

December 13, 2016

## 21<sup>st</sup> Century Cures Act

Hi, I'm Al Cacoza, a partner in the Washington, D.C. office of Ropes & Gray and a member of the firm's life sciences practice group. Today we will discuss the recently enacted 21<sup>st</sup> Century Cures law. This is part of the *Capital Insights* podcasts series we are hosting to examine the issues and potential regulatory changes emanating from Washington, D.C., as we transition to a new Federal administration. Today, I am joined by two of my Washington, D.C. partners, Kellie Combs and Greg Levine. Kellie, let's start with you. Can you highlight those issues in the new law of most relevance to a drug company?

**Attorneys**  
[Al Cacoza](#)  
[Kellie Combs](#)  
[Greg Levine](#)

**Kellie:** Sure Al, I'd be happy to. With the Act coming in at about 1000 pages, there are too many provisions for us to talk about today. But a central aim of the Act is to streamline and expedite the drug development and review process. Importantly, the Act doesn't modify FDA's substantial evidence standard for drug approval, but manufacturers may now have greater flexibility in how they satisfy that standard. To highlight just one example, Section 3022 of the Act requires FDA to issue guidance about the reliance of real-world evidence to help support the approval of new indications for drugs and biologics that are already on the market and to fulfill post marketing study requirements. Real-world evidence is steadily risen in importance over the last several years as big data from electronic medical records and prescription claims databases now provide the opportunity to analyze how products actually perform in the real-world setting. That consideration of these types of evidence hasn't formally been baked into the FDA approval process. Under the Act, FDA has five years to issue guidance to discuss the circumstances under which they may rely on real-world evidence in the review process, as well as the standards and methodologies that may be applicable to real-world evidence. So while we're waiting for the guidance, it remains to be seen precisely what the impact will be, but over the long term this could really have a significant effect on the approval process for follow-on indications of drugs and biologics.

**Al:** Greg, same question for you, but this time from the perspective of a device company.

**Greg:** Like Kellie, I'll focus on just one of the key provisions. Probably for devices one of the most important provision will be the breakthrough device provision. This provision requires the FDA to establish a program for the expedited development and priority review of devices that treat or diagnose life-threatening or irreversibly debilitating diseases or conditions and that represent breakthrough technologies for which no approved or cleared alternatives exist. Under the statutory provision, FDA will have considerable discretion in determining which devices qualify for this program.

**Al:** How is this different from the current FDA expedited approval program?

**Greg:** Well the EAP that's in place now applies only to devices that are subject to PMA approval and so this new program, by statute, will also apply to 510(k) devices and to de novo petitions, so that's the significant expansion of the current program. FDA is going to have to respond to requests for designation

of such products within 60 days, and also under the statute, FDA may not withdraw a breakthrough designation on the basis that another device was subsequently cleared or approved.

**AI:** We know that priority review means shorter review timelines under user-free goals. What does expedited development mean?

**Greg:** So expedited development will have a number of elements to it. There are certain provisions that are mandatory. For example, FDA will have to assign a team of staff, including a team leader with appropriate subject matter expertise for each such device; adopt an efficient process for timely dispute resolution; provide for interactive and timely communication with a sponsor; and expedite FDA's review of manufacturing and quality system elements where that's applicable to an application. FDA also will have to disclose to a sponsor at least 5 business days in advance of any topics that require consultation with an advisory committee or other outside experts, and allow the sponsor to recommend such experts. There also are additional elements that are permissive, not mandatory, but that also could further expedite development programs for these kinds of products.

**AI:** Can you touch on how the law addresses so-called combination products that might contain both a drug and a device?

**Greg:** The combination product provision provides that FDA must establish a process to assign a primary agency center to regulate combination products, based on the primary mode of action of those products. It requires FDA to conduct pre-market reviews of a combination product under a single application whenever appropriate. This is the agency's policy, currently, to try to attempt to do that. This would make it a statutory requirement. In addition, this provision prohibits FDA from determining that a product's primary mode of action is that of a drug merely because a product has any chemical action. Instead FDA will be able to determine that a product has a drug primary mode of action only if the chemical action is the single mode of action of the product as a whole, expected to make the greatest contribution to the overall intended therapeutic effects of the product. There's no time limit on which FDA must make a primary mode of action determination, but once made, if a sponsor disagrees with FDA on primary-mode-of-action determination, the sponsor may propose studies to demonstrate the primary-mode-of-action for a product, and FDA must seek to reach agreement with a sponsor within 90 days on the studies that will be conducted. And if agreement is reached, those studies will be binding during reevaluation of the primary mode of action of the product. In addition, the provision clarifies the applicability of Hatch-Waxman exclusivity periods to combination products that contain a drug component subject to exclusivity, and also requires FDA to issue guidance within 4 years of enactment describing a structured process for managing presubmission interactions with sponsors developing combination products, best practices for ensuring that feedback in such presubmission interactions represents the best advice of the agency, and certain other elements must be included in this guidance as well. So it will remain to be seen whether this provision is considered enough on combination products. There are certainly those who are calling for further reforms in this area, and we'll see whether this becomes one of the subjects that might be covered during the upcoming MDUFA and PDUFA reauthorization legislation later on during 2017.

**AI:** Kellie, you testified in November at the FDA regarding regulation of manufacturer speech. Does this new law offer any clarifications on that issue?

**Kellie:** Yes, Al. 21<sup>st</sup> Century Cures does affect manufacturer speech in one key respect. So the law updates and clarifies some language in FDAMA 114, which is a safe harbor that was passed by Congress in 1997 and regards communications with formulary committees and similar entities. Under FDAMA 114, as originally passed, pharmaceutical manufacturers could talk to these entities so long as the information was directly related to a drug's approved indication and was supported by competent and reliable scientific evidence, as opposed to the substantial evidence required for safety and effectiveness claims. FDAMA 114 relates specifically to the communication of healthcare economic information, but it's not been used to its full potential because the law, as passed, contains some undefined terms, and FDA has never issued guidance on the law despite repeated promises to do so. So the Act amends FDAMA 114 to clarify that it applies to communications with payors, as well as formulary committees and similar entities, and that healthcare economic information merely needs to relate rather than directly relate to the approved indication. The new law also requires that manufacturers, when communicating with payors and formulary committees under FDAMA 114, include a statement that prominently describes any differences between the information that is being conveyed and the information that's in the drug's approved labeling. Importantly, the law also provides now that the competent and reliable scientific evidence standard applies not only to the economic analysis, but also to any clinical data or assumptions. If for example, about safety and efficacy of the drug that may be underlying that healthcare economic information. And that's a particularly important amendment because some at FDA had taken a different view.

**Al:** Thank you so much, Kellie and Greg, for your insights. And thank you for listening. Please visit our newly launched Capital Insights page at [www.ropesgray.com](http://www.ropesgray.com) for additional news and analysis about noteworthy regulatory and enforcement issues.