December 13, 2016

21st Century Cures Act – Provisions to Promote Drug Development

On December 13, 2016, President Obama signed into law the 21st Century Cures Act (the Act), just days after it passed in the U.S. House of Representatives and Senate. With an overarching goal of advancing biomedical innovation, the Act makes numerous changes to laws that govern Food and Drug Administration (FDA) programs, clinical research regulations, and Medicare coverage and reimbursement rules.

To see Ropes & Gray's analysis of key provisions of the Act, please click on the hyperlinks below:

- Development Incentives for Certain Classes of Drugs
- Medical Device Innovation
- Digital Health
- Regulation of Clinical Research
- Reimbursement & Fraud and Abuse

Partners in Ropes & Gray's FDA Regulatory practice have also recorded a podcast to discuss some key implications of the Act for biopharmaceutical and medical device manufacturers. Click here to listen to the podcast.

This Alert highlights select provisions of the Act related to drug development. These provisions aim to expand the types of evidence that FDA will consider in reviewing drug applications and to facilitate the use of novel clinical trial designs and surrogate endpoints, such as biomarkers, in the drug development process. While the Act retains the substantial evidence standard for approval, drug companies may have more flexibility in how to satisfy that standard.

Patient-Focused Drug Development [Sections 3001-3004].[1]

Consistent with recent efforts to increase the role of patient experience data in the clinical research process, the Act includes several 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.

Of note, within six months of enactment, FDA must develop a plan 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. Specifically, FDA is required to issue guidance addressing methodologies for collecting and assessing patient experience data as well as how the FDA intends to use patient experience data in regulatory decisions. FDA is already engaged in patient-focused drug development activities, including meetings with patient advocacy groups, but the Act's provisions are intended to force FDA to develop broadly applicable policy on patient experience data.

[1] Sections cited in this Alert refer to the relevant provisions in the Act.

Qualification of Drug Development Tools [Section 3011].

This provision codifies a process for qualifying drug development tools, which may be used to support a new drug application (NDA), a biologics license application (BLA) or an investigational new drug application (IND). Drug development tools can include biomarkers (including surrogate endpoints), clinical outcome assessments, or other methods, materials, or measures determined to aid drug development and regulatory review. This provision will bolster FDA's existing drug development tool qualification program.[2]

Novel Clinical Trial Designs [Section 3021].

The Act requires FDA to issue guidance addressing the use of complex adaptive and other novel trial designs in the development and approval of drugs or licensure for biological products. The guidance will address how novel trial designs help to satisfy the NDA substantial evidence standard, how sponsors may obtain feedback on technical issues related to modeling and simulations, the types of quantitative and qualitative information that should be submitted for review, and recommended methodologies. This provision, which builds upon FDA's 2010 draft guidance on *Adaptive Design Clinical Trials for Drugs and Biologics*, is consistent with a primary objective of the Act, which is to modernize and make more efficient clinical trials to support regulatory decision-making.

Real-World Evidence [Section 3022].

The Act requires FDA to establish a program and issue guidance to increase the collection, use, and reliance of real-world evidence to help support regulatory decision-making. This section would encourage the use of real-world evidence to help support (i) approval of a new indication for a drug already approved pursuant to an NDA, 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 real-world evidence, and (ii) the appropriate standards and methodologies for collection and analysis of real-world evidence submitted for regulatory purposes. The provision clarifies that it does not alter the statutory standards of evidence for NDA approval or biological product licensing, and does not alter the Secretary's authority to require post-approval studies or clinical trials, or the standards of evidence under which studies or trials are evaluated.

By facilitating the use of real-world evidence, 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.

Summary Level Review [Section 3031].

This provision allows FDA to rely upon qualified data summaries to support the approval of a supplemental application for a drug or biologic, with respect to certain qualified indications. The term "qualified data summary" means a summary of clinical data that demonstrates the safety and effectiveness of a drug with respect to a qualified indication, whereas a "qualified indication" is an indication that FDA determines to be appropriate for summary level review. FDA would be able to shorten the clinical development phase previously required for expanding indications of approved drugs and biologics by authorizing sponsors to rely on data summaries rather than conduct full clinical investigations.

[2] *See, e.g.*, FDA webpage on Drug Development Tools (DDT) Qualification Programs; and FDA Guidance on "Qualification Process for Drug Development Tools" (January 2014).

Expanded Access Policy [Section 3032].

The Act requires that manufacturers and distributors of investigational drugs for serious diseases publicly post their expanded access policy. The public posting must be readily available, such as on an internet website. The posting must include, among other information, the firm's contact information, requesting procedures, and the criteria used to evaluate requests. However, the posting does not guarantee a patient access to an investigational product under the firm's policy. The Act would broaden recent legislation that required expanded access policies to be posted on www.clinicaltrials.gov for certain studies. [3]

If you have any questions, please contact any member of Ropes & Gray's FDA regulatory or health care practices or your usual Ropes & Gray advisor.

[3] *See* 42 U.S.C. § 282(j)(2)(A)(ii)(II)(gg).