THE PEW CHARITABLE TRUSTS

2005 Market Street, Suite 2800 215.575.9050 Phone
Philadelphia, PA 19103-7077

901 E Street NW 202.552.2000 Phone
Washington, DC 20004
www.pewtrusts.org

August 13, 2018

Commissioner Scott Gottlieb, M.D.
Dockets Management Staff (HFA-305)
Food and Drug Administration
5630 Fishers Lane, Rm. 1061,
Rockville, MD 2085

RE: Docket No. FDA-2018-D-2032*: Limited Population Pathway for Antibacterial and Antifungal Drugs*

Dear Commissioner Gottlieb,

The Pew Charitable Trusts is an independent non-profit organization that applies a rigorous, analytical approach to improve public policy, and has been committed to advancing strategies to spur the development of new antibacterials. This letter is to provide comments on the draft guidance for industry entitled, "Limited Population Pathway for Antibacterial and Antifungal Drugs." Pew is a part of a broader group of stakeholders that have long supported this approach, which will help bring new medicines to patients who have few or no treatment options and will ultimately save lives. Pew is committed to the implementation of this important pathway and appreciates the opportunity to comment on the draft guidance.

Drug-resistant bacterial infections are becoming more common, and few antibiotics are available to treat them. A majority of infectious disease doctors report having treated patients who have infections that do not respond to any antibiotic. In the past decade, scientific and economic barriers have contributed to the decline of antibiotic innovation as evidenced by a decreasing number of large pharmaceutical companies engaged in antibiotic discovery. Without a robust pipeline of antibacterial candidates, increasing numbers of patients will succumb to these resistant infections, and other common medical interventions like transplants, chemotherapy, and surgeries would become more dangerous.

The limited population antibacterial drug (LPAD) pathway provides a mechanism for the FDA to review and approve new antibiotics specifically for use in patients with unmet medical needs. Drug developers focused on highly resistant bacterial infections often face challenges in identifying and enrolling patients with these pathogens in sufficient numbers for large-scale clinical trials. These infections are very serious and often deadly, but are still rare enough to make large trials difficult. LPAD allows approval of antibiotics in limited populations of patients with unmet medical need by considering the benefits and risk for patients with few or no treatment options. Pew supports the polices and processes in the draft document and offers recommendations on proper use, labeling, and stewardship.

Appropriate use is critical to delivering optimal patient care, while also limiting the likelihood of antibiotic resistance developing to these new drugs. LPAD has several provisions to help guide the proper stewardship of antibiotics approved under this new pathway. Specifically, any new

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antibiotic approved under the LPAD pathway must prominently display a special designation clearly labeling it as "Limited Population." In addition, the guidance requires FDA to preapprove any promotional materials from the drug sponsor to ensure that the drugs are only marketed for use as intended in the target population and not for any other purpose. Pew appreciates the inclusion of these provisions in the draft guidance and their role in providing safeguards to help ensure that these drugs are only used when appropriate for approved patient populations.

The legislation requires the collection of aggregate antimicrobial drug use and resistance trends, including those approved under the LPAD pathway. Additional language should be included in the finalized guidance on how FDA proposes to monitor the use of the LPAD-designated drugs and whether the limited population indication is working as intended or whether the drugs are being used in the broader population for whom they have not been evaluated. FDA has been forward looking in taking steps to promote rational prescription of opioids and the agency should similarly coordinate with other federal agencies such as the Centers for Disease Control and Prevention and the Centers for Medicare and Medicaid Services (CMS) to support polices focused on judicious use and antibiotic stewardship.

Antibiotics should only be used to treat bacterial infections and prescribed in doses and durations that are appropriate for the patient and infection being treated. When implemented correctly, antibiotic stewardship programs (ASP) improve patient outcomes and appropriate antibiotic use and demonstrate reductions in adverse events and health costs.[1] Pew supports the CMS proposed Conditions of Participation rule which requires all hospitals to implement an ASP. Broad implementation of ASPs in the hospital settings would help ensure the long-term efficacy of LPAD drugs by mitigating overuse. Pew recommends FDA work closely with CMS to ensure finalization of this rule and its important role in the stewardship of these essential medicines.

Pew thanks FDA for the opportunity to comment on this draft guidance and appreciates your agency's efforts to ensure a strong pipeline of new antibiotics and promote appropriate use and stewardship of these essential drugs. If we can be of assistance to you in these efforts, please do not hesitate to contact Sarah Despres, sdespres@pewtrusts.org.

Sincerely,

Allan Coukell
Senior Director

[1] "A Path To Better Antibiotic Stewardship in Inpatient Settings." The Pew Charitable Trusts, Washington, D.C. (April 2016) http://www.pewtrusts.org/en/research-and-analysis/reports/2016/04/a-path-to-better-antibiotic-stewardship-in-inpatient-settings