

## LIFE SCIENCES

### CHANGES ON THE HORIZON FOR CLINICAL RESEARCH AND DRUG AND DEVICE DEVELOPMENT: 21ST CENTURY CURES ACT BECOMES LAW

By: Michael J. Lerner, Esq., Tara P. D'Orsi, Esq., and James C. Shehan, Esq.

Life sciences companies can expect sweeping changes in how drugs and medical devices are developed and approved in the wake of the enactment of the 21st Century Cures Act (the "Cures Act" or the "Act").<sup>1</sup> While the \$6.3 billion law is a voluminous 996 pages and mandates changes to numerous federal and state agencies and the programs they administer, this Client Alert focuses on the most significant changes to the development of drugs and devices.

The drug and device portions of the Cures Act aim to accelerate the discovery, development, and delivery of lifesaving and life-improving therapies. The legislation echoes the desire of patient advocacy groups, drug and device manufacturers, and research organizations to minimize administrative and financial barriers to innovation. Research-based life sciences companies can expect to benefit from many of these provisions that streamline and relax certain research regulations, create new opportunities for priority review, and increase funding for research. But don't expect most of these changes to occur soon – the Act allows FDA several years to implement many of the most sweeping provisions and, on top of, that FDA has a long tradition of missing deadlines set in legislation.

#### Adaptive Clinical Trial Designs

The Cures Act requires FDA to hold a public meeting and then issue guidance on the use of complex adaptive and other novel clinical trial designs in the development and regulatory review and

approval of drugs and biologics. The guidance will address the use of novel trial designs, the types of quantitative and qualitative information that should be submitted to FDA, and how such clinical trials may satisfy the Federal Food, Drug, and Cosmetic Act's<sup>2</sup> requirement of a showing of "substantial evidence" of safety and effectiveness.

An adaptive clinical design is one which uses prospectively planned modifications of one or more aspects of the study design based on analysis of interim data. Adaptive designs, which are already being used in the development of some products, may make studies more efficient (e.g., shorter duration, fewer patients), more likely to demonstrate an effect of the drug if one exists, or more informative (e.g., by providing broader dose-response information).

The Act calls for FDA to hold the public meeting and gather input from stakeholders within 18 months of enactment. FDA is then supposed to issue guidance within 18 months of the public meeting and to finalize that guidance within one year after the comment period on the guidance closes.

#### Greater Use of Patient Experience Data in Approvals

Expanding upon existing legislative mandates aimed at increasing the role of patients in the drug approval process, the Cures Act requires FDA to issue guidance on the use of patient data in the drug approval process. FDA is directed to explain how to collect patient experience data

and what it should consist of, how patient advocacy groups may propose draft guidance to FDA, and how FDA plans to use patient experience data when evaluating the risks and benefits of a new drug application in a structured risk-benefit assessment framework. Patient experience data includes data collected by patients, parents, caregivers, patient advocacy organizations, disease research foundations, medical researchers, and drug companies that is intended to facilitate FDA's risk-benefit assessments.

The Act provides FDA with a five-year timetable for implementing the patient-focused drug development guidance.

#### Use of Real-World Evidence and Qualified Data Summaries for New Indications

In two separate sections of the Cures Act, Congress also directs FDA to make it easier for drug companies to win approval for new indications of previously approved drugs. The first provision may ultimately allow applicants to use "real-world evidence" to support approval of new indications. The Act defines real-world evidence as "data regarding the usage, or the potential benefits and risks of, a drug derived from sources other than randomized clinical trials." Implementation of real-world evidence has a particularly long and somewhat ambiguous deadline — FDA is given six and a half years to issue a final guidance or a "revised draft guidance."

The second change to new indication approval allows FDA to rely upon

“qualified data summaries” when approving supplemental applications. A qualified data summary is a summary of clinical data that demonstrates the safety and effectiveness of a drug for a “qualified indication,” which is an indication that FDA “determines to be appropriate for summary level review.” The Act does not require FDA to issue guidance on the use of qualified data summaries, and apparently this section of the law takes effect immediately.

## Priority Review for Breakthrough Devices and Easing of Device Regulation

The Cures Act makes some significant changes to device regulation as well, the most significant of which is the establishment of a new breakthrough device pathway. “Breakthrough devices” are devices that “offer significant advantages over existing approved or cleared alternatives, including the potential, compared to existing approved alternatives, to reduce or eliminate the need for hospitalization, improve patient quality of life, facilitate patients’ ability to manage their own care (such as through self-directed personal assistance), or establish long-term clinical efficiencies.” FDA is expected to build on the existing priority review device pathway covered in a guidance issued April 13, 2015.<sup>3</sup>

Other significant changes to device regulation include (i) the permitted use of centralized IRBs for device clinical trials; (ii) a mandate that FDA consider the least burdensome appropriate means for demonstrating safety and effectiveness when reviewing pre-market approval applications; (iii) the designation of five categories of medical software that will not be regulated as medical devices; and (iv) a raising of the cap for humanitarian device eligibility from 4,000 to 8,000 patients.

