To: Collaboration for Research Integrity and Transparency at Yale
From: Collaboration for Research Integrity and Transparency at Yale
Date: October 31, 2016
Re: 21st Century Cures and FDA’s Regulation of Medical Devices

The Collaboration for Research Integrity and Transparency (CRIT) is a joint initiative of Yale Law School, Yale School of Public Health, and Yale School of Medicine. Our mission is to promote health by improving the integrity and transparency of biomedical and clinical research. At Congresswoman Rosa DeLauro’s request, we prepared this memorandum to provide resources that discuss the current problems with the FDA’s regulation of medical devices and to raise concerns with how the 21st Century Cures bill will further weaken regulatory standards and could lead to less safe and effective devices on the market.

1. Many medical devices are approved by the FDA without adequate clinical evidence

A 2011 research paper by Diana Zuckerman, Paul Brown, and Steven Nissen found that of the medical devices that have been recalled for life-threatening or very serious risks, over 70% were cleared via less stringent review pathways and 7% were not even reviewed by the FDA.[1] This accompanying commentary by Rita Redberg and Sanket Dhruva discusses the need for reliable evidence of safety and effectiveness before approval.[2] While it is impossible to discover all safety concerns before a device is marketed, conducting rigorous clinical trials helps to ensure that we have adequate evidence of safety and effectiveness. Even the highest-risk devices are approved on the basis of just one clinical trial, which enrolls fewer than 250 patients on average.[3] Furthermore, although randomization and blinding are the gold standards for reliable clinical evidence, only about half of these trials are randomized and fewer than half are blinded.[3]

2. The FDA lacks the resources for adequate post-market surveillance of devices

Because pre-approval studies have limitations, the hope is that post-market studies – studies that occur after a device receives FDA approval – will provide helpful data. However, recent research has shown that post-market studies are usually less rigorous and reliable as they often lack randomization and blinding, and nearly half do not focus on clinical outcomes that are likely to be meaningful to patients.[3] They are also often delayed – only 13% are completed between 3 to 5 years of approval of a high-risk device.

The FDA also relies on voluntary reports of adverse events to determine if devices are unsafe. However, the FDA noted last week (October 24, 2016) that hospitals sometimes do not file these reports, and thus, the voluntary surveillance is limited.[4] Additionally, according to
3. Consequences for patients – Examples of defective/recalled devices

Approving medical devices without adequate clinical evidence could increase risks for patients. Many high-risk devices are permanently implanted, making their removal difficult and possibly dangerous. Defibrillators are permanently implanted medical devices that are intended to provide lifesaving therapy to patients with heart failure if their heart develops an abnormal heart rhythm. In the last decade, there have been multiple recalls of defibrillators approved without clinical data, including Medtronic’s Sprint Fidelis & St. Jude’s Riata and Riata ST defibrillators, which were found to fail and have led to substantial health risks, including death.[5, 6]

Thirteen models of St. Jude’s defibrillators provide a very recent example. An FDA Safety Communication (dated October 11, 2016) issued for these 13 models warns of sudden battery failure that can occur within one day.[7] (In normal functioning defibrillators, cardiologists have several months warning before a battery dies, thereby providing sufficient time for replacement). 398,740 affected devices have been sold worldwide, and this battery complication has been linked to at least 2 deaths, 10 people fainting, and 37 people feeling dizzy due to the sudden and unexpected failure of their defibrillator’s battery. St. Jude has issued a Class I recall, the most serious type of recall, and stated that there are 199,642 active implants within the United States.[8] A Wall Street Journal article on this FDA Safety Communication links to a paper published in December 2014 that had identified these safety concerns.[9, 10] Thus, the risks were known for at least 22 months before the FDA issued its Safety Communication and before St. Jude issued the recall.

For more recent examples, here is the FDA’s list of medical device recalls in 2016.[11]


The approval of ineffective or defective medical devices, in addition to possibly placing patients at risk, increases national spending on devices that have not been proven to be safe and effective. This recent article discusses the U.S. Health and Human Services Inspector General’s report demonstrating that Medicare spent $1.5 billion because of recalls and device failures of 7 defective heart devices implanted in 375,991 beneficiaries.[12, 13] Additionally, Medicare beneficiaries spent approximately $140 million in co-payments and deductibles for these devices and their related complications. Implanting medical devices that are untested can lead to severe adverse events and place a great financial burden on society.

5. 21st Century Cures will further weaken regulatory standards

This New York Times op-ed by Rita Redberg and Sanket Dhruba describes several problems with the 21st Century Cures bill concerning medical devices.[14]
a. Priority review for breakthrough devices

Section 2201 of the House bill expands the expedited pathways program for “breakthrough” devices, which would permit the FDA to approve more devices through a less stringent review process. The provision broadens the definition for “breakthrough” and encourages the FDA to rely on “shorter or smaller clinical trials” and “surrogate endpoints.” This January 2016 article by Aaron Kesselheim and Thomas Hwang, entitled “Breakthrough Medical Devices and the 21st Century Cures Act,” discusses how drugs billed as “breakthrough” have often not been clinically effective, and it is critical that a breakthrough designation for medical devices is reserved for those devices that are truly transformative and beneficial technologies.[15]

The Advancing Breakthrough Medical Devices for Patients Act (S. 1077) is the Senate’s companion bill to this provision. This Blog Post in The Hill (May 2016) discusses the problems with the Senate’s bill.[16] While not as extreme as the House version, the Senate’s bill has a vague definition for “breakthrough” and raises similar concerns of allowing more devices to qualify for expedited review when they may not truly be “breakthroughs” that benefit patients.

b. Weaker scientific evidentiary standards for high-risk devices

Section 2222 of the House bill permits the FDA to approve high-risk devices on the basis of less rigorous evidence, such as case studies (i.e. anecdotal evidence), registries, and medical journal articles. While it is impossible to discover all safety concerns before a device is marketed, conducting controlled clinical trials helps to ensure that there is adequate evidence of safety and effectiveness. Pressuring the FDA to rely on uncontrolled studies or journal articles could prevent the FDA from learning and assessing important safety risks.[14] There is no companion provision in the Senate bills.

c. Third-party quality assessment for devices changes

Section 2221 of the House bill allows devices makers to select and pay a nongovernmental third-party to certify that changes to devices are safe and effective, in lieu of submitting an application to the FDA. Such a system creates a conflict of interest and makes it difficult for physicians and patients to trust the safety or effectiveness of modified devices.[14] Device makers could make changes to even the highest risk medical devices (such as artificial heart valves) without first notifying the FDA or demonstrating to the FDA that the modified device remains safe and effective.[17] According to an FDA report from 2012, the use of third-party review for medical devices in Europe has resulted in unsafe devices on the market that were not approved for distribution in the U.S.[18] There is no companion provision in the Senate bills.
Sources


