



November 5, 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: "21<sup>st</sup> Century Cures: Examining Ways to Combat Antibiotic Resistance and Foster New Drug Development," September 19, 2014

Dear Chairman Pitts:

Thank you again for the opportunity to testify on the important topic of antibiotic resistance and policy options for fostering new drug development. Below please find my responses to questions posed in writing by Subcommittee Members in follow-up to the hearing.

**The Honorable Joseph R. Pitts**

**1. What are the 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?**

In recent years, a number of countries have acknowledged and begun to respond to the need to foster research and development (R&D) for areas of high unmet medical need, including drug-resistant infectious diseases. In the European Union (EU), at least several policy initiatives to this end have been substantial. The EU's primary model for spurring R&D for anti-infectives has centered on public-private partnerships (PPPs).

The EU launched its "Priority Medicines for Europe and the World Project" in collaboration with the World Health Organization in 2004. The Project's stated goal was and remains "to help bridge the gap between public health needs and the development priorities of the pharmaceutical industry."<sup>1</sup> The Project aims to bridge these gaps through a large-scale PPP launched in 2008, known as the Innovative Medicines Initiative (IMI). With a budget of €2 billion in its initial phase, the IMI embraced a novel funding model in which public funds are targeted toward Product Development Partnerships (PDPs). These PDPs aim to

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<sup>1</sup> Kaplan, Warren, Veronika J. Wirtz, Aukje Mantel-Teeuwisse, Pieter Stolk, Beatrice Duthey, & Richard Liang. *Priority Medicines for Europe and the World 2013 Update*. Geneva: WHO Publications, 2013.

stimulate "open innovation" between pharmaceutical companies and other key actors in the healthcare system, including academic institutions, small- and medium-sized enterprises (SMEs), patients, and regulatory authorities. The current IMI budget is €3.3 billion for the period 2014-2024 (€1.638 billion from the EU, and €1.425 billion committed by participating innovator pharmaceutical companies).<sup>2</sup> Important to note is that the largest portion of that funding is dedicated to projects related to chronic disease research for which markets of significant size exist.

For anti-infectives, available IMI funding is disproportionately smaller, though not insignificant: The IMI has reportedly set aside €700 million for a PPP to boost innovation under the "New Drugs for Bad Bugs" (ND4BB) program.<sup>3</sup> An ultimate aim of this program is the clinical development of antibiotics to treat resistant Gram-negative pathogens. Research programs to date have focused on basic antimicrobial resistance (AMR) research.

Outside of AMR, IMI-funded research activities have yielded some notable successes. However, due in part to the disconnect between available short-term funding commitments (3 to 5 years) and necessarily long-term development periods, PDPs have not yet produced hoped-for medical breakthroughs in antibiotics. PPPs for R&D as structured in the EU system are subject to a number of additional limitations. These include, for example, the following:

- The EU has settled on a "consortium management" model, which attempts to integrate academic institutions and SMEs with large pharmaceutical companies through PPPs. While this mechanism is intended to create internal synergies in innovation, conflicts can arise in consortium leadership and project management given the disparate set of competencies and skills represented.
- The intellectual property structure for consortium participation is not fully defined. To date, the EU has not developed specific intellectual property protocols that can be readily allocated against the contributions made by each of the public and private partners participating in the consortium.

At present, with these and other operational questions still outstanding, the ability of the consortium management model to successfully drive the development of new therapies, including new antibiotics, remains uncertain.

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<sup>2</sup> IMI. *Innovative Medicines Initiative 2 Joint Undertaking Budget Plan 2014, Including Staff Establishment Plan 201*. IMI. 2014.

<sup>3</sup> IMI. "New Drugs 4 Bad Bugs." IMI.europa.eu. IMI, n.d. Web. 23 Oct. 2014.

Those uncertainties notwithstanding, the EU has clearly demonstrated global leadership in the fight against drug-resistant infectious disease. We applaud efforts undertaken in the EU to date, which include but also go beyond PDPs.<sup>4</sup>

Among EU member states, at least several have demonstrated leadership in their own capacities on matters pertaining to antibiotic resistance. The United Kingdom (UK), for example, has created an independent review commission on the economic impediments to antibiotic drug development, the results of which will likely support new legislation to help mitigate current hurdles. Additionally, a high-level working group established in the UK is actively exploring new business models for antibiotics (an initiative known as "Chatham House"). The output of the Chatham House efforts will support the newly launched DRIVE-AB<sup>5</sup> initiative, a multi-year IMI-funded program that will further assess the economics of antibiotic drug development.

