

# UPDATE

Food and Drug Law Institute



## 2017 ANNUAL CONFERENCE RECAP



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## 21st Century Cures Act Implementation

by Jean W. Frydman

This year's Food and Drug Law Institute Annual Conference marked nearly five months since the 21<sup>st</sup> Century Cures Act (the Act) became law, the first major legislation in four years to amend the Federal Food, Drug, and Cosmetic Act (FDCA). The keynote addresses at the conference touched on the transformational potential of the Act.

A breakout session on "FDA's Implementation of the 21<sup>st</sup> Century Cures Act" with Wade Ackerman (Covington & Burling LLP), Jonette Foy (CDRH, FDA), and Julia Tierney (CBER, FDA) was moderated by Carla Cartwright (Johnson &

Johnson). At lunch on the second day of the conference, a facilitated table topic discussion, "The Drug Approval Process—Life After 21<sup>st</sup> Century Cures," attracted nearly a dozen participants representing diverse stakeholders for informal discussion.

In addition to this dedicated programming, key provisions of the new law, their implementation, and how they will impact industry stakeholders were much discussed throughout the event.

The following discussion focuses on the key provisions of interest to the food and drug law community highlighted at the conference: 1. Real World Evidence; 2. Patient-Focused Drug Development; 3. Breakthrough Medical Devices; 4. Healthcare Economic Information; and 5. Patient Access to Regenerative Medicine.



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## Key Provisions:

### 1. Real World Evidence (RWE)

The Act requires FDA to establish a program and issue guidance to increase the collection, use, and reliance on RWE to help support regulatory decision-making. This section<sup>1</sup> is designed to encourage the use of RWE to help support (i) approval of a new indication for a drug already approved pursuant to an NDA or BLA, and (ii) post-approval study requirements. The Act defines “real-world evidence” to mean data regarding the use, benefits, or risks of a drug “derived from sources other than randomized clinical trials,” which would include, for example, ongoing safety surveillance, observational studies, and registries. Under the Act, FDA also must issue draft guidance within five years addressing (i) the circumstances under which sponsors may rely on RWE, and (ii) the appropriate standards and methodologies for collection and analysis of RWE submitted for regulatory purposes. The provision clarifies that it does not alter the statutory standards of evidence for NDA approval or BLA licensing, and does not alter the Secretary’s authority to require postapproval studies or clinical trials, or the standards of evidence under which studies and trials are evaluated.

By facilitating the use of RWE, the need to conduct randomized clinical trials to support certain expanded indications for use or to satisfy post-market study requirements may decrease. Over the long term, this could lead to significant changes in the approval process for follow-on indications of previously approved drugs and biologics.

Presently Congress has asked FDA to work with NIH on ways to harmonize data collected from electronic health records, claims data, and registries, and to facilitate the provision of actual data

that does not require external review or interpretation.

The concerning issue among conference participants was whether FDA has the expertise in statistics, meta-analysis, and other technical areas needed for developing and applying effective standards to analyze RWE sources of information in support of regulatory decision making. This was an ongoing discussion with members of FDA who attended the lunch discussion focused on the 21<sup>st</sup> Century Cures Act. Select attendees from FDA stated the agency does not have the expertise and bandwidth to properly address the needed statistical analysis to support RWE. The general concern is that the new administration may overlook the need to properly implement standards for the support of RWE.

### 2. Patient-Focused Drug Development

This section of the Act<sup>2</sup> increases the role of patient experience data in the clinical research process. There are several sections in the Act that include provisions aimed at encouraging drug sponsors and FDA to incorporate so-called “patient experience data” into the drug development and review process. “Patient experience data” is defined as data that are intended to provide information about patients’ experiences with a disease or condition, including (i) the impact of such disease or condition, or a related therapy, on patients’ lives, and (ii) patient preferences with respect to treatment of such disease or condition.

Within six months of the enactment date of December 13, 2016, FDA must develop plans to issue draft and final versions of one or more guidance documents over a period of five years regarding the collection of patient experience data and the use of such data in drug development. FDA is already engaged in

patient-focused drug development activities, including meetings with patient advocacy groups, the National Institutes of Health (NIH), and Congress. FDA has conducted discussions with Congress on its focus to better understand the perspective of the patient. In particular, the agency is looking at what tools can be used to more quantitatively assess tradeoffs patients are willing to make in treatments.

The Act also provides NIH with critical tools and resources such as support for high-priority initiatives, funds for a biomedical research workforce, enhancement of data sharing and reduction of paperwork formerly needed for NIH-conducted research, to advance biomedical research across the spectrum from basic research studies to advanced clinical trials of promising new therapies. Affecting everyone from researchers to research participants to patients suffering from numerous conditions, these measures will cut bureaucratic red tape that slows the progress of science, and further enhances data sharing and privacy protections for research volunteers.

