Key Insights from BARDA in the United States

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Summary

The world needs powerful antibiotics, but the way they are being used today is jeopardising their effectiveness. Overuse of antibiotics in animal production and misuse in everyday therapeutic medicine (along with many other factors) has supported the evolution of antibiotic-resistant bacteria already rendering some medicines useless. This problem could be overcome through the development of new antibiotics. However, the commercial market for such products is perceived to be small in comparison to other drugs – not least because it is expected that any new antibiotic will be held back by medical authorities as a last line of defence to fight off resistant bacteria. Pharmaceutical investment thus tends to shy away from new antibiotics, focusing on more profitable markets instead. The U.S. government has sought to address the resulting lack of commercial investment in this area by creating the new Biomedical Advanced Research and Development Authority (BARDA), which launched a Broad Spectrum Antimicrobial Program in 2010. This policy brief outlines the way that BARDA has tried to encourage the commercial development of new antibiotics, and what lessons can be learned from its experience.

The Challenge

The use of antibiotics has become commonplace in many areas of society. The creation of antibiotics has paved the way for major advances in cancer treatment, organ transplantation, and surgery – irrevocably changing the scope of modern medicine. The use of antibiotics in animal farming has also made possible the intensive production of meat and other products. Antibiotics are thus essential to many economic and medical practices. For those same reasons, the lack of access to powerful antibiotics also remains a pressing issue in many parts of the world today. At the same time, there is growing concern amongst medical experts that overuse or misuse of antibiotics around the world is rendering them less and less effective. The challenge of curbing the rise of antibiotic resistance is thus threefold: 1) creating new efficacious drugs, 2) managing the usage practices of antibiotics, and 3) enabling equitable access to such medicines in many low-income countries.

The Research

This five-year project analysed the ways that the United States government has supported the development of new medicines that have little to no commercial market other than government purchases. The U.S. government did so by establishing a new organization in the form of BARDA in 2006. BARDA was initially set up to support companies in the development of medical countermeasures against bioterrorist threats. However, the development of antibiotics also falls under its remit, provided they could have an application against types of bacteria such as *Bacillus anthracis* that could conceivably be used as agents of bioterrorism. BARDA was chosen as the focus of this research as it is the most significant organisation dedicated to supporting companies in the development of medical countermeasures that would not ordinarily be made without government support. In recent years BARDA has supported numerous companies in development in this area and is an exemplar for similar efforts.

Key Messages

- Antibiotic resistance is a major challenge for many countries around the world
- Pharmaceutical companies will need to develop new antibiotics to meet this challenge
- The U.S. government has fostered new public-private collaborations for developing antibiotics
- Funding, regulatory advice and contracting are potentially key areas of government support
- Longer-term sustainability of these efforts remains a significant challenge

Key Information

- The research leading to these results has received funding from the European Union's Seventh Framework Program (FP/2007-2013) ERC Grant Agreement n. 312567: 'Pharmaceuticals and Security: The Role of Public-Private Collaborations in Strengthening Global Health Security'.

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The Findings

The project found that the U.S. government has used a range of policy mechanisms to incentivise pharmaceutical companies, and to adapt to the key challenges that arise when supporting such companies in the development of new antibiotics. The three most significant of these are:

Funding: Medical countermeasure development is an extremely arduous process characterised by the 'valley of death' – i.e., the lack of funding that often occurs in the mid- to late stages of development and which prevents innovative products from being seen through to completion. BARDA is unique in that it can offer 'non-dilutive' funding (funds that do not require the sale of a company's shares), and hence does not cause dilution of the existing shareholder value. This allows companies to carry out risky development studies without the fear that they will be out of pocket should these studies fail. In this way milestone payments can be used to incentivise companies to work with BARDA and to push products through the advanced development pipeline.

Regulatory: BARDA and the Food and Drug Administration (FDA) also support companies in the development of certain products through regulatory incentives – such as fast track product designation and priority review. Incentives like these can help expedite the review of certain products at the FDA, so reducing the development time helping push a product through the pipeline.

Contracting: One key obstacle when collaborating with large pharmaceutical companies has been the contracting requirements set out in the Federal Acquisition Regulations (FAR) that any partner with the government must abide by. To overcome the industry view that these requirements are too cumbersome, BARDA has begun to use the Other Transaction Authority (OTA) instead. This supports more flexible contracting when compared to FAR. It is also not tied to the success of one drug alone, so it can be used to support a portfolio of potential products – allowing partnerships to continue despite the failure or limitations of one candidate. OTA has already been used to partner with GSK and AstraZeneca in the development of a portfolio of drugs in the antibiotic pipeline. The partnerships that BARDA has set up using the OTA with such companies have also involved a cost sharing arrangement under which both sides are expected to provide funds in contrast to BARDA being the sole source of funding in traditional contracts.

Policy Implications

This assessment of the way that BARDA has supported companies in the development of antibiotics has revealed some significant issues that can serve as guidelines for any future efforts in this area.

Long Term Funding: When incentivising private companies, nothing is more effective than funds in the form of non-dilutive capital. Recently funding for medical countermeasure development and procurement shifted from multiyear advance appropriation to a system of annual appropriations. Dedicated funds for development not only give confidence to companies working in this area, they also reflect their future profitability to potential investors. This shift in funding thus provides no long-term guarantee that the U.S. government will decide to continue the development and procurement of products in this area. Indeed, companies have not received this as a confident statement of government dedication. To generate sustained company involvement in this area long-term funding strategies must be deployed.

Regulatory Development: Medical countermeasure development is at best an uncertain science with the nature of the agents preventing efficacy trials in human beings. The pathways through which medical countermeasures can be developed must be advanced with the relevant science to the benefit of companies. Regulatory pathways must be as clear as possible with viable and realistic avenues for companies to confidently approach antibiotic development and approval. There must also be clear channels of communication and division of responsibilities between regulatory and government agencies when supporting private companies in the development of medical countermeasures in this area.

Flexible Contracting: The use of the OTA has proved successful when trying to collaborate with large and experienced pharmaceutical companies in the development of new antibiotics. Wherever possible this mechanism should be utilised to encourage collaboration and more practical and amenable partnerships.

Enterprise Sustainability: The funding for medical countermeasures is closely linked to the threat environment. The waning threat of bioterrorism has led to the restructuring of the funding offered, noted above. One significant issue in the funding and development of medical countermeasures is their limited shelf life. Indeed, as the government is the only buyer for particular medical countermeasures, upon expiry they can be seen as a wasted investment. This has led to calls for a more sustainable investment and development strategy. A considerable advantage of developing antibiotics is the, albeit limited, commercial market that is available. Going forward the development of antibiotics should be linked as closely as possible to market needs and requirements. In this way public health benefit can be used to maintain significant and sustainable government investment in this area.

Resources

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