# QUARTERLY TREND ADVISORY

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## The 21st Century Cures Act: Research Focus and Information – Part 2

Previously, this publication reviewed the "Development" subsection of the 21st Century Cures Act of 2016 ("Cures Act"). While not reviewed here, the legislation also included another division regarding mental health care and components of Medicare, much of which was met with overwhelming support. In this edition, we will review other subsections within the Cures Act.

A subsection, titled "Innovation Projects and State Responses to Opioid Abuse," authorizes $4.8 billion over 10 years to the National Institutes of Health (NIH) for the Precision Medicine and Cancer Moonshot initiatives. It also establishes the NIH and U.S. Food and Drug Administration (FDA) innovation accounts and outlines funding for the Brain Research through Advancing Innovative Neurotechnologies (BRAIN) Initiative and regenerative medicine using adult stem cells. The Cures Act also establishes the Account for the State Response to the Opioid Abuse Crisis, which provides grants for states to supplement opioid misuse prevention and treatment activities.

The "Discovery" subsection encourages research. It includes provisions to fund research targeting significant advancements and improved health outcomes and provides intramural loan repayment programs. It also includes funding for collaborative research in neurological and vector-borne diseases, such as Lyme disease. By encouraging a global clinical study network with research funding and cooperative agreements, the Cures Act promotes research in pediatrics and other underrepresented populations in clinical trials. Finally, much of this subsection focuses on NIH planning, administration, accountability, advancement, and data access.

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The "Delivery" subsection focuses on dissemination of information to key stakeholders, including reducing documentation burdens associated with electronic health records (EHRs) and encouraging the adoption of this technology by Medicaid providers. Other key provisions focus on empowering patients and improving access to personal EHR information by increasing the use of health information exchanges and other relevant platforms.

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In addition, it provides for an ombudsman within the Centers for Medicare & Medicaid Services (CMS) who will receive and respond to complaints and requests from key stakeholders. This section also requires reporting information to Congress on use of telehealth services, particularly in Medicare- and Medicaid-eligible populations.

Although the Cures Act authorized $6.3 billion in new spending over the next 10 years, it did not appropriate the majority of this funding. Overall, the law's objectives have received broad congressional support, but future appropriations will depend on congressional priorities and funding availability; thus, its final effects remain to be seen.

## Genetic Tests: A Voyage of Human Discovery

The genetic voyage begins in the 19th century with the father of genetics, Gregor Mendel. It transitions to the 20th century with the discovery of the deoxyribonucleic acid (DNA) double helix and arrives in the 21st century at the ambitious Human Genome Project (HGP), which mapped the human genetic blueprint. These scientific milestones have made present day genetic testing a reality (see Figure 1). Most genetic tests, which look for certain mutations in a person's genes to assess risk, screen, diagnose, and inform therapy decisions, are not regulated. CMS regulates the clinical labs that perform genetic testing to ensure Clinical Laboratory Improvement Amendments (CLIA) compliance. The FDA can regulate genetic tests as medical devices, but has only regulated a limited number of genetic tests sold to labs as kits. Many genetic tests require an order by a healthcare professional (HCP).

Recently, direct-to-consumer (DTC) genetic tests have become available without HCP involvement. Currently, only one at-home test is FDA-cleared. 23andMe, where a patient simply mails a saliva sample, recently received FDA clearance to run tests on 10 diseases, including Parkinson's disease and late-onset Alzheimer's. Along with this approval, the FDA has put a regulatory pathway in motion for approval of DTC risk assessment tests. Notably, these tests only deliver genetic risk information; they are not diagnostic and do not take environmental or lifestyle factors into consideration. While DTC genetic tests can empower patients with knowledge regarding their risks, results can be difficult to interpret and even be misleading. Consensus in the medical community is that patients should talk to an HCP and genetic counselor before deciding to be tested to aid patients in test expectations, pros and cons, and future options. For example, testing may be recommended in select high-risk patients for certain genetic mutations associated with breast cancer. With DTC genetic tests, this layer of professional guidance prior to testing is absent. The Genetic Information Nondiscrimination Act (GINA) currently prohibits health insurers from denying health coverage based on genetic test results; however, this federal law does not apply to life, disability, or long-term care insurance. Moreover, potential legislation in development could allow companies, as part of workplace wellness programs, to require employees to undergo genetic testing or risk financial penalties. This possibly could compromise patient privacy and protection for sensitive genetic health information. In a 2015 *New England Journal of Medicine* study in which results of genome sequencing data would be stored in patients' medical record, 25% of patients declined to participate, citing fear of discrimination from life insurance companies as the main reason.

