

## 21<sup>st</sup> Century Cures Act Could Speed Drug Approval Process

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### ABSTRACT

**On Friday, July 10<sup>th</sup> the U.S. House voted overwhelmingly to streamline the approval process of prescription drugs and medical devices by the FDA. If passed in the Senate and signed by President Obama, the 21<sup>st</sup> Century Cures Act would foster significant regulatory changes in the introduction of new drugs to the market. The Act would allow for shorter clinical studies involving fewer individuals for certain kinds of drugs and would expand use of biomarkers as a measure of drug efficacy. Opponents raise ethical questions related to patient safety. The Act is analyzed in light of these objections and with a historical perspective of prescription drug regulatory policy.**

**Keywords:** FDA, 21<sup>st</sup> century cures act, Health care reform, Health care policy, Regulatory reform.

On Friday, July 10<sup>th</sup> the U.S. House voted overwhelmingly to streamline the approval process of prescription drugs and medical devices by the FDA. If passed in the Senate and signed by President Obama, the 21<sup>st</sup> Century Cures Act (“The Act”) would foster significant regulatory changes in the introduction of new drugs to the market. The main focus of the 352-page Act<sup>1</sup> is a reduction of bottlenecks in the regulatory process that slow the development of new drugs. The Act would allow for shorter clinical studies involving fewer individuals for certain kinds of drugs. It passed 344-77 with strong, bipartisan support<sup>2</sup>, though opponents raise concerns about The Act’s lack of assurances of patient safety.

**EXPANDED USE OF BIOMARKERS:** The Act would allow for expanded use of surrogate endpoints as evidence of the efficacy of drugs. Surrogate endpoints are biomarkers such as lab measurements which are thought to predict clinical

benefit, but are not outright measures of such benefit. Use of surrogate endpoints has been shown decrease the time of clinical trials without compromising safety of patients<sup>3</sup>. For example, instead of having to wait to learn if a drug extends survival for diabetic patients, the FDA could approve a drug based on evidence that it reduces hemoglobin A1C levels. Surrogate endpoints have been used in this manner since 1992 when the FDA instituted Accelerated Approval regulations; however, those regulations limited use of surrogate endpoints to drugs being developed to treat a serious condition that filled an unmet medical need. The 21<sup>st</sup> Century Cures Act would expand the FDA’s authority to use surrogate endpoints. It requires The Secretary of Health and Human Services to collaborate with the medical community to issue appropriate standards to support the development of biomarkers as evidence of drug efficacy and develop a taxonomy for the classification of biomarkers for use in drug development.

Supporters have long called for greater flexibility in the regulatory process both quicken the pace of clinical trials and introduce greater personal drug therapy and precision medicine approaches. Greater use of surrogate endpoints would do just this. A person-centered focus tailored to each individual’s unique biometric needs could supplement the traditional disease-focused approach to drug development.

If a drug that is already on the market is shown to have a new use, The Act will allow case studies to suffice as evidence of the new benefit rather than require additional clinical trials. The Act will also increase use of patient registries and existing health care data to speed up clinical trials. These regulatory changes would be enhanced by a five-year, \$8.75 billion increase in funding to the National Institutes of Health – a major financier of biomedical

research in the U.S. The NIH would also host a new Cures Innovation Fund which would support breakthrough biomedical research. The Act would enhance funding to the FDA by \$550 million.

#### **OPPONENTS RAISE ETHICAL QUESTIONS:**

The Act includes several controversial measures that are beyond a general concern for patient safety. Informed consent has been a hallmark of clinical trials since the fallout following the Tuskegee syphilis experiments that stretched from 1932-1972<sup>6</sup>. Waivers are granted only when it is impossible to obtain informed consent or when doing so is contrary to a patient's best interest. The Act adds a measure whereby informed consent can be denied when "clinical testing poses no more than minimal risk" to the study's participants<sup>7</sup>. This is problematic, as The Act does not define who determines what constitutes "minimal risk". The FDA has endorsed this provision of The Act as a means to provide adequate flexibility while maintaining protections for individuals participating in clinical trials. Supporters maintain that this provision would allow investigators to conduct important research that may contribute substantially to the development of drugs and devices to diagnose or treat serious or life-threatening conditions or understand advantages and disadvantages of varying treatment options in clinical practice.

Several other controversial provisions were included in The Act. It would speed up the regulatory process for antibiotics that treat drug-resistant infections by allowing for approval based on laboratory and animal testing with smaller clinical trials, and would provide financial incentives to hospitals that prescribe these antibiotics. The Act includes a six-month extension of market exclusivity for already-approved drugs that treat rare diseases. Finally, the Act would allow the FDA to grant breakthrough status to drugs based on early stage testing, with drug makers performing clinical trials following approval of the drug. Opponents of The Act have expressed concerns over how these reforms will compromise patient safety.

