BMJ 2015;351:h4013 doi: 10.1136/bmj.h4013 (Published 23 July 2015)

FEATURE

BRIEFING

21st century cures: is US medicines bill a colossal mistake?

A massive proposed US law claims to accelerate the discovery, development, and delivery of new medicines, but critics warn about the implications for drug and device safety. **Peter Doshi** sets out some of the more controversial changes

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The 21st Century Cures Bill is so large that is it impossible to summarize it in a sentence. But that has not stopped its proponents and critics from doing so. "Improve lives, save money," declares one press release sent out by the House Committee on Energy and Commerce, which introduced the bill to the full House of Representatives in May. "All about the patients," declares another. Public Citizen, the health watchdog, has a different catchphrase: "Don't buy the snake oil." At over 350 pages, the bill is far reaching and proposes major changes to America's central medical institutions.

What do people agree on?

One core component with broad support aims to boost funding for the National Institutes of Health by $1.75bn (£1.1bn; €1.6bn) a year for five years, with provisions to invest in younger, emerging scientists and "high-risk, high-reward" research. The increase, however, would still leave the NIH's funding—now around $30bn a year—well below what it would have been if there had not been a 20% fall over the past decade.[1]

How will it affect drug regulation?

The bill encourages the FDA to broaden the types of data it considers when evaluating new drug or device applications, allowing for expedited review and approval of new medicines based on trials using surrogate endpoints, in vitro data, animal studies, modeling studies, and smaller, early stage clinical trials in humans. Section 2222 of the bill, for example, says that in the context of the FDA's evaluation of medical devices, "valid evidence" can include results published in journal articles. Other sections (2221 and 2224) call for changing regulatory processes by requiring the FDA to accredit third parties to conduct quality system assessment and develop standards. Certification by such third parties would allow device companies to apply to bypass certain current FDA approval requirements when making changes (such as design or material) to their moderate and high risk devices. The bill also directs $110m a year for five years to the FDA.

Although the bill's website says that "Dr Woodcock, who runs the FDA's drug center, stated publicly in June that [21st Century] Cures does nothing to lower FDA's gold standard (safety standard),"[2] not everyone is so confident. Concern that the bill will expose consumers to unsafe drugs and devices, thereby undermining public health, is at the heart of some of the bill's biggest critics such as Public Citizen, the National Center for Health Research, the National Physicians Alliance, the HIV/AIDS Treatment Action Group, and faculty from UCSF, Yale, and Harvard. On 20 July, the editorial board of the *New York Times* weighed in, declaring the bill to be "loaded with bad provisions," and identified special interest money as key to fueling its bipartisan support.[3]

Will it increase off label use?

Section 2102—titled "responsible communication of scientific and medical developments"—directs the FDA to issue guidance to manufacturers for acceptable dissemination of information that is not included in FDA approved drug and device labeling. This may make it permissible for industry to promote products for "off label" uses, something currently illegal but increasingly litigated in the US as a first amendment freedom of speech issue.

What are the provisions for rare diseases?

Delivering "cures" for rare diseases, those affecting fewer than 200 000 people in the US, is another major focus of discussion around the bill. Section 2151 attempts to incentivize drug manufacturers to repurpose major market medicines for rare diseases by offering a six month extension of patent protection for all indications and certain exclusivity periods on already approved treatments if the sponsor obtains approval of a new indication for a rare disease. The exclusivity extensions cannot be revoked "for any reason" even if the drug is later found to

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be ineffective or unsafe, with one exception: the initial application "contained an untrue statement of material fact." These incentives will be in addition to the incentives already put in place by the Orphan Drug Act of 1983, pediatric exclusivity, and exclusivity for antibiotics deemed qualified infectious disease products.[4]

Who has proposed it?

The bill was introduced to the House of Representatives by Diana DeGette, a Democrat from Colorado, and Fred Upton, a Republican from Michigan who chairs the Energy and Commerce Committee. Although it was formally introduced to the house only this May, substantially different draft versions of the bill—some running to over 400 pages—have been circulating for months. The introduction of the bill was long expected after DeGette and Upton began convening numerous roundtables and congressional hearings in April 2014.

What are people saying about it?

The website of the Energy and Commerce Committee boasts a list of over 700 groups in support of the bill, "encompassing patient advocacy groups, rare disease groups, cancer centers, technology groups, top universities, biopharmaceutical companies, medical device companies, and others from across the country."

But former FDA commissioner David Kessler, writing in the *New York Times* with two members of AIDS Coalition to Unleash Power (ACT UP), contends that the "21st Century Cures Act could substantially lower the standards for approval of many medical products, potentially placing patients at unnecessary risk of injury or death."[5]

Recently departed FDA commissioner, Margaret Hamburg, showed her concern before leaving the FDA. "It is foolish—in fact dangerous—to believe that reducing regulatory standards will make new treatment interventions appear if the science is not there," she stated in her final speech as commissioner, in what is widely assumed to be a reference to 21st Century Cures.

Is it likely to pass—and if so, when?

Proponents point to the bill's bipartisan support in a time of great partisan gridlock as evidence of its "non-partisan" nature. And its momentum thus far is hard to miss. Entering the floor of the House after a 51-0 vote in subcommittee, the full House voted 344-77 on 10 July to approve the bill.

Now in the Senate's hands, and seeing increasing public debate, the bill's ultimate fate is difficult to predict. One major sticking point that emerged in the lead up to the House vote was whether the proposed spending on NIH and FDA should be mandatory or subject to later Congressional negotiation. Upton has said that he aims to have the bill on the president's desk for signing by the end of the year.

Competing interests: I have read and understood BMJ policy on declaration of interests and declare I am employed by the University of Maryland, Baltimore, which has signed a group letter in support of the bill.

The full bill is downloadable from www.congress.gov/bill/114th-congress/house-bill/6 and the House Energy and Commerce Committee has set up a dedicated promotional website (http://energycommerce.house.gov/cures).

Provenance and peer review: Commissioned; not externally peer reviewed.

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Cite this as: *BMJ* 2015;351:h4013