This new law recognizes that patients should play an essential role in development of drugs and devices to diagnose and treat their disease. Patients are in a unique position to provide essential insights about what it is like to live with and fight their disease. A patient with a life-threatening disease may prefer to accept certain side effects in a new breakthrough therapy that traditionally were considered unsafe if the benefits of the treatment are valuable to that patient. Conference attendees discussed the impact of the Act’s potential to result in more liberal safety profiles allowing side effects not traditionally permitted: How will these new standards be established? And what will the consequences be for



Carla Cartwright, Director, Federal Affairs, Johnson & Johnson, moderates the panel FDA's Implementation of the 21<sup>st</sup> Century Cures Act, with presentations from Jonette Foy, Acting Associate Director for Policy, CDRH, FDA; Julia Tierney, Senior Policy Advisor for Strategic Planning and Legislation, CBER, FDA; and Wade Ackerman, Partner, Covington & Burling LLP.

product liability and medical malpractice suits in the future?

### 3. Breakthrough Medical Devices

This section<sup>3</sup> expands FDA's Expedited Access Pathway program, which allows for expedited development and review of devices that represent breakthrough technologies for life threatening or irreversibly debilitating diseases/conditions. The Breakthrough Devices program requires frequent and extensive interactions between device companies and FDA staff during the device development phase, as well as priority review for designated breakthrough medical devices.

To accommodate this new process the agency will need to expand its personnel over the next 10 years. This mandate poses challenges to FDA for efficient implementation and successful recruitment of personnel with the requisite technical skills. Comments at the conference reflected concern over the agency's resources and whether these were sufficient to meet the required staff expansion. The timeline contemplated in the statute implies acquisition of IT systems to fully implement this program at a rate of growth of 20 percent a year.

Additional implementation challenges are presented by the fact that many of these breakthrough technologies, no doubt, will be drug delivery mechanisms regulated as combination products.

### 4. Healthcare Economic Information

The 21<sup>st</sup> Century Cures Act addresses the ability to discuss Health Care Economic Information (HCEI)<sup>4</sup> with payors and other sophisticated audiences. It allows for "any analysis (including the clinical data, inputs, clinical or other assumptions, methods, results, and other components underlying or comprising the analysis) that identifies, measures, or describes the economic consequences, which may be based on the separate or aggregated clinical consequences of the represented health outcomes, of the use of a drug. Such analysis may be comparative to the use of another drug, to another health care intervention, or to no intervention."

The current state of the law has led to confusion within industry over what appear to be contradictory standards. The new definition is potentially a far-reaching change from the previous definition of HCEI, as it seems to allow

for communication of pre-approval information, but at the same time requirements that such information shall not be false or misleading are in effect. Does this mean sharing HCEI with payors prior to the approval of an expedited medical device is permissible? According to FDA Draft Guidance released in January 2017, which cites the statute on the appropriate scope of the audience, such information can be disseminated to payors, formulary committees or other similar entities, with knowledge and expertise in the area of health care economic analysis, carrying out responsibilities for the selection of drugs for coverage or reimbursement.<sup>5</sup> However, Section 3037 of the Act states that a communication must relate to an approved indication of the product and that HCEI that relates only to an unapproved indication is not protected. Industry representatives expressed the need for more guidance around communications of health economics so that manufacturers do not run the risk of sharing data that is considered false or misleading. Will FDA enforce this provision, and if so, how?

## 5. Patient Access to Regenerative Medicine

The Act creates a new program for the development of regenerative medicine products, an important and exciting new field that deserves this special focus. The program designates certain therapeutic products as “regenerative advanced therapies,” or what FDA called “regenerative medicine advanced therapies” or RMATs, and takes appropriate actions to improve the efficiency of development and to enhance the exchange of information among FDA, researchers, and developers. An especially important element of this program is the creation of a research network and a public-private partnership to assist developers in generating definitive evidence about whether their proposed therapies indeed provide clinical benefits that are desired.

In order to obtain a RMAT designation, the treatment must be a “cell therapy, therapeutic tissue engineering product, or any combination product using such therapies or products, intended to treat, modify, reverse, or cure a serious or life-threatening disease” and have preliminary clinical evidence that the drug has the potential to address unmet needs.

The first publicly disclosed RMAT designation (for Humacyte’s product Humacyl) was announced on March 20, 2017, so the program appears to be up and running. However, as with the medical device breakthrough designation, conference attendees expressed concern over the availability of sufficient resources and time needed by FDA to implement fully this provision of the Act.

Time will tell how well this provision is executed under the new law.

## Conclusion

The next five years will be critical for implementation of the 21<sup>st</sup> Century Cures Act. Implementation will no doubt lead to evolving regulatory decision making, and new standards and practices in the medical products industry. There will be plenty to discuss at future FDLI Annual Conferences as the agency continues to face the challenges of new approaches to data use and clinical metrics, emerging technology, and expediting medical breakthroughs. Many issues are immediately salient, especially regarding whether sufficient resources can be secured to support the needed expansion of personnel and information infrastructure to implement the Act, how to resolve

questions surrounding the definition, standardization, and application of evidence-based data, and the agency’s stance on enforcement of prohibitions on off-label communications going forward. ▲

1. 21<sup>st</sup> Century Cures Act, Section 3002.
2. 21<sup>st</sup> Century Cures Act, Section 3001-3004.
3. 21<sup>st</sup> Century Cures Act, Section 3051.
4. 21<sup>st</sup> Century Cures Act, Section 3037.
5. Food and Drug Administration Draft Guidance, Drug and Device Manufacturer Communications With Payors, Formulary Committees, and Similar Entities – Questions and Answers, at 4 (citing 21 U.S.C. 352(a) (section 502(a)), <https://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM537347.pdf>).

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