



215 Pennsylvania Avenue, SE • Washington, D.C. 20003 • 202/546-4996 • www.citizen.org

September 19, 2014

Chairman Joe Pitts (PA-16)
Ranking Member Frank Pallone (NJ-6)
Committee on Energy & Commerce, Subcommittee on Health
United States House of Representatives
Washington, D.C. 20003

Chairman Pitts, Ranking Member Pallone, and members of the Subcommittee:

We write today to register our comments on your subcommittee hearing, “21st Century Cures: Examining Ways to Combat Antibiotic Resistance and Foster New Drug Development,” and the broader public health debate around the growth of antibiotic resistance.

Public Citizen is a national consumer and public health organization with 40 years of history and more than 350,000 members and supporters around the country.

Public Citizen commends the subcommittee for taking the time to consider the public health impacts of the problem of antibiotic-resistant bacteria. In the United States, an estimated two million people are infected with antibiotic-resistant bacteria every year. At least 23,000 people die as a direct result.¹ Antibiotic resistance costs our healthcare system dearly. The economic burden is estimated at \$20 billion in direct healthcare costs and more than \$35 billion in lost wages, extended hospital stays, and premature deaths.²

Members of the subcommittee are right to be concerned about the public health implications surrounding antibiotic resistance. However, the Antibiotic Development to Advance Patient Treatment (ADAPT) Act is not the right proposal to address this issue and boost the discovery of safe new drugs. The ADAPT Act would not address the core economic challenges and bottlenecks regarding the development and discovery of new antibiotics. Moreover, the legislation places patient safety at risk by compromising the U.S. Federal Drug Administration’s (FDA) drug approval process.

The ADAPT Act would create an expedited approval pathway that attacks the standards of FDA review of specific antibiotics intended to treat limited patient populations. Under the legislation, approval could be based on smaller datasets with alternative endpoints, which could be construed to include findings in test tubes, laboratory animals, or mathematical models, and not patient

¹ Centers for Disease Control and Prevention (CDC). Antibiotic Resistance Threats in the United States, 2013. Atlanta, GA: CDC, 2013. Available at <http://www.cdc.gov/drugresistance/threat-report-2013/pdf/ar-threats-2013-508.pdf>.

² Ibid

outcomes such as improvements in symptoms, function, or survival. The drug approval standards for new antibiotics are already low. Creating another so-called “streamlined” approval pathway could drastically compromise patient safety.³

The bottleneck in drug discovery in this area is mainly due to scientific constraints and a weak economic model that allows drug sales to dictate the focus of scientific research. The FDA’s drug approval process is not hampering how we address the growth of antibiotic resistant pathogens. Data regularly cited by the pharmaceutical industry itself demonstrate that the drug discovery bottleneck issue is not regulatory, but scientific.⁴ Since 1964, antimicrobials have had the highest rates of regulatory agency approval of any therapeutic class of drugs.⁵ Scientific discovery in this area is obviously challenging, and as a result, no new classes of antibiotics with novel mechanisms of action (i.e., how a drug works) have been discovered since 1987.⁶

The ADAPT Act would not be the best way to tackle this problem. Indeed, the bill would compromise patient safety and has the potential to place key parts of the approval process in the hands of private stakeholders that may be unduly influenced by industry.

For example, the ADAPT Act would place the FDA standard-setting of antimicrobial susceptibility criteria in the hands of private entities that are vulnerable to industry influence. Under the ADAPT Act, the Secretary would perform quarterly evaluations of susceptibility standards including those from private entities. These test criteria are used to classify whether bacteria are resistant to new drugs. During the process, breakpoints for antibiotic resistance have the potential to be heavily influenced by a private group with close ties to the pharmaceutical industry. The Clinical and Laboratory Standards Institute (CLSI) is a nonprofit group with diverse membership. However, at least a quarter of the members of the CLSI are pharmaceutical industry employees. Only two of the twelve members, excluding the Chair and Vice-Chair, disclosed having no financial conflict of interest.⁷

Another problem with the bill is that it would fail to address the central determinant behind antibiotic resistance. Antibiotic use is the most important factor that leads to resistant pathogens.⁸ ADAPT fails to provide safeguards to conserve novel antibiotics for use in limited populations. Although antibiotics may have favorable results in small populations of critically ill patients, the

³ Carpenter D, Zucker EJ and Avorn J. "Drug-Review Deadlines and Safety Problems." *New England Journal of Medicine* 358, no. 13 (2008): 1354-1361. Available at <http://www.nejm.org/doi/full/10.1056/NEJMsa0706341#t=articleResults>

⁴ Payne DJ, Gwynn MN, Holmes DJ, Pompliano DL. "Drugs for Bad Bugs: Confronting the Challenges of Antibacterial Discovery." *Nat Rev Drug Discov* 6, no. 1 (2007): 29-40. Available at <http://www.nature.com/nrd/journal/v6/n1/full/nrd2201.html>

⁵ DiMasi, J.A., Success rates for new drugs entering clinical testing in the United States. *Clin Pharmacol Ther*, 1995. 58(1): p. 1-14.

