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February 20, 2014

The Honorable Fred Upton, Chairman

Energy and Commerce Committee

United States House of Representatives

Washington, DC 20515

Dear Chairman Upton,

As members of the Patient, Consumer, and Public Health Coalition, which includes groups representing physicians, scientists, consumers, and patients, we are writing to express our concerns about H.R. 3742, the Antibiotic Development to Advance Patient Treatment (ADAPT) Act of 2013.

We share your concerns that antibiotic resistance is a serious public health problem. As the Centers for Disease Control and Prevention (CDC) has noted, more than 2 million Americans fall ill and more than 20,000 die each year due to pathogens that are antibiotic resistant. All of us want to “do something” about this terrible situation.  However, the current version of the ADAPT Act could contribute to antibiotic resistance rather than protect patients from it.

Below are our specific concerns:

**Protecting New and Old Drugs from Resistance**

Most new antibiotic that have been approved have eventually been overused, resulting in resistance to the new antibiotic as well as greater resistance to older antibiotics that have similar chemical structure to the new ones.

“Stewardship” refers to protecting the new drugs, and the old ones, from being used when they are not needed, and saving them for when other drugs are ineffective.  Strong stewardship must be a part of any new bill in order to protect antibiotics from overuse, and unfortunately is missing from the ADAPT Act, and was missing from previous antibiotics legislation, the GAIN Act that passed in 2012.  We strongly agree with the CDC that **“Perhaps the single most important action needed to greatly slow down the development and spread of antibiotic resistant infections is to change the way antibiotics are used.”****[[1]](#endnote-1)** The CDC points out that “as much as 50% of the time, antibiotics are prescribed when they are not needed or they are misused.”

Unfortunately, stewardship is contrary to the goals of pharmaceutical companies, which is to sell more of their products to as many patients as possible.  That is why they strongly support the ADAPT Act, which devotes only one sentence to “ensuring appropriate stewardship” and has no specific strategies to ensure effective stewardship.

Since new antibiotics in the same *class* as current antibiotics can harm the effectiveness of the entire class of antibiotics, responsible public policy requires gathering more information to prevent that from happening.  **If the ADAPT Act is to succeed in saving lives, it needs to be revised to add protections that would reduce the dangerous misuse of new or old antibiotics.** Unfortunately, the current version of the ADAPT Act falls far short of doing that.

**Safe and Effective for the Patients who Need Them**

We need new antibiotics that are safe and effective as measured by patients’ health and survival.  Unfortunately, the ADAPT Act encourages the use of “surrogate endpoints” rather than the **outcomes that really matter to patients: their health.**   For example, last year the FDA approved a new TB drug that was more effective than older drugs at killing bacteria in patients’ spit; unfortunately, the patients randomly assigned to taking that drug were 5 times more likely to die than patients randomly assigned to older TB drugs in a double blind clinical trial.  This is the kind of dangerous and nonsensical approval decision that is likely to become more frequent under the methodological suggestions included in the ADAPT Act.  Physicians and patients deserve the information they need to make medical decisions that are based on clear evidence of whether a patient is likely to benefit rather than be harmed by a new antibiotic.  **Since Congress is not expert on research methodology, it should not include methodological recommendations in legislation.**  That section of the ADAPT Act should be deleted.

It is essential that the FDA ensure the benefits of antibiotics outweigh the risks. More than half of all antibiotics approved by the FDA from 1980 to 2000 were removed from the market because of their risks.[[2]](#endnote-2)

The ADAPT Act also encourages the use of smaller clinical trials, which would make it difficult, if not impossible, to determine if new antibiotics affect specific types of patients differently. For example, it is vital that the FDA be able to evaluate how safe and effective a new drug is in specific subpopulations such as women, men, minorities, seniors, or patients with common illnesses such as diabetes or heart disease. Ironically, in 2012 Congress passed legislation requiring the FDA to issue a report regarding women, minorities, and the elderly in clinical trials used by the FDA, and an action plan aimed at improving the analyses of the safety and effectiveness of new medical products for those demographic subgroups, and inclusion of that information in product labels.  By encouraging the FDA to conduct fewer and smaller clinical trials focused on patient outcomes, **the ADAPT Act would discourage the FDA from improving information about the safety and effectiveness of new drugs for women, minorities, and the elderly, contrary to this previous Congressional legislation that you supported.**

**Labels with Clear Warnings and the Risks of Off-Label Use**

The Act would encourage the FDA to approve drugs that are not carefully tested on a sufficient number of patients, and then warn doctors and patients of those lower standards with a warning on the label stating, “This drug is indicated for use in a limited and specific population of patients.”   If drugs are not tested on a large group of patients to determine safety, then ADAPT should require that the label include a large logo that clearly states that the drug is approved for a limited population and may not be safe or effective for other patients. Without that visible reminder, the drug is likely to be used by many patients for whom the approval was not intended.  **It makes no sense to take the risk of lowering the approval standards in order to approve a drug for desperate patients who are most likely to benefit, and then provide no safeguards to ensure that the drug is used appropriately for that specific patient group**.  It is worrisome that the pharmaceutical industry opposes a logo or special warning at the same time that they claim that their goal is to have drugs approved only for a targeted, well-defined smaller group of patients.

