July 31, 2013

The Honorable Phil Gingrey
U.S. House of Representatives
442 Cannon House Office Building
Washington, DC 20515

The Honorable Gene Green
U.S. House of Representatives
2470 Rayburn House Office Building
Washington, DC 20515

Dear Representatives Gingrey and Green,

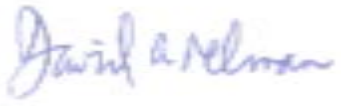
We are writing today to applaud your leadership in supporting the creation of the Limited Population Antibacterial Drug (LPAD) approval pathway to expedite patient access to critically-needed antibiotics to treat serious or life-threatening infections for which there are currently few or no satisfactory treatment options. Antibiotic development has declined dramatically, while drug resistance continues to soar, leaving a very serious unmet medical and public health need.

Regulatory and economic challenges have contributed to the decline in antibiotic innovation—particularly for drugs to treat resistant infections. The LPAD pathway will encourage the development of antibiotics to treat highly resistant infections by creating a new mechanism to allow FDA to more quickly approve novel antibiotics on the basis of trials conducted on smaller subpopulations with the most serious illnesses. In contrast, antibiotics are now studied in large patient populations with a wide range of disease symptoms. A properly constructed LPAD pathway could make clinical trials shorter and less expensive and at the same time would allow for special labeling that would reflect the more limited data and help ensure limited use.

We urge you to enact legislation to create an LPAD pathway based on the principles outlined in the attached document in order to make development more feasible for the antibiotics needed

most by patients. These principles also call for data collection to ensure the pathway meets its intended public health goals, including limiting the use of these new drugs to the patients for whom they are intended in order to preserve the drugs' utility and protect patients' health.

Thank you for your leadership on this critical public health issue. We look forward to working with you as you continue to develop policies to further stimulate antibiotic development. If you would like any additional information, please do not hesitate to contact our organizations at acoukell@pewtrusts.org or ajezek@idsociety.org.



Allan Coukell
Senior Director, Drugs and Medical Devices
The Pew Charitable Trusts

David Relman, MD, FIDSA
President, IDSA

**Core Principles for a limited population antibacterial drug (LPAD) pathway**

As drug-resistant bacterial infections grow more common, few antibiotics are available to treat them. Today, patients need new drugs to treat increasingly common infections, particularly highly resistant serious or life-threatening ones such as those caused by carbapenem-resistant Enterobacteriaceae (CRE), a family of dangerous pathogens that pose special risk to patients in the hospital. Thomas Frieden, Director of the Centers for Disease Control and Prevention recently warned that these "nightmare bacteria" are spreading rapidly across the U.S. and are resistant to our strongest antibiotics.

Regulatory and economic challenges have contributed to the decline in antibiotic innovation for more than a decade—particularly for drugs intended to treat resistant infections in small numbers of patients. Last year, as part of the Food and Drug Administration Safety and Innovation Act, Congress enacted Generating Antibiotic Incentives Now provisions, which give additional exclusivity to qualifying new antibiotics. This law was a good first step to address some of the financial disincentives to antibiotic innovation. However, to overcome the dearth of antibiotic innovation, we need a sustained and multi-pronged strategy to spur industry and investor interest in reinvigorating the antibiotic pipeline.

As one next step, the undersigned organizations urge Congress to support creation of a new regulatory pathway for antibiotics that target special or limited patient populations—namely those suffering from serious or life-threatening infections with few or no satisfactory treatment options. The new pathway will encourage the development of antibiotics that address the greatest unmet needs (mainly caused by resistance) and get them to patients faster (preferably before the serious or life-threatening pathogen is widely spread). This pathway would speed patient access to important antibiotics by allowing them to be approved based on clinical trials with smaller numbers of patients than the trials for more widely used antibiotics. It is not feasible for antibiotics that treat serious infections due to highly resistant bacterial pathogens to be developed using traditional, large clinical trials due to the limited numbers of patients in whom these infections occur. This pathway must be designed to balance the immediate needs of patients and physicians with measures to monitor drug use in appropriate populations without placing undue

burdens on Infectious Diseases physicians, nurses, hospitalists, hospital administrators, and antibiotic innovators.

The limited population antibacterial drug pathway should be created through new legislation based on the core principles outlined below.

Specifically, the new law should:

1) Create a special designation and label (with logo) distinguishing products approved under the limited approval pathway from traditional antibiotics (e.g., drugs approved for more common infections or for infections for which satisfactory therapeutic options exist);
2) Acknowledge that the benefits of an antibiotic approved under the pathway outweigh the risks for the limited population for which the drugs are indicated based on smaller datasets, taking into account the seriousness of the infection and the unmet medical need. For the purposes of the legislation, the definition of unmet need should allow for the approval of multiple antibiotics per indication to ensure the antibiotic pipeline is sufficiently diverse;
3) Include a mechanism to collect information in order to evaluate the utility of the pathway, preferably including the FDA's Sentinel System and/or the CDC's National Healthcare Safety Network;
4) Require FDA to issue guidance, within one year of enactment, on acceptable clinical trial designs to demonstrate the safety and effectiveness of antibiotics approved under the pathway;
5) Ensure that the option to pursue this pathway for limited approval be voluntary for drug sponsors;
6) Allow removal of the limited population designation if FDA approves a broader indication sought by the sponsor under the traditional approval pathway;
7) Provide for submission and FDA review of promotional materials of products approved under this pathway, using the processes FDA has already established for accelerated approval products; and
8) Not attempt to regulate the practice of medicine.

The special limited population pathway could have a number of important effects. First, the streamlined process would provide patients more rapid access to potentially life-saving therapies by lowering regulatory barriers to the development of antibiotics they most need, providing an incentive for companies that otherwise would be discouraged by prohibitively high development costs and lengthy testing timelines. Second, narrow indications could create conditions for value-based or premium pricing for high-need antibiotics, which will encourage greater research and development investment. Third, Congress' support for this new drug pathway and FDA's special designation and labeling will send a strong signal to the health care community and patients about the critical need to use these drugs prudently, given that their approval will be based on a benefits/risks assessment that supports use in limited, high-risk populations, but not in the broad population of patients suffering with infections that can be treated effectively with existing drugs. The designation and labeling will also help encourage judicious use of limited population antibiotics—an important goal if we are to preserve the effectiveness and promote stewardship of these vital medicines over time.

Many companies have abandoned antibiotic development during the past decade, citing regulatory challenges as the primary reason. By making the approval pathway for high-need antibiotics more feasible, the limited population pathway may encourage drug developers to invest once again in the field.

Affinium
American Academy of Otolaryngology—Head and Neck Surgery
American Medical Association
American Society for Microbiology
Antibiotics Working Group (Cempra, Optimer, Rib-X, Trius, Durata, The Medicines Company, Theravance)
Association for Professionals in Infection Control and Epidemiology
Cempra
Infectious Diseases Society of America
Michigan Antibiotic Resistance Reduction Coalition
National Association of County and City Health Officials

National Foundation for Infectious Diseases

The Pew Charitable Trusts

Rempex

Society for Healthcare Epidemiology of America

Society of Critical Care Medicine

Society of Hospital Medicine

Society of Infectious Diseases Pharmacists

Tetraphase

Treatment Action Group

Trust for America’s Health