## Drug Companies Must Publicize Their Expanded Access Policies

The Act makes one big change to regulation of the compassionate use of unapproved drugs outside of clinical trials. Drug companies that are developing drugs for “serious diseases” must, within 60 days of enactment, post on a website their policies for expanded access, that is, their policies for making investigational drugs available to patients who are not in their clinical trials. These expanded access policies must include procedures for making requests, the company’s criteria for evaluating and responding to requests, and the length of time required to typically respond to a request. While less extensive than some proposals advocated by the right-to-try movement, this provision will require significant and immediate action by most drug companies.

## Streamlining Human Subject Research Regulations

The Cures Act simplifies human subject and informed consent research regulations. It requires harmonization of the Department of Health and Human Services and FDA regulations within three years of enactment, directs FDA to allow the use by researchers of joint or shared IRB review, and allows use of an independent IRB or an IRB of an entity other than the sponsor of the research. Further, the Act provides additional opportunities for obtaining waivers of informed consent and allows medical device and drug trials posing “no more than minimal risk” to bypass the informed consent process if other safeguards are in place to protect the rights, safety, and welfare of patients.

## Miscellaneous Provisions

The Cures Act contains a number of other provisions of significance to research-based life sciences companies. For example, it extends the pediatric priority review voucher program for drugs until September 30, 2020. Another provision adds to FDA’s 2012 Drug Development Tools Qualification Program, by establishing a review pathway at FDA for biomarkers and other drug development tools that can be used to shorten drug development time and reduce the failure rate in drug development.

The Cures Act aims to speed the approval of drug-device combination products by clarifying how the “primary mode of action” of a product is to be determined and by requiring FDA to meet with sponsors and agree early in development how best to study the combination product to meet approval standards. The Act also establishes procedures governing disagreements between sponsors and FDA on how to treat a combination product.

In addition, the Act clarifies FDA’s authority over genetically targeted drugs by allowing sponsors to rely on data for the same or similar technology from previously approved applications by the same sponsor.

## What Is Missing from the Cures Act?

While the Cures Act contains many provisions favorable to the life sciences industry, there are a few notable industry-friendly provisions in earlier drafts that are missing from the law. For example, prior drafts of the Act included provisions that would amend the Open Payments program under the Physician Payments Sunshine Act as it relates to educational materials and continuing medical education (CME) for physicians. The Act, as ultimately passed, does not include the

provisions that would have exempted manufacturers from disclosing certain educational materials, including peer-reviewed journals, reprints, medical conference reports, and medical textbooks. The signed version of the Act also does not include the language that would have excluded certain physician speaker fees from mandatory reporting.

Another notable omission is a proposed six-month extension of the orphan drug exclusivity period when sponsors receive approval of new orphan indications for existing orphan drugs.

### Looking Forward

The 21st Century Cures Act is rightfully regarded as landmark legislation. Although implementation will be slow and it is not clear how many of the Act's mandates will be interpreted by FDA, it is clear that as we prepare to ring in the New Year, we are also ringing in a new era of drug and device development. There will be challenges in navigating this brave new world that will require collaboration with legal counsel in order to take full advantage of opportunities and avoid pitfalls.

## contacts

**Please contact any of the following Life Sciences attorneys for further information on the matters discussed herein.**

**Michael J. Lerner, Esq.**  
973 597 6394  
mlerner@lowenstein.com

**Tara P. D'Orsi, Esq.**  
973 597 6202  
tdorsi@lowenstein.com

**James C. Shehan, Esq.**  
646 414 6897  
jshehan@lowenstein.com

<sup>1</sup> See 21st Century Cures Act, S. 298 114th Congress (2016), available at <http://docs.house.gov/billsthisweek/20161128/CPRT-114-HPRT-RU00-SAHR34.pdf>.

The House of Representatives passed the bipartisan bill on November 29, 2016 by a 392-26 vote, and an amended version sailed through the Senate with a 94-5 vote on December 7.

<sup>2</sup> 21 U.S.C. 355(d).

<sup>3</sup> FDA, Center for Devices and Radiological Health and Center for Biologics Evaluation and Research, Guidance for Industry and FDA Staff: "Expedited Access for Premarket Approval and De Novo Medical Devices Intended for Unmet Medical Need for Life-Threatening or Irreversibly Debilitating Disease or Conditions," April 13, 2015, available at <http://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/UCM393978.pdf> (announced in the Federal Register, 80 Fed. Reg. 19669 (April 13, 2015)).

Follow us on [Twitter](#), [LinkedIn](#), and [Facebook](#).

[www.lowenstein.com](http://www.lowenstein.com)

New York Palo Alto Roseland Washington, DC Utah

© 2016 Lowenstein Sandler LLP.

This Alert has been prepared by Lowenstein Sandler LLP to provide information on recent legal developments of interest to our readers. It is not intended to provide legal advice for a specific situation or to create an attorney-client relationship. Lowenstein Sandler assumes no responsibility to update the Alert based upon events subsequent to the date of its publication, such as new legislation, regulations and judicial decisions. You should consult with counsel to determine applicable legal requirements in a specific fact situation.