TAG
Treatment Action Group

Oral comment re: docket number FDA-2018-D-2032
Public Meeting on
Limited Population Pathway for Antibacterial and Antifungal Drugs

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Thank you to the U.S. Food and Drug Administration for this opportunity to offer comment on behalf of Treatment Action Group, or TAG.

TAG is an independent, activist and community-based research and policy think tank fighting for, among other improvements, better treatments and a cure for HIV, and related co-morbidities tuberculosis and hepatitis C virus.

From our founding over 25 years ago, we have understood that both ambitious research agendas and a flexible but rigorous regulatory authority are necessary for achieving these advances.

TAG was instrumental in advocating for the development of accelerated approval and parallel track pathways, which paved the way for earlier but conditional drug approval in response to urgent unmet medical needs, as well as pre-approval access under the current expanded access framework. These regulatory flexibilities were vital to progress against the HIV epidemic. We are proud that they have endured and been improved upon to allow similar progress in other disease areas.

Since then, other initiatives to stimulate investment in neglected diseases, including orphan drug, priority review, fast track, and breakthrough therapy designations have been introduced. These initiatives have had utility in facilitating product development in at least the disease areas on which TAG works.

But we cannot ignore that pivotal to progress on HIV, hepatitis C, and more recently, tuberculosis, has been investment in rigorous research. We understand the challenges of securing such investments, especially for diseases of little commercial interest or with limited or hard-to-enroll patient populations. In our current work on TB, this is a problem we face routinely. And let's not forget that HIV was once a disease that no one paid attention to, especially not pharmaceutical companies or their shareholders.

With existing incentives and regulatory flexibilities, we are concerned that already the trade of rigor for speed may compromise the FDA's ability to ensure drug safety and efficacy, and undermine equitable access. For example, the Orphan Drug Act's exemption for pediatric research means children—the most orphaned of all when it comes to drug development—don't benefit from advances that are made.

We are deeply concerned that further lowering the evidentiary bar for regulatory approval will do a disservice, rather than a favor, to patients.

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At the core of FDA's mission is the responsibility "for protecting the public health by ensuring the safety, efficacy, and security of [...] drugs."[1] As Professor Susan Ellenberg remarked at a recent FDA hearing regarding a new anti-infective drug candidate, "People in these desperate situations are every bit as entitled, if not more entitled, to have drugs where there's a definitive evidence that they are going to work."[2]

We support the remarks submitted by the National Center for Health Research and the questioning by survivor Jonathan Furman on safety issues that could come under the Limited Population Pathway for Antibacterial and Antifungal Drugs.

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If the FDA does decide to go ahead with this pathway despite these appeals, we are concerned that the pathway could be applied to tuberculosis, the active, infectious form of which (particularly its drug-resistant strains) affects a relatively small number of patients in the U.S. However, millions of people are affected by tuberculosis globally. This creates a risk that drugs approved under lower evidentiary standards given limited patient numbers in the United States could be applied to large patient populations abroad. As such, we ask the FDA to ensure that, if this pathway does advance, it makes clear that conditions that affect a large number of patients in other settings outside the U.S. are ineligible.

Further, if this pathway does proceed in some form, we do not agree that compliance with the labeling and promotional material requirements currently in the draft guidance is sufficient to alert patients or providers to the lax evidentiary standards under which benefits and risks were assessed for a drug. And we are alarmed to see comments from pharmaceutical companies asking for even fewer labeling requirements.

There is also insufficient protection against off-label use, an extremely common practice in the U.S.

Additionally, noting that "the LPAD pathway should also not be used to salvage a trial that fails to demonstrate its objective or an inadequately designed development program" seems difficult to enforce.

We welcome and encourage efforts to attract and appropriately incentivize further research into health areas that have not attracted and are unlikely to attract commercial investment in research. But cutting corners for research is not the way to do this. We need appropriate incentives that facilitate development and promote rigorous science, not merely more incentives.

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[1] U.S. Food and Drug Administration. What We Do. 2018 Mar 28. Available from: https://www.fda.gov/about-fda/what-we-do

[2] Ravelo JL. Will a new TB treatment be available soon? Devex. 2019 July 05. Available from: https://www.devex.com/news/will-a-new-tb-treatment-be-available-soon-95140