At Janssen, we believe the U.S. has a special opportunity to complement the PDP and other programs advanced by the EU and EU Member States, and to demonstrate its own global leadership with a set of fresh, bold policy incentives capable of surmounting current barriers and sparking a new era of antibiotics innovation.

### **The Honorable Marsha Blackburn**

- 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 21<sup>st</sup> 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 considers for FDA designated QIPDs?**

Looking ahead to "GAIN II"-related efforts, we recommend that Congress advance a "menu" or "basket" of incentives capable of attracting a larger number and wider range of innovators to the field of antibiotics R&D. At Janssen, our analysis of various incentive

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<sup>4</sup> Beyond IMI, its PDPs and ND4BB program, the EU has initiated a number of other efforts that educate Member States and their citizens with regard to the need to stimulate R&D for anti-infectives in the EU. These additional efforts include the following initiatives:

- In 2009, during its tenure in the EU presidency, Sweden advanced antimicrobial resistance as an EU-wide priority.
- In 2011, the EC issued a five-year "Action Plan against the Rising Threats from Antimicrobial Resistance (AMR)." The EC added additional research funding through the IMI 6th Call on AMR, which supported a part of the Action Plan.
- The European Parliament approved a Resolution in 2012 to address the "Rising Threats of Antimicrobial Resistance."

<sup>5</sup> DRIVE-AB stands for Driving Reinvestment in R&D and Responsible Antibiotic Use.

models suggests that three in particular merit inclusion among those contemplated for GAIN II legislation.<sup>6</sup> They are as follows, listed here in order of anticipated effectiveness:

1. A Transferable Regulatory Exclusivity Incentive (TREI) program;
2. Public-sector underwriting of both early- and late-stage development;
3. Prize models.

As underscored in my testimony, the creation of a special incentives framework for antibiotics innovation, sufficient to attract the world's best and brightest to this great challenge, must be a primary point of focus as Congress examines solutions to the current crisis. Combinations of these and other incentives would, in our view, substantially expand the pool of innovators participating in antibiotics R&D.

- 2. Congress via the GAIN Act gave the FDA a very important tool, to designate certain anti-infectives such as QIDPs; and the agency is 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?**

At Janssen, we agree that definitions should be simple and focused. The GAIN Act included such a designation when it was crafted, targeting its incentives to areas of the greatest and most urgent unmet medical need. For new reforms, we suggest maintaining this narrow focus, even limiting eligible products further to those that both meet an unmet medical need and address infections associated with high mortality rates or significant patient morbidity.

#### **The Honorable Gene Green**

- 1. We have heard a lot of talk about the inherent lack of incentives for drug companies to develop new and novel antibiotic medicines. Why is it that the package of current incentives is not enough to stimulate new drug development? And from your perspective, what is required to solve this problem?**

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<sup>6</sup> Of note, per our internal analysis, less effective incentive models include reimbursement adjustments and tax credits.

The package of current incentives for antibiotics R&D in the U.S. is insufficient because it fails to overcome a major challenge facing antibiotics developers today: no clear commercial viability, no clear return-on-investment potential. While current incentives have streamlined the regulatory pathway for new antibiotics, and provided some modest financial incentives for their development, the overall costs and risks of antibiotics R&D remain disproportionately high relative to the potential for financial reward. This area of research is unique for many reasons,<sup>7</sup> and thus requires a unique and uniquely robust set of incentives to drive progress.

While the GAIN Act certainly recognized the uniqueness of antibiotics, and while it marked an important first step toward spurring greater investment in antibiotics R&D, the need for bolder action remains.<sup>8</sup>

As a next step, to help create the potential for innovator rewards while promoting antibiotic stewardship principles that do not tie financial rewards to the overuse of novel antibiotics, we recommend the establishment of a new package of policy incentives that include, for example,

1. A Transferable Regulatory Exclusivity Incentive (TREI) program;
2. Public-sector underwriting of both early- and late-stage development; and
3. Prize models.

From our company's perspective, no proposed U.S. legislation in view at present offers incentives sufficient to turn the tide against drug-resistant bacteria. Though laudable in their intent, proposals such as those included in the current DISARM<sup>9</sup> Act lack the potency to support meaningful progress. Incentive models such as TREI, by contrast, offer a viable pathway forward for investment in this and other categories of medical products marked by high social value but limited to no commercial value.

2. **We have heard from witnesses on the issue of antibiotic incentives also discussed the importance of stewardship, and you brought up the importance of appropriate use in your testimony. When we are thinking about strategies to combat antibiotic drug resistance, how should incentives for innovation be considered in relationship to stewardship strategies?**

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<sup>7</sup>On this point, it is reasonable to suggest that some new antibiotics developed against drug-resistant bacteria may have different revenue profiles entirely, in some cases developed "in trust," to be placed under the stewardship of others such as public-sector disease control agencies. This scenario is particularly out of concert with standing business models for pharmaceutical R&D.

