Haffner Associates
Expertise Orphan Products & Rare Diseases

11616 Danville Drive, Rockville, MD 20852
Office: 301-984-5729
www.mhaffner.com

21st Century Cures Act as it Impacts the Rare Disease Community

Kelly Austin, PhD, Sandra K. Heibel, PhD, and Marlene E. Haffner, MD, MPH

The 21st Century Cures Act (21CCA) will impact the way treatments are developed for the rare disease community. It was signed into law by President Obama on December 13, 2016 and is a far-reaching regulatory package containing five main sections and The Helping Families in Mental Health Crisis Reform Act of 2016. The five sections are titled: Title I: Innovation Projects and State Responses to Opioid Abuse, Title II: Discovery, Title III: Development, Title IV: Delivery, and Title V: Savings. Patients with rare diseases will be most impacted by the section on development, but may also benefit from some of the other sections of this law.

Three aspects of the Development section directly impact rare diseases. The first new incentive was introduced to spur development of targeted drugs for rare diseases. Drugs that directly modify genes or variant proteins causing rare diseases will have relaxed regulations, allowing the sponsor to use data from previously approved applications using the same technology. By reducing the financial burden of additional clinical trials while maintaining the existing safety and efficacy standards for drug approval, the FDA is incentivizing drug manufacturers to focus on potential cures and treatments for rare diseases.

Second, the pediatric rare disease (PRD) priority review voucher (PRV) program was extended until 2020. This program incentivizes research into PRDs. A PRD is defined as a serious disease in which more than half of the population impacted by the serious or life-threatening nature of the disease is under 19 years of age, and the most serious aspects of the disease occur in the less than 19 years of age group. The total patient population with the disease must be fewer than 200,000 people in the United States. If a drug receives a PRD designation by the Food and Drug Administration (FDA), upon marketing approval of the drug, the sponsor receives a voucher for the priority review of another drug application. The number of applications for PRD designation continues to increase substantially. It is hoped this will translate into new drugs for patients with PRDs. However, since PRV programs are relatively new, and only 9 PRVs had been awarded as of January 9, 2017, the 21CCA also mandates investigation into any unintended consequences of PRV programs.

Lastly the FDA orphan products grants program is amended so that grants are to be made not only for drug development studies, but also for natural history studies of rare diseases. Qualifying studies will either create drug development tools for rare diseases or contribute to a more complete understanding of how a rare disease manifests, including variability in genotype, phenotype and subpopulations. These studies can be part of the drug development process, and will help health practitioners and researchers understand rare diseases.

While not directly targeting the rare disease community, the new Regenerative Advanced Therapy (RAT) designation will likely promote research that could eventually lead to treatments for some rare diseases. To be considered a RAT, the drug must be “a cell therapy, therapeutic tissue engineering product, human cell and tissue product, or any combination product using such therapies or products, except for those regulated solely under Section 361 of the Public

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Health Service Act and part 1271 of Title 21, Code of Federal Regulations."[i] To receive RAT designation, the sponsor must demonstrate the RAT will be used to treat a serious or life-threatening disease and provide preliminary clinical evidence supporting the use of the drug to fulfil unmet medical need. Once designated, RATs are potentially eligible for expedited review and accelerated approval. These incentives, along with mandates to set standards for reviewing RATs, are intended to promote advancement in cell and tissue therapies.

Other provisions in the Development section impact drug discovery as a whole, but might especially benefit the rare disease community. There is a push to include patient data and feedback in the drug development process. The FDA will be required to issue a guidance on how patients and caregivers can communicate their experiences with the FDA and how that data will be used. The FDA will also review how patient data is being incorporated into drug development, with reports on the subject due in 2021, 2028 and 2031. Another subsection of the 21CCA is intended to make clinical trials easier to conduct and more likely to result in drug approval. The FDA is to hold public meetings on novel trial designs, then issue guidance on how clinical trials can provide substantial evidence of efficacy using new clinical trial methodology. The guidance must also detail how sponsors can get feedback from the FDA, what types of information should be submitted, and which analytic techniques should be used. Consideration of real-world evidence is another topic covered in the new law. Real-world data refers to information gathered outside clinical trials, and is currently not part of the approval process. The FDA will evaluate whether real-world evidence should be used to support approval of drugs or in post-market studies. Various stakeholders, such as drug developers and patient advocacy groups, are expected to contribute to development of a process by which non-clinical data could be used, and a guidance on the role of real-world data in drug development must be issued within five years.

While the bulk of the impact to the rare disease community is found in the Development section, the other four sections and the mental health reform act might have some effect. The Savings section primarily addresses Medicaid and reimbursement issues. This will likely affect which treatments are perceived as profitable by drug and device developers, indirectly impacting rare disease patients. The Delivery section creates a new position, an ombudsman tasked with addressing Medicare coverage of new and life-saving technologies. The section on discovery promotes genomic technologies and research into pediatric diseases. The Helping Families in Mental Health Crisis Reform Act of 2016 is intended to provide better services to those with mental or behavioral issues. Additionally, the section on opioid abuse includes provisions for special funding of certain National Institute of Health (NIH) projects, including research on cancer, the brain, regenerative medicine using adult stem cells, and precision medicine. Individual patients with rare diseases might benefit from some of these initiatives.

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Helpful links:

Committee of Energy and Commerce 21st Century Cures Act
https://energycommerce.house.gov/cures

Regulatory Explainer: 21st Century Cures Redux and What it Will Mean for FDA
http://www.raps.org/Regulatory-Focus/News/2016/11/28/26242/Regulatory-Explainer-21st-Century-Cures-Redux-and-What-it-Will-Mean-for-FDA/

The President Signs 21st Century Cures into Law; Highlights of Drug and Biologic Related Provisions (Part One) http://www.fdalawblog.net/fda_law_blog_hyman_phelps/2016/12/the-president-signs-21st-century-cures-into-law-highlights-of-drug-and-biologic-related-provisions-p.html

(Part two) http://www.fdalawblog.net/fda_law_blog_hyman_phelps/2016/12/highlights-of-drug-and-biologic-related-provisions-of-21st-century-cures-part-two.html

[i] http://www.fda.gov/BiologicsBloodVaccines/CellularGeneTherapyProducts/ucm537670.htm