⁶ World Economic Forum. *Global Risks 2013*. 8 ed. Geneva, Switzerland: World Economic Forum, 2013. Available at <http://www.weforum.org/reports/global-risks-2013-eighth-edition>.

⁷ Clinical and Laboratory Standards Institute, Subcommittee on Antimicrobial Susceptibility Testing—Disclosure Summary, 5/27/14. Available at: http://clsi.org/wp-content/uploads/sites/14/2013/07/Disclosure-of-Interest_June-2014.pdf

⁸ Centers for Disease Control and Prevention (CDC). *Antibiotic Resistance Threats in the United States, 2013*. Atlanta, GA: CDC, 2013. Available at <http://www.cdc.gov/drugresistance/threat-report-2013/pdf/ar-threats-2013-508.pdf>

lack of adequate testing before new drugs are released to the general population may lead to inappropriate usage based on incomplete safety and efficacy data – making antibiotic resistance *worse* and not better.

The ADAPT Act also would fail to control the overprescribing of antibiotics. The final section of the Act states that “nothing in the bill shall restrict the prescribing of antibiotics or other products by healthcare providers” including those for limited populations. This statement may be interpreted to imply that although antibiotics may only be approved for use in limited populations, providers may prescribe them for any patient. Wide use leads to more widespread antibiotic resistance, exacerbating the public health concerns ADAPT seeks to address.

Finally, the ADAPT Act would not mandate the disclosure of data that would improve innovation of new antibiotics and their effective stewardship. The lack of transparency occurs in several venues. First, the ADAPT Act would not require disclosure of drug company sales of their antibiotics, some only approved for limited populations. Second, it wouldn’t require the release of clinical trial data of shelved products. Third, it wouldn’t require the release of clinical trial data of products receiving five more years of exclusivity under the GAIN Act as qualifying infectious disease products, or of drug trials conducted after approval for this limited population use. All of these failures lead to huge knowledge gaps that will hinder innovation and patient safety.

To effectively combat antibiotic resistance in the 21st century, we require incentives that spur the development of truly novel antibiotics. We should not and cannot instead undermine necessary drug approval protections that are in place to tackle antibiotic resistance.

A more comprehensive approach to tackle this public health concern would do the following:

- 1) **Bolster a coordinated federal government approach by the National Institutes of Health to address the scientific challenges in drug innovation.** The National Institute of Allergy and Infectious Diseases’ research program can study antibiotic drug resistance mechanisms that help drug firms and academic groups bring new drugs forward for testing in humans.
- 2) **Provide incentives only for antibiotics that address unmet medical needs** that are studied in patients with these needs and show added benefits for these patients. Approved drugs should improve efficacy and decrease harm to patients.
- 3) **Strengthen and not undermine the FDA approval process.** Clinical trial design should reflect the clinical benefits of an unmet medical need. For example, if an unmet medical need in question is patient death, then the trial endpoint should be mortality, not an alternative endpoint.
- 4) **With FDA expedited approval of novel antibiotics, there should come responsibilities of ensuring antibiotic stewardship.** Measures might include limiting prescribing and dispensing to certain trained providers or certified institutions or requiring administration in specific healthcare settings.

- 5) **Remove any conflict of interest in standard setting of antimicrobial susceptibility testing of drugs.**
- 6) **Ensure data transparency to ensure greater innovation and better antibiotic stewardship.** Beyond monitoring the use of antibiotics, confidential clinical trial data should be released publicly so that treatment decisions are based on the most complete clinical data available and drug developers can avoid placing patients through unnecessary risks.

Again, we are very encouraged to see the subcommittee choosing to tackle the issue of antibiotic resistance. However, despite its intentions, the ADAPT Act would not go far enough to appropriately tackle the grave public health concern caused by antibiotic resistance. In fact, it undermines the current safeguards in place intended to protect the public. We encourage members of the subcommittee to oppose this legislation and to go further towards solving the problem by supporting stronger proposed recommendations as mentioned above. These recommendations align incentives for appropriate antibiotic drug discovery while maintaining the public's trust that approved antibiotics are both safe and effective for treatment.

Sincerely,



Vijay Das
Healthcare Advocate
Public Citizen's Congress Watch