They claim that a less rigorous review process could introduce the possibility of faulty drugs entering the market and that effectiveness can be proven only when there is substantial evidence from well-controlled clinical trials – not from alternative measures like surrogate endpoints. Opponents recall that regulatory fast tracking has been traditionally reserved for only urgent circumstances where no other

reasonable clinical alternative exists, and that this Act turns the exception into the rule.

It has been a longtime statutory requirement for drugs to be proven safe and effective before entering the U.S. market. Some believe that the reforms in The Act are a departure from decades of regulation that guarantee safety and efficacy through a sometimes burdensome and lengthy regulatory process; however, this is by no means the first time that Congress has acted to speed up the drug approval process.

#### **FIFTY YEARS OF REFORM TO THE DRUG APPROVAL PROCESS:**

In 1950, over half of medications in common use in the U.S. had been unknown a decade earlier<sup>8</sup>. That rate of growth slowed tremendously following a 1962 scare in Europe when pregnant women were prescribed Thalidomide which led to birth defects<sup>9</sup>. The *Kefauver-Harris Amendments* were passed which made proof of efficacy and rigorous clinical trials explicit requirements for approval of new drugs by the FDA. These new regulations significantly increased R&D costs to pharmaceutical companies, which soon stopped developing drugs to treat rare diseases, as the new regulations made such drugs unprofitable. Congress responded by passing the *Orphan Drug Act* in 1983 which introduced market exclusivity periods for drugs treating rare diseases to allow for a return on pharmaceutical R&D investments before other drug makers could compete.

The HIV/AIDS epidemic fostered in a series of reforms aimed at speeding up the regulatory process. A *fast track designation* was approved in 1988 for drugs treating serious or life-threatening illnesses for which there were no approved treatments and unmet need. Congress again acted in 1992 to introduce *priority review*, which shortened the review process to six months for drugs that hold a promise of significant improvement over existing therapies for serious or life-threatening illnesses. That same year, *accelerated approval* regulations were introduced which allowed for the use of surrogate endpoints as evidence of drug efficacy for drugs treating serious conditions that filled an unmet need. The *FDA Modernization Act* was passed in 1997 which codified many of these regulatory designations and also cleared a path for a single clinical investigation for some drugs which previously were required to go through multiple phases. Finally, in 2012, Congress passed a *breakthrough therapy designation* which expedited the approval process for drugs which demonstrate preliminary clinical evidence of substantial improvement over existing therapies.

In some ways, the 21<sup>st</sup> Century Cures Act represents a paradigm shift in policy-makers' thinking about the drug approval process. Unlike the reforms introduced in past decades, we are now in an age of electronic medical records, health information exchanges, and personalized, precision medicine which provide unprecedented opportunity to use biometric data to gauge the impact of new drugs and devices and share that data with researchers, providers, and patients. The traditional large scale clinical trial which has been the anchor of an often burdensome, lengthy regulatory process is now supplemented by our ability to see data in new ways which can shorten and strengthen that process. This has the potential to reduce the cost and quicken the pace of clinical trials, providing Americans with faster access to new therapies<sup>10</sup>.

#### THE ACT IS SILENT ON COST REDUCTIONS:

While many proponents of The Act claim that its reforms would decrease the cost of drugs through streamlining regulatory requirements and introducing flexibility into the clinical trial process<sup>11</sup>, the legislation is silent on outright cost reductions. Unlike the Affordable Care Act which imposed restrictions on profit by insurance companies, the 21<sup>st</sup> Century Cures Act includes no provisions pertaining to profits within the pharmaceutical industry. The pharmaceutical industry's strong support of the legislation would have waned had controversial price control measures been included. Significant R&D costs are borne by drug makers through a high-risk process to take drugs to the market. Few drugs make it through the process, and among those that do, few are profitable. Those profits must cushion losses taken on other drugs, must compensate for losses experienced in other industrialized nations that place price ceilings on pharmaceuticals (i.e.: Europe, Canada, Japan), and must fund future R&D investments<sup>12</sup>. These variables complicate the science of how to leverage cost savings in the pharmaceutical sector from a regulatory standpoint, as any kind of price control could result in less expenditures into research and development. The provisions of the 21<sup>st</sup> Century Cures Act would certainly reduce costs to drug makers; however, it remains to be seen whether those cost savings will be shared with the consumer or whether they will bolster additional R&D investments and profits.

The 21<sup>st</sup> Century Cures Act will now go to the Senate, where revisions are likely. President Obama has expressed concerns for patient safety and has not been a vocal supporter of The Act, although its strong bipartisan support, if continued through the Senate, would make a veto improbable.

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**NOTE TO THE EDITOR:** A portion of this work has previously appeared in a health law blog which I authored and published in the days following passage of The Act<sup>13</sup>. It can be found here: <http://www.healthlawgurus.com/2015/07/21st-century-cures-act-passes-house-could-usher-in-broad-reforms-to-drug-approval-process/>

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