Whenever the FDA approves a drug, it is for a specific use that the agency determines is likely to benefit patients more than it will hurt them.  It does not mean that the drug is safe and effective for all types of medical uses.  Off-label use of drugs refers to a drug that is prescribed for a use that was not approved by the FDA.  Doctors are free to prescribe drugs for these other uses, but companies are not allowed to promote them for off-label uses. The ADAPT Act should include increase penalties for off-label promotion.

In recent years, major pharmaceutical companies have paid billions of dollars in fines for such illegal promotion activities, and those fines are considered worth it to the company because of the profits that off-label uses provide.  Even though ADAPT Act proposes labeling for use of the new antibiotics only for a limited “population” of patients, such as those with MRSA, the final section of the bill states that nothing in the ADAPT Act “shall be construed to restrict, in any manner, the prescribing of antibiotics.”  That means that the **bill provides no enforcement authority to restrict the drugs to those patients that are most likely to be helped and least likely to be harmed** by the new drug. A recent study makes it clear that this type of overuse of antibiotics “can speed the development and spread of antibiotic resistance.”2

**Antibiotic Use in Animals**

The vast majority of antibiotics are used in animals. The CDC report cites the use of antibiotics for animals as an example of how antibiotic resistance spreads.  It stated that “drug-resistant bacteria can remain on meat from animals” and if the food is “not cooked properly, the bacteria can spread to humans.”  In 2011, “80% of antibiotics sold by weight in the U.S. were used for meat and poultry production.”[[3]](#endnote-3) The FDA recently issued a *voluntary* guidance on the use of antibiotics for animals but it has been sharply criticized as being weak and ineffective. The **ADAPT Act does not address this major issue**. **If the Act truly wants to slow antibiotic resistance, it must include provisions in the ADAPT Act to help to reduce antibiotic use in animals.**

**Prevention**

The CDC recommends preventing infections by focusing on immunizations and strategies as simple as hand washing.  The CDC recommends tracking the *causes* of infections and the *risk factors* that led to resistant infections. **The ADAPT Act would just monitor the use of antibacterial and antifungal drugs, but would not examine the *causes* of infections, which is what the CDC recommends.**  The ADAPT Act should follow the CDC’s recommendation.

**Incentives**

The ADAPT Act assumes that the incentive of faster approvals would encourage companies to develop new antibiotic and antifungals.  The GAIN Act of 2012 already provides incentives to antibiotic drug makers, and according to its author, Representative Phil Gingrey, GAIN’s incentives are working.  He stated in a July 2013 press release that “12 new antibiotics are currently in the final stages of approval process.”  A recent *Wall Street Journal* article noted that more companies are working to develop new antibiotics.[[4]](#endnote-4) **There is no evidence that more incentives are needed at this point – especially if those incentives could cause additional resistance.**

The ADAPT Act also includes unnecessary incentives for developing new antifungal drugs.  **Antifungals are expensive and not in short supply. They should not be included in the legislation.**

**FDA’s Authority to Help Patients with Urgent Needs**

The ADAPT Act does not give the FDA new authority to change its scientific standards or help desperate patients get access to new medications more quickly.  **There is no reason to pass the ADAPT Act unless it provides greater safeguards for the use of existing authority, such as logos that warn physicians and patients that a new drug is not approved for a general population because it was tested on a small sample of targeted patients**.  Moreover, for intensive care patients or others who desperately need new antibiotics, the existing compassionate use pathway can provide access to drugs that are still under study. In addition, the FDA already has several programs that speed drug approvals for antibiotics and other drugs.  These programs include breakthrough therapy designation, fast track approval, accelerated approval, and orphan drug status.

**Conclusion**

Antibacterial resistance is an important public health issue but the ADAPT Act, as currently written, does not provide the protections needed to make sure that the bill will help rather than harm the current situation.

The ADAPT Act could easily be improved.  We would like to work with your office to address all of the concerns we listed above.  If antibiotics are speedily approved but are not safe or effective, then we have caused more harm than good to patients.

American Medical Student Association

American Medical Women’s Association

Connecticut Center For Patient Safety

Jacobs Institute of Women’s Health

National Physicians Alliance

National Research Center for Women & Families

National Women’s Health Network

The TMJ Association

WoodyMatters

*For more information, contact Paul Brown at (202) 223-4000 or pb@center4research.org*

1. U.S. Department of Health and Human Services Centers for Disease Control and Prevention.  Antibiotic Resistance Threats in the United States, 2013.  Accessed February 5, 2014.  <http://www.cdc.gov/drugresistance/threat-report-2013/>. [↑](#endnote-ref-1)
2. Kesselheim, AS, Outterson K (2011). Improving Antibiotic Markets for Long Term Sustainability. *Yale Journal of Health Policy, Law, and Ethics, Volume 11.* Accessed February 5, 2014. <http://www.ncbi.nlm.nih.gov/pubmed/21381513>. [↑](#endnote-ref-2)
3. Plumer B, (December 14, 2013). The FDA is cracking down on antibiotics on farms. Here’s what you should know. *The Washington Post.* Accessed February 5, 2014. <http://www.washingtonpost.com/blogs/wonkblog/wp/2013/12/14/the-fda-is-cracking-down-on-antibiotics-at-farms-heres-what-you-should-know/>. [↑](#endnote-ref-3)
4. Drug Makers Tiptoe Back Into Antibiotic R&D. *The Wall Street Journal (January 2014).* [↑](#endnote-ref-4)