



Senator Lamar Alexander
Chairman, US Senate Committee on Health, Education, Labor, & Pensions

Senator Patty Murray
Ranking Member, US Senate Committee on Health, Education, Labor, & Pensions

cc: members, US Senate Committee on Health, Education, Labor, & Pensions

March 4, 2015

Dear Senators Alexander and Murray,

On behalf of the National Physicians Alliance (NPA), we are writing to express concern over the *Promise for Antibiotics and Therapeutics for Health* or PATH (S. 185) bill introduced by Senators Orrin Hatch and Michael Bennet. In the interest of our patients' health and the public health of our nation, we ask you to **withhold** support for this bill.

The NPA represents physicians across medical specialties who are dedicated to promoting evidence-based medicine; the organization accepts no funding from pharmaceutical companies. Antibiotic resistance is a major problem worldwide and the US needs a comprehensive, scientifically-based approach to deal with this issue. PATH as written presents a fast-track pathway for FDA drug approval based on data from animals, test tubes, and mathematical modeling instead of clinical trials in humans with diseases. This will result in new drugs which are ineffective and unsafe for our patients while actually adding to antibiotic resistance and fostering the growth of "superbugs." In the interest of our patients' health and the public health of our nation, we ask you **not to support** this bill.

Our specific concerns regarding PATH are:

- (1) **PATH only addresses antibiotic resistance by introducing another fast-track pathway, which is not needed.**

FDA regulations already give the agency the authority to approve drugs in limited well-defined sets of patients. Compared to other drug classes, antibiotics already have higher rates and speed of approval. In addition, the agency has just issued a new draft guidance to expedite the "compassionate use" of investigational drugs for individual patients. Physicians can make requests far more readily than in the past for individual patients with unmet medical needs who are willing to take an informed risk. The drugs can remain under investigation for the wider public.

- (2) **PATH allows drug approval based on smaller datasets with alternative endpoints, animal studies, test tube studies and mathematical models in place of clinically relevant endpoints and appropriate clinical trials in humans.**

Such intermediate surrogate clinical endpoints and data from test tube studies, laboratory animal tests, or mathematical models do not necessarily reflect outcomes that matter to patients and clinicians. We want to see improvements in symptoms, function, or survival. Approving antibiotics based on these criteria would only undermine the FDA and violate its mission to protect public health by ensuring the safety and efficacy of these drugs.

- (3) **PATH further reduces standards for approving new drugs by allowing drug approval based on “non-inferiority” trials that do not provide better drugs to counter antibiotic resistance.**

Under Section 2b, “approval ...shall not be denied due to a lack of evidence to fully establish a favorable benefit-risk profile” in a broader population. As drugs may be approved based on preclinical data, this would then allow drugs on the market that are actually inferior to existing drugs. Drugs approved by the FDA should improve efficacy (superiority, not just non-inferiority) and/or decrease harm to patients. PATH fails to target incentives towards developing truly novel antibiotics as opposed to “me-too” products. Drugs without evidence of added benefits should not be rushed to approval.

- (4) **PATH has no safeguards to conserve novel drugs for use in these limited populations.**

Drugs that are beneficial in critically-ill patients should be subjected to confirmatory testing before being released for use in the general public for more minor infections. The lack of additional testing before further release may lead to inappropriate usage due to the lack of safety and efficacy data. Since the most important factor leading to antibiotic resistance is antibiotic use, this would only exacerbate the problem further.

- (5) **PATH fails to call for better diagnostics in order to decrease the prescribing of antibiotics, which will result in more widespread resistance.**

Section 9B of this bill state that “nothing...shall...restrict the prescribing of antibiotics or other products, including drugs approved under the limited population pathway, by health care professionals, or to limit the practice of health care.” Clinicians need better diagnostics in order to use antibiotics appropriately, decrease unnecessary side effects from drugs that won’t benefit patients, and decrease the spread of resistance. FDA does not regulate the practice of medicine, but it should provide evidence and tools to aid doctors in practicing better medicine.

- (6) **PATH goes beyond antibiotics, extending its fast-track approval pathway approach to any other drug class.**

Most egregiously, under Section 10, “the limited population pathway for antibiotic drugs may be expanded to apply to approval of other drugs intended to treat a serious or life-threatening illness.” This goes beyond the wording of the companion ADAPT bill (HR. 3742) in the House of Representatives, setting a troubling precedent that would allow unsafe and ineffective drugs of any kind to reach our patients. Shortcuts that allow drug approval without adequate, scientifically-based confirmatory studies in humans should not be expanded to even further classes of drugs. This would take clinical trials science very far back and result in even further harm to our patients.

Rather, the standard that Congress set up over 50 years ago of adequate and well-controlled studies in human diseases should remain the scientific gold-standard.

In summary, the PATH bill as written would allow for the approval of unsafe and ineffective antibiotics as well as all other classes of drugs. The bill fails to address antibiotic resistance and could potentially worsen the problem. Combating antibiotic resistance requires a much more comprehensive solution. Our recommendations in place of this bill are as follows:

- (1) New antibiotics are needed, but they must be shown to improve efficacy (superiority, not non-inferiority) or at least be less harmful compared to existing drugs.
- (2) Legislation to combat antibiotic resistance must include safeguards to conserve our current antibiotics and ensure effective antibiotic stewardship.
- (3) Legislation should strengthen, not lower the FDA approval standard for adequate and well-controlled trials in humans for all classes of drugs.
- (4) To hasten the development of truly innovative antibiotics, legislation should increase support for research and development at the NIH.

As the PATH bill fails to substantively address antibiotic resistance and lowers FDA standard for testing of all drugs, **we urge you not to sign onto the bill**. Instead, we urge you to consider a broader, more effective approach such as that in the newly-released House bill, the **Helping Effective Antibiotics Last or HEAL**, sponsored by Representatives DeLauro, Schakowsky and Meng—a bill we do support. We invite you to contact us for further discussion.

Sincerely,



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