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October 28, 2014

The Honorable Joseph R. Pitts
Chairman, Subcommittee on Health
House Energy and Commerce Committee
2125 Rayburn House Office Building
Washington, DC 20515-6115

Re: "21st Century Cures: Examining Ways to Combat Antibiotic Resistance and Foster New Drug Development," September 19, 2014

Dear Chairman Pitts,

Thank you for the opportunity to testify on this important matter. We cannot allow the most important drug class in human history to be lost. Today we face Ebola; next time it could be drug-resistant bacteria originating in our hometowns. We need urgent action that is much bolder.

You asked me to respond to written questions from Members. The questions and my responses are as follows:

<u>The Honorable Joseph R. Pitts</u>

1. **What are other countries or the European Union doing to help spur research and development for anti-infectives? Which initiatives are working well and which will likely have the most significant impact to draw more companies to anti-infective product development moving forward?**

My response:

The most advanced efforts abroad are in Europe, particularly in England, Sweden and the European Union. Current antibacterial R&D initiatives in Europe are larger than in the US, and include significant studies on the economics of antibacterial drug development.

In England, the Chief Medical Officer, Dame Sally Davies has long championed the issues of antibiotic resistance. Earlier this year, the Prime Minister, David Cameron, created an independent review commission to study the economic problems relating to antibiotic drug development. An interim report is due next year and the UK government is expected to take up legislation in response to this report. Over the past two years, I have led a high-level Working Group on New Business Models

for Antibiotics for the Royal Institute of International Affairs (Chatham House). England is making significant strides to building a better business model for antibiotics.

England is also home to the Longitude Prize, which has announced a £10 prize for a rapid point of care diagnostic that would help reduce unnecessary antibiotic use globally. Most antibiotics are prescribed without diagnostic certainty and in many cases the antibiotic is entirely unnecessary.

Sweden held the Presidency of the EU in 2009 and focused on antibiotic resistance. These efforts raised the profile of resistance across Europe, leading to the €700 million New Drugs for Bad Bugs ("ND4BB") program in the Innovative Medicines Initiative. The first three ND4BB projects focused on basic antibacterial research. The fourth project, DRIVE-AB examines economic problems with antibacterial drug development. I serve as a consultant on DRIVE-AB, which has a funded budget exceeding €9 million. Three additional projects will focus on bringing Gram-negative drugs through the development pipeline to market. ND4BB is an impressive program.

Several things are notable about the European efforts.

First, the magnitude is very large, more than ten times the unofficial cost estimate of DISARM. Every expert agrees that the European efforts are still too small for the problems we face, but their efforts dwarf ours.

Second, every European initiative includes industry, government, academics and civil society working together.

Third, much of the European focus is on the economics, trying to build a new business model for antibiotics. Prominent among these is a concept called "delinkage." For antibiotics, we do not want to drive sales inappropriately. Volume-based sales lead to resistance. Delinkage provides generous rewards for innovative R&D, paying for value rather than volume.

Fourth, stakeholders in the EU are very impressed with BARDA and hold it up as a model for their efforts as well.

In conclusion, several valuable initiatives are underway on both sides of the Atlantic that may be opportunities for the US to coordinate a global response to resistance.

<u>The Honorable Marsha Blackburn</u>

1. **Our committee has enacted important reforms like the GAIN Act to stimulate development of new antibiotics, but realize more work needs to be done. It is my hope that as part of the 21st Century Cures effort we will put additional incentives in place for antibiotics that are designated as Qualified Infectious Disease Products (QIDPs). What other specific incentives do you recommend Congress consider for FDA designated QIDPs.**

My response:

The ERG Report described in my written testimony lays bare the economic problems facing antibacterial drug development. We require economic incentives that change company investment decisions. I suggest five actions:

- Invest in surveillance, infection control and public health. The easiest way to address resistant pathogens is to prevent infection.
- Double NIAID funds for antibacterial R&D over the next decade, without reducing funding for important work on viruses, AIDS, TB or malaria. We need research to feed ideas to industry;
- Expand BARDA's funding and mandates on a stable basis, at a funding level larger than Europe's NB4BB program. BARDA has carried several important Gram-negative antibiotics across the "valley of death;"
- Give refundable tax credits for qualified infectious disease clinical trial expenses; and
- Significantly increase reimbursement for antibiotics, increasing US spending by more than $1 billion per year, approximately 100 times larger than the unofficial annual cost estimate for DISARM. That bill correctly focuses on reimbursement, but it is far too small in size to have an appreciable effect.

Every industry and academic leader that I have spoken with agrees with the basic thrust of these five actions, even if they might be unwilling to be so plain spoken about the limits of DISARM.

In conclusion, act boldly to significantly improve economic incentives for antibiotics.

2. **Congress via the GAIN Act gave FDA a very important tool, to designate certain anti-infectives as QIDPs; and the agency has made good progress on QIDP guidance, as well as designating over 30 developmental antibiotics as QIDPs. If we create other incentives as we should – real incentives are needed – we must avoid a situation where there is confusion and differences over what qualifies for which type of incentive across different agencies of HHS. Will you respond to this statement?**

My response:

QIDP was appropriate for GAIN because the incentive -- 5 years of additional exclusivity -- had a zero CBO score. But when we start spending real money, as I suggest is imperative, then we need to be more carefully tailored across the life cycle of drug development:

- For the doubling of NIAID funds, QIDP is not needed. Let NIH/NIAID manage the grants, looking for both basic research and major breakthroughs;
- BARDA already demands a much higher standard than QIDP. This model works very well and deserves additional funding that is stable over time. BARDA is a truly innovative and important program to carry antibiotics across the "valley of death;"
- Limit tax credits to qualified infectious disease clinical trial expenses, perhaps built on QIDP; and
- For reimbursement after approval, QIDP is far too broad for DISARM or any more powerful version of DISARM. To be blunt: every new molecular entity (NME) antibiotic will probably qualify for QIDP. Probably every NME antibiotic from the past several decades would have qualified. The standard is too easy to meet if we have limited funds and have to prioritize. We should pay for value, not just FDA approval.

In conclusion, business realities are different at various stages of the antibiotic product life cycle. We need carefully designed incentives at each stage. QIDP is not a "one size fits all" solution.

<u>The Honorable Michael C. Burgess</u>

1. **Some in Europe are debating a new system that would change the traditional drug commercialization model, whereby an antibiotic company would receive payment from some third-party for developing a valuable product but then would not handle the sales/distribution of that product. That is, the company would not need to deploy sales teams and whose profit would not be tied to volume sales – they call it "delinkage." What kind of promise does a system like this have? The closest U.S. analog seems to be BARDA. Can we improve the BARDA model to work specifically in this context?**

My response:

Antibiotic delinkage is simply paying for value rather than volume. Paying for volume drives resistance.

I lead the Working Group at Chatham House on antibiotic delinkage. Delinkage will also be a major part of the European Union's DRIVE-AB research project over the next three years and will feature prominently in the UK Independent Commission appointed by the Prime Minister. Delinkage is indeed an important effort to stimulate new antibiotics without boosting resistance. Supporters include governments, universities, and several of the global companies, most notably GlaxoSmithKline and AstraZeneca.

But I must emphasize that many of the details of delinkage will require some additional time to work out. The Chatham House Report from our Working Group will be published in December 2014; the UK Commission will issue a preliminary report in 2015; DRIVE-AB is a three-year project, ending in 2017.

My suggestion is for the US to closely collaborate with this process in Europe and to adapt these ideas to the US context. Our health care system is different from those in Europe and the precise contours of delinkage might well differ here. A study provision should be attached to DISARM to evaluate delinkage in the US context.

In any event, US and European efforts should be coordinated at the highest levels, together with any other nation willing to work together to ensure that antibiotics are not destroyed. That coordination might require some significant diplomatic work around a framework that moves every country in the correct direction.

You also mentioned BARDA. I strongly support BARDA; it is a very effective program, acting like a venture capital fund providing non-dilutive capital. Expanding BARDA to include delinkage will require significantly larger funding that must be stable over a number of years. Companies need to be able to count on those funds being available when their drug is ready. My suggestions for BARDA:

- Expand the Congressional mandate beyond biodefense to include all resistant pathogens that threaten US health;
- Replenish funding on a stable, long-term basis;
- The funding amount should be larger than the European Union's ND4BB program; and
- Also emphasize vaccines, diagnostics and other technologies that blunt resistance as well.

In conclusion, deepen our commitment to BARDA, evaluate delinkage, and coordinate with other countries to counter the threat of resistance.

Thank you for this opportunity. I will send you a copy of the Chatham House report when it is finalized in December.

Sincerely,

Kevin Outterson
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Boston University