Targeted education and mindful regulation must safeguard our life's code. Knowledge is power. As research advances DTC genetic tests, the real inflection point in this voyage is widespread access to and the accurate application of our genetic blueprint to inform treatment choices and prevent disease.

## Keep on Your Radar: Clearing out America's Medicine Cabinets

Ensuring safe disposal of unused prescription medications has been an ongoing challenge. The problem of leftover, undisposed opioid prescription medications is an especially troubling problem. Drug overdose is now the leading cause of accidental death in the U.S. Many people who abuse prescription drugs report the

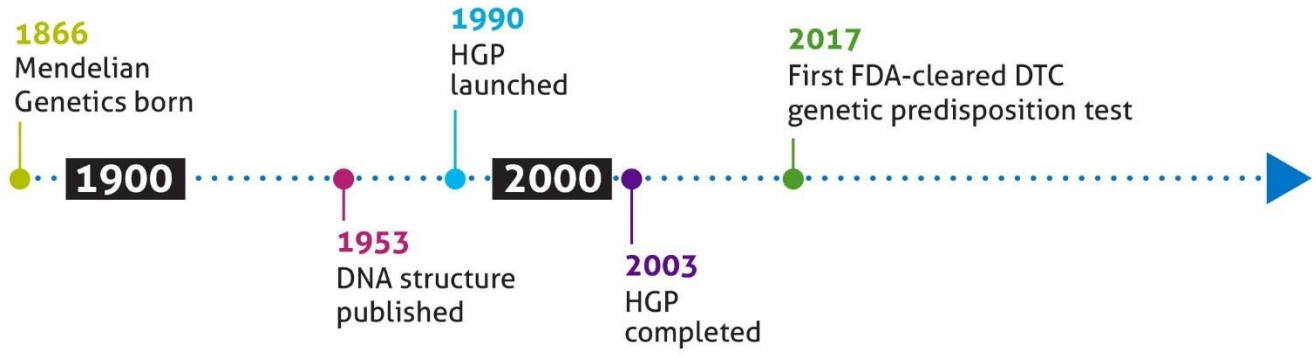


Figure 1. Major Genetic Milestones

opioids are given to them for free by a friend or relative. In addition, 80% of new heroin users started out misusing prescription opioids. Safe disposal options for controlled substances include national and community drug take-back events, mail-back programs, and collection receptacles. Despite these options, a national survey found that 61% of patients opted to keep leftover opioids for possible future use and 21% indicated they had shared their opioid prescription medication with another person. Another study in Wisconsin found that when opioid prescriptions were returned for disposal, greater than 60% of the dispensed doses remained unused. Taken together, these studies paint a picture of excess quantities of unused prescription opioids being available for potential diversion or misuse.

A possible solution for this problem is addressed by the Reducing Unused Medications Act of 2016. This proposed legislation would amend current laws and allow for partial filling of Schedule II (CII) controlled substances such as opioids. Under current federal law, a CII prescription may not be refilled (if partially filled on the initial fill) unless the patient is terminally ill or resides in a long-term care facility. The Reducing Unused Medications Act would remove this prohibition and provide the flexibility to allow partial fills of a CII prescription at the request of the provider or patient. The prescription would expire at the end of the original written day's supply. Many physician groups, including the American Medical Association, have voiced their support; however, several pharmacy groups, such as the American Pharmