



February 10, 2014

The Honorable Joseph R. Pitts, Chairman, Committee on Energy & Commerce
The Honorable Frank Pallone, Jr., Ranking Member, Committee on Energy & Commerce
2125 Rayburn House Office Building, Washington, DC 20515

Cc: Members of the U.S. House Committee on Energy & Commerce, Subcommittee on Health
Senator Tom Harkin, Chairman, U.S. Senate Committee on Health Education, Labor & Pensions
Senator Lamar Alexander, Ranking Member, U.S. Senate Committee on Health Education, Labor & Pensions
Members of the U.S. Senate Committee on Health Education, Labor & Pensions

Dear Congressmen Pitts and Pallone,

On behalf of the National Physicians Alliance (NPA), we are writing to express concern over **H.R.3742**, the *Antibiotic Development to Advance Patient Treatment Act of 2013* (ADAPT). The NPA represents more than 15,000 physicians across medical specialties, dedicated to promoting conflict-free medicine. We have grave concerns that ADAPT's primary beneficiaries would be the pharmaceutical and clinical laboratory supply industries rather than our patients. In the interest of our patients' health and the public health of our nation, we ask you to withhold support for this bill.

Our specific concerns with ADAPT are as follows:

- 1) **Another fast-track pathway is not needed.** The FDA already has the authority to approve drugs in a limited subset of patients under its basic labeling regulations. In addition, we have "compassionate use" pathways in place for individual patients and their providers wishing to try investigational drug choices. If we aim to hasten the development of new antibiotics and biologics, we should do this through an agency such as the National Institutes of Health, which is not tied to industry.
- 2) **ADAPT allows drug approval based on "alternative endpoints" in place of traditional, clinically-relevant endpoints.** Our concern is that these "alternative endpoints,"—which may be "surrogate" clinical endpoints or endpoints found in laboratory animals or even just in mathematical models—do not necessarily reflect significant patient outcomes, such as improvement in symptoms, function, or survival.
- 3) **Changes in interpretation of susceptibility criteria are now to be made by a private group closely tied in with industry, presenting a conflict-of-interest.** Such groups have the potential to benefit from adjusting sensitivity levels in a way that leads providers to order newer, more expensive antibiotics. Clearly such basic decisions in patient care should be based on unbiased science. Additionally, the Act forces the Secretary to perform quarterly evaluations of these criteria and to change such criteria based on clinical and pre-clinical "pharmacokinetic, pharmacodynamics and statistical" data, as well as "Bayesian and pharmacometric statistical methodologies." We are concerned that Congress does not have the scientific expertise to specify which technical methods the FDA should be allowing to direct its decisions.

- 4) **This Act allows for ready expansion in use of initially-restricted drugs to a general population, without specifying what studies should be done.** Drugs or biologics found helpful in critically-ill patients should be subjected to much broader testing before they are released for the general public for use in more minor infections. Our standards for proving efficacy, comparing these drugs with older drugs, and judging safety must be broader and more thorough. The FDA should not put the larger population of patients with susceptible infections at risk while trying to develop drugs for far less common resistant infections.

- 5) **The use of investigational drugs should be restricted; prescribing practices must be regulated.** The final section (4) of the Act states that “nothing (in the bill) shall be construed to restrict in any manner, the prescribing of an antibiotic or other products by health care providers or to limit the practice of health care.” This is a dangerous statement. Does it imply that, despite the fact that these new antibiotics/biologics are to be approved for a limited subset of the population, doctors are free to prescribe them for any patient?

In summary, this bill is unnecessary for the protection of extremely ill patients; is potentially hazardous to the general population; could lead to the development of earlier resistance to newer agents through widespread, unregulated use; relies on untested hypotheses instead of valid clinical data; would increase cost to our health care system by shifting prescription patterns to newer, more expensive antibiotics; and would place an unnecessary administrative burden on our regulatory agencies by mandating they evaluate data submitted by private organizations.

Given the many serious problems in this bill, we strongly ask you to withhold your support of ADAPT and we invite you to contact us for further discussion.

Sincerely,



Jim Scott, MD
NPA President



Lisa Plymate, MD
Chair, NPA-FDA Taskforce

References:

The drug doripenem increased mortality in hospital acquired pneumonia despite favorable animal models and promising in vitro testing. A second trial was stopped early due to increased mortality despite dosing in the second trial based on pharmacodynamic modeling. See FDA warning: <http://www.fda.gov/drugs/drugsafety/ucm285883.htm>

The drug tigecycline increased mortality in various infections despite non-inferiority on "traditional" endpoints and promising animal models and in vitro testing. See FDA warning: <http://www.fda.gov/Safety/MedWatch/SafetyInformation/SafetyAlertsforHumanMedicalProducts/ucm370170.htm>

The drug televancin increased mortality in one of two trials in hospital acquired pneumonia (in the trial with more patients with renal and heart failure) and showed "non-inferiority" on "traditional endpoints" while it increased mortality. Again the drug had promising animal models.

The drug bedaquiline was approved for multi-drug resistant TB based on a single phase 2 trial with a surrogate endpoint despite increasing death by 5-fold compared to older TB drugs.

A recent AHRQ panel showed a lack of evidence that pharmacodynamic modeling resulted in improved outcomes for patients.

Studies at Johns Hopkins looking at shifting susceptibility criteria in their patients found that changes would have led to 300% of patients being taken off older antibiotics but that this would not have affected clinical outcomes. Tamma et al. *Ped Inf Dis J* 2013 Sep PMID: 23470679