<sup>8</sup> Tellingly, the CBO Score for the GAIN Act was zero.

<sup>9</sup> DISARM stands for *Developing an Innovative Strategy for Antimicrobial Resistant Microorganisms*.

At Janssen, we support vigorous antibiotics stewardship policies such as those proposed by the U.S. Centers for Disease Control and Prevention (CDC)<sup>10</sup> and others discussed at the hearing on September 19. Stewardship programs play a vital role in managing the overuse of antibiotics and preserving their effectiveness over time. Such programs should be pursued in parallel with, and should be seen as on par with, programs to stimulate R&D toward new antibiotic medicines. Some programs can achieve both innovation and stewardship aims simultaneously: The Transferable Regulatory Exclusivity Incentive (TREI), for example, furthers stewardship aims by de-linking the financial return for a new antibiotic from its use.

**3. You mentioned Transferable Market Exclusivity (TME) as a pull-based incentive that could encourage innovation by affording companies a defined risk period of market exclusivity that can be applied to any compound. Will you elaborate on how you believe TME could be structured to maximize its advantages and minimize downside risks? What guardrails you see necessary to incorporate in any such program?**

As described in my testimony, one of the main barriers to industry investment in antimicrobial drug development is the fact that the expected revenues for such drugs are uncertain and significantly lower, and the risks of research higher, than for drugs in other therapeutic areas. Transferable Market Exclusivity—referred to here as the Transferable Regulatory Exclusivity Incentive (TREI)—can help to address this imbalance by enhancing the expected returns from approval of a qualifying antimicrobial drug. This improved equilibrium is accomplished by permitting the company responsible for the antimicrobial drug to transfer a portion of that drug’s regulatory exclusivity to another drug (the “recipient drug”). The increased revenues from the recipient drug partially compensate for the lower revenues from the antimicrobial drug, thereby increasing incentives for companies to invest in research and development activities for antimicrobial drugs.

TREI can be structured in a variety of ways. The TREI proposal outlined below includes a number of “guardrail” provisions designed to protect potentially impacted stakeholders, such as generic drug manufacturers, while stimulating new and sustained investments in antibiotics R&D. These proposed provisions are as follows:

- Limitation to qualifying antimicrobial drugs. By passing the GAIN Act, Congress recognized that the failure of antimicrobial product development to keep pace with the evolution of pathogens constitutes a public health crisis. Like the GAIN Act, the TREI proposal is limited to antimicrobial drugs intended for serious or life-

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<sup>10</sup> CDC. "Core Elements of Hospital Antibiotic Stewardship Programs." Centers for Disease Control and Prevention. Centers for Disease Control and Prevention, 04 Mar. 2014. Web. 23 Oct. 2014.

threatening infections. The TREI proposal is further limited, however, to drugs that meet an unmet medical need and address infections associated with high mortality rates or significant patient morbidity.

- Maximum transfer of 12 months. Although qualifying antimicrobial drugs are granted a number of years of regulatory exclusivity upon approval, the 12-month maximum for transfers of exclusivity reduces the potential that a company will receive a windfall for its development of a qualifying antimicrobial drug.
- Minimal disruption of generic development. A recipient drug must have at least four years left of its own regulatory exclusivity or at least four years of patent life remaining on a patent covering the drug. Because generics of the recipient drug generally cannot be approved by FDA until expiration of the recipient drug's regulatory exclusivity and patents, this provision gives generic companies significant notice of the additional exclusivity and allows generic companies to make informed decisions about product development.
- Private sector donations to NIH. The owner of a recipient drug must make donations to NIH, not to exceed 5 percent of TREI-derived sales, for purposes of funding grants for basic antimicrobial research. Such donations would provide a stream of new funds for infectious disease research.
- Patient assistance programs. The owner of the recipient drug must make donations to patient assistance programs that are designed to help financially needy patients obtain access to FDA-approved drugs in the therapeutic area the recipient drug is intended to treat. These donations would provide important safety-net assistance for patients who cannot afford their cost-sharing obligations for prescription drugs.

The ways in which this TREI proposal is structured helps to maximize its public health advantages and minimize downside risks, including risks to generic manufacturers. We believe this TREI model is an especially strong option for reinvigorating development of antimicrobial drugs and getting more innovative therapeutic options to patients, sooner.

It is my hope that the written responses provided here have proven helpful to Members of the Subcommittee. Please feel free to contact me should you or your colleagues wish to discuss these topics in greater detail.

Sincerely,



Adrian Thomas

Vice President, Global Market Access & Global Public Health