nature medicine

A closer look at the 21st Century Cures Act

The proposed 21st Century Cures Act is a potential boon to the funding woes faced by the US National Institutes of Health and the Food and Drug Administration. But a careful look at the provisions within the bill is warranted to avoid enacting policies that could undermine the progressive translation of research into clinical products.

In July, the US House of Representatives passed the 21st Century Cures Act with overwhelming bipartisan support, a rare occurrence in the current American political climate. But as *Nature Medicine* went to press in mid-September, the US Senate had yet to schedule a hearing or vote to decide the fate of the bill. If approved by the Senate and enacted into law, the 21st Century Cures Act would provide an extra $8.75 billion to the US National Institutes of Health (NIH) over five years. The Act would also benefit the US Food and Drug Administration (FDA), adding $110 million to its yearly funding over the same period to help to accelerate the drug and device review process.

But several stipulations in the 21st Century Cures Act that deal with the drug and device approval processes are of concern. In its current form, the bill could relax oversight of these processes.

High-risk devices include those used to support and sustain human life. For their approval, the FDA currently accepts as evidence peer-reviewed articles, case histories and controlled investigations showing that the benefits provided by the device outweigh the risks. Yet although the new bill stipulates that documented case histories and peer-reviewed journal articles can be submitted as evidence for the approval of new devices, it notably omits controlled investigations.

To help expedite the process of getting devices to the market, the bill also suggests adopting "adaptive" clinical trial designs, including shortening the length of the trial and reducing the sample size. Moreover, one section of the bill says that the FDA could forego requirements demonstrating efficacy if a device would benefit fewer than 8,000 individuals.

The 21st Century Cures Act aims to accelerate the delivery of drugs and devices to patients, and this is important and laudable. But valuing speed over safety and efficacy gives cause for concern. A recent study evaluating the life cycle of high-risk devices that received the FDA's approval in 2010 and 2011 found that, on average, the approval of a device relied on the results of only two clinical studies (*JAMA* **314**, 604–612, 2015). Of the 33 post-market studies that the FDA requested for the 28 devices approved, only six had been completed at the time of the *JAMA* study, roughly five years after their approval. Post-market follow-up is often a contingency for the approval of these high-risk devices, but as this study demonstrates, manufacturers aren't fully complying. The 21st Century Cures Act, if passed, could lead to an even lower threshold for the approval of high-risk devices as well as for other, less risky medical devices.

To expedite the approval of orphan drugs, the bill states that the FDA may rely upon data that was previously submitted as part of a different approved drug or application, even if the indication for that drug was different. Currently, the FDA accepts previously submitted data to aid a new drug application as a reference, but not as evidence. But as a recent article in *Forbes* pointed out, the FDA's approval rate for new drugs is greater than 95%, and given that, according to the FDA, all reviews are completed within six to ten months, it is debatable whether the approval process needs further streamlining.

Of serious concern is that the bill seems to waive the need to obtain informed consent for clinical trials in certain instances. The bill stipulates that consent from participants in a trial is not required as long as "the proposed clinical testing poses no more than minimal risk to the human subject," without any indication of what constitutes "minimal risk" or who would make that determination. Without strict guidelines on what constitutes risk, such a relaxed informed consent process could be dangerous.

The FDA told *Nature Medicine* that the language in the bill must strike a balance between making new products available to those who need them while also preserving the agency's high standards. Others, such as former FDA commissioner David Kessler, have expressed similar concerns about the FDA's role as outlined in the bill. Meanwhile, the health advocacy organization Research!America has lauded the bill as a "victory for patients and their loved ones."

The 21st Century Cures Act has many provisions to recommend itself, particularly the added funding to the NIH for basic and translational research. Although the proposals are well intended, the language in the bill needs some adjustment to ensure that future drugs and devices undergo appropriate review before hitting the market.