April 28, 2017

Members of the House Energy and Commerce Committee
Members of the Senate Health, Education, Labor and Pensions Committee
via mailto:FDAsuserfees2017@help.senate.gov

Dear Senators and Representatives:

The Collaboration for Research Integrity and Transparency at Yale is heartened to see bipartisan efforts toward prompt passage of the Food and Drug Administration (FDA) Reauthorization Act of 2017. The work of the 5,000 FDA employees funded by the user fee amendments is crucial to protecting and advancing public health. We are concerned, however, by the federal Right to Try bill as well as legislative efforts to permit off-label marketing by restricting how the FDA determines the “intended use” of medical products. We urge you to reject any amendments that would introduce provisions of these other bills or efforts into the Food and Drug Administration (FDA) Reauthorization Act of 2017.

The “Right to Try” Creates False Hope

Right to try legislation fails to advance the interests of people with terminal illnesses and makes an empty promise of access to unapproved treatments. Current policy already allows those with terminal illnesses to obtain experimental treatments through compassionate use, emergency use, and treatment IND programs managed by the FDA, if the use is approved first by the manufacturer.

The FDA is not Denying Experimental Treatments to Patients
Manufacturers have often been reluctant to approve requests based on limited experimental drug supplies, desire to enroll patients in clinical trials, and financial and liability concerns. In the ten years between 2005 and 2014, the FDA approved 99.7% of patient applications for expanded access that had manufacturer approval. The FDA application forms for expanded access take less than an hour to complete.

Risk to Patients and the Drug Development Process
The federal right to try bill would allow patients to take unapproved medications after preliminary safety studies (Phase I) are completed, but before studies are done to further establish safety and to determine effectiveness. This would risk patients’ health and safety. Roughly 90% of drugs that enter the first phase of clinical testing do not reach the market because of unanticipated toxicity or because of a failure to show clinical benefits. In January 2017, the FDA released a report on 22 cases studies where
promising results of Phase II trials were not confirmed by Phase III trials, due to a lack of safety and/or efficacy. In an attempt to allay manufacturers’ reluctance to provide access to experimental agents, the federal right to try bill provides misguided incentives that would compromise the drug development process. The bill appears to allow manufacturers to commercially profit from drugs provided under “right to try,” while relieving them of liability from any harms to patients and barring the FDA from considering the outcomes from such uses. These provisions essentially lower the bar for companies to market drugs targeting terminally ill patients and could threaten the clinical testing process that is critical to generating evidence that demonstrates whether drugs are safe and effective. While allowing companies to profit, the bill could also place patients at financial risk, since private and government-funded insurance programs typically do not cover experimental treatment.

**Off-label Marketing Risks Patient Health and Undermines Incentives for Rigorous Research**

Currently, drugs and biologics are only approved based on adequate and well-controlled studies, demonstrating safety and efficacy for particular uses. Some off-label uses are supported by substantial evidence and are recommended in clinical practice guidelines. While physicians are allowed to prescribe drugs for off-label uses, pharmaceutical companies are prohibited from marketing medicines for these purposes. The FDA has justifiably intervened when drugs and biologics are marketed for unapproved or off-label uses, due to the health risks involved. A recent study found that 80% of off-label prescriptions lacked strong evidence to support their use, and that patients who received drugs prescribed for off-label use that were not supported by strong evidence were 54% more likely to experience an adverse drug event than those who received a drug for an approved use. Restrictions on off-label marketing protect patients, primarily by ensuring that companies generate data before they market, thus giving companies incentives to create the information that doctors need to properly prescribe.

Recent bills – such as the Medical Product Communications Act of 2017 – have proposed restricting the government’s ability to regulate the pharmaceutical promotion of “off-label” uses. Like previous proposals, the current bill limits what evidence the FDA can use to determine that a medical product has an “intended use” that differs from an approved use – the primary mechanism in which the government demonstrates that a company has engaged in promoting an unapproved use. The bill prohibits the FDA from demonstrating the “intended use” of a product by relying on a company’s actual or contributive knowledge of off-label uses or a company’s “scientific exchange” about off-label uses. The latter is particularly problematic because the bill also sets a less rigorous bar for what can be considered “scientific exchange” and broadens the categories of permissible “scientific exchange” about off-label uses, including articles in lay, non-peer-
reviewed journals, letters to editors, and communications at conferences. If this bill were passed, companies would be permitted to disseminate information about off-label uses under the guise of “scientific exchange,” and the government would be prohibited from using such communications to show that the company marketed off-label uses.

Permitting off-label promotion would discourage companies from investing in clinical research to support new uses of drugs.\(^7\) In fact, companies might be tempted to obtain approval for one narrow indication and then expand the market for the drug without generating strong evidence that is independently scrutinized by the FDA. This would undermine the regulatory system that ensures that a drug’s safety and efficacy is tested and validated with respect to every use marketed by a company. This result is not mandated by the First Amendment, properly understood, and the FDA should continue to prohibit off-label promotion.\(^8\)

Thank you for your attention to this matter.

Sincerely,

Margaret McCarthy
Executive Director