

## **Conversation with the Pew Charitable Trusts, July 17, 2013**

### **Participants**

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- Brian Hill – Senior Associate, Philanthropic Partnerships Group, The Pew Charitable Trusts
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**Note:** This set of notes was compiled by GiveWell and gives an overview of the major points made by Allan Coukell, Brian Hill, and Nicole Mahoney in the conversation.

### **Summary**

GiveWell spoke to Pew Charitable Trusts as part of its investigation of antibiotic resistance. The conversation addressed the problem of antibiotic resistance, the drug development pipeline, ways of addressing antibiotic resistance, Pew's work on this issue, and other organizations in the field.

### **What is the problem of antibiotic resistance?**

#### **Magnitude of antibiotic resistance today**

Antibiotic resistance is a major public health problem, though it is difficult to quantify. In the developed world, the number of infections that are difficult to treat with existing drugs is increasing. In the developing world, the problem is likely even more acute, because of underlying health status and patterns of antibiotic use. Without effective antibiotics, many medical procedures would not be possible, such as organ transplants and many types of acute care.

There is no national or global morbidity or mortality data for antibiotic resistance as a whole. It is difficult to distinguish between deaths from non-resistant and resistant bacterial illnesses. Experts from the Infectious Diseases Society of America (IDSA) have said that the majority of deaths from hospital-acquired infections, of which there are about 99,000 per year in the US, are caused by resistant infections.

## **Potential future impacts of antibiotic resistance**

It is difficult to estimate the potential future impacts of antibiotic resistance, because there are no reliable methods for predicting the emergence of resistance. A few years ago, a "superbug" emerged in India due to a gene called NDM-1. This gene directs production of an enzyme that makes the bacteria in which it is found resistant to many, and possibly all, existing antibiotics. If this "superbug" or something similar were to spread around the world, it could bring society back to the pre-antibiotic era, when common infections would often cause death and overall life expectancy was considerably lower. This is a feasible scenario. There are major open questions here, such as how fast could such a bacterium spread and would there be any way to stop it.

## **Decline in the creation of new antibiotics**

The rate of production of new antibiotics has slowed, so as strains of bacteria develop resistance to existing antibiotics, there are fewer alternatives in the pipeline. In the 1980s, 29 new systemic antibiotics were approved; in the 1990s, 23 were approved; in the 2000s, 10 were approved; and in 2011-2012, none were approved. (Systemic antibiotics work throughout the body, rather than only in one area, such as the skin.)

The last new class of antibiotics was discovered in the 1980s, and the last new class was approved for use in people in 2003. A new class of drugs targets bacteria in different ways than existing drugs. Often, companies will make small modifications to existing antibiotics to combat resistance. Most of the antibiotics approved since the 1980s have been modifications of existing classes of drugs.

The Infectious Diseases Society of America (IDSA) has analyzed the pipeline of antibiotics and found that there are some infections emerging for which there are no antibiotics in development at all.

## **Challenges to creating new antibiotics**

There are three reasons why the rate of production of new antibiotics may have slowed:

1. The financial return on producing a successful antibiotic is smaller than producing a "blockbuster drug."
2. There are some aspects of antibiotics that make them particularly difficult to study in a clinical setting.
3. There are scientific challenges to discovering new antibiotics, such as the shortage of natural products from which to derive new antibiotics.

## **What are possible approaches to addressing this problem?**

### **Incentivize the creation of new antibiotics**

It is well accepted that there are still new antibiotics to be discovered; this is not the limiting factor. The challenge is in improving the drug development process, from discovering new chemicals that could make good antibiotics, to identifying new ways of targeting bacteria, to creating better mechanisms for studying antibiotics in people during clinical trials.

Pew was a key player in the Generating Antibiotic Incentives Now (GAIN) Act, which was passed by Congress in 2012. The act provides additional market protection and expedited FDA application review for certain new antibiotics. There has been significant interest in using the provisions of the legislation: companies have already applied for 12 different antibiotics to be included under its provisions.

There was some opposition to the act because it was seen as benefitting the pharmaceutical industry by adding market protections, which would increase profits for companies. On the other hand, there were pharmaceuticals companies that wanted the act to go further, by including more new antibiotics or changing the FDA approval process. Pew worked with the major stakeholders to create an acceptable compromise. Pew was involved in both crafting and advocating for the bill with policymakers. The act was added on as a component of a much larger piece of FDA legislation, which passed with overwhelming support.

Most new drugs have been produced in the US and the EU, but as China and India develop their own biopharmaceuticals research sector, they may play a larger role.

### **Improve stewardship of existing drugs**

More evidence is needed for what stewardship strategy (optimal management of antibiotic use) would work best in the US. Once there is strong evidence for a certain stewardship strategy, the path to implementation may become clearer.

In many other parts of the world, antibiotics are sold over the counter and much more freely used than in the US. Recently, China has set targets for reducing antibiotic use and India has begun to require prescriptions for many previously over-the-counter antibiotics.

Counterfeit and substandard drugs, more prevalent in the developing world, are a serious problem that contributes to antibiotic resistance.

## **How quickly could we respond to an antibiotic resistance emergency?**

Under normal circumstances, it takes more than a decade to bring a drug to market. If an emergency of some kind occurred, this process could be expedited by changing the rules around drug testing and approval. For example, a drug that looked promising during animal testing might be used on humans more quickly than it would under current rules; however, this approach is only used when human testing is unethical or not feasible.

## **Why did Pew choose to work on antibiotic resistance?**

The field of antibiotics and bacterial resistance is one of the Pew Charitable Trust's priority areas because it is a crosscutting issue in public health that has significant potential for positive impact. Unlike other disease areas, to stay still on this issue is to go backwards, because without new antibiotics being developed, society will be more vulnerable to growing bacterial resistance. This area does not receive as much attention as it should, partly because patients don't identify as patients of bacterial resistance, they identify as patients of their primary disease.

## **What does the Pew Charitable Trusts do in this area?**

The Pew Charitable Trusts works on a variety of initiatives relating to antibiotics and bacterial resistance, including:

- Advancing policy that will stimulate the development of antibiotics, either by improving the feasibility of drug development or making it more attractive for companies to be in the field.
- Advocating for a pathway under which the FDA could approve drugs for patients with life-threatening infections and few or no treatment options. These antibiotics would be approved based on smaller studies and for limited use (in patients with no good alternatives).
- Trying to ensure that publicly-funded science addresses important questions about antibiotic resistance and antibiotic discovery, such as finding the best strategy for effective stewardship of existing antibiotics.
- Reducing the use of antibiotics as additives in industrial agriculture.

## **Who else is working on this?**

### **Non-governmental organizations**

- **Center for Disease Dynamics, Economics & Policy** is a group that tracks data on antibiotic resistance.
- **Alliance for the Prudent Use of Antibiotics** published a study a few years ago, funded in part by the Robert Wood Johnson Foundation, that assessed the cost of antibiotic resistance in Cook County, Illinois based on hospital claims forms.
- **Infectious Diseases Society of America** is a group of healthcare professionals who specialize in infectious diseases.
- **Foundation for the National Institutes of Health** and **Critical Path Institute** are two non-profits working to tackle some of the scientific challenges associated with antibiotic development and the challenges posed by the regulatory system for antibiotics.
- **ReAct**, a European-based group that is working to fill knowledge gaps in antibiotic resistance, convene relevant players, and publish reports.

### **Governmental organizations**

- **World Health Organization (WHO)** has published reports on antibiotic resistance.
- **Food and Drug Administration (FDA)**, **National Institutes of Health (NIH)**, and **Centers for Disease Control and Prevention (CDC)** have some resources devoted to antibiotic resistance. They also lead the Interagency Task Force on Antimicrobial Resistance.
- **Veterans Affairs** and **Department of Defense** play a role in all healthcare-related issues, as they run some of the largest and most sophisticated healthcare systems in the US.
- **State and local health departments** perform much of the "on the ground" work in controlling infections and collecting information about the epidemiology of infections.

### **Public-private partnerships and coalitions**

- **Innovative Medicines Initiative (IMI)** is a public-private partnership composed of representatives from the pharmaceutical industry, universities, and some European organizations that are working on antibiotic resistance. IMI is funded by the European Union and the European pharmaceuticals industry. Until recently, this group has focused on basic science and clinical trials. It has now expanded to working on creating business models for antibiotics that provide a sufficient return on investment while also promoting good stewardship, and to assessing the societal value of antibiotics.
- **Pew Charitable Trusts** is working in partnership with the **CDC** and **Urban Institute**

to conduct an ongoing study assessing the costs of antibiotic resistance.

- **Keep Antibiotics Working** is a coalition of advocacy groups primarily focused on reducing the use of antibiotics in industrial agriculture; it works closely with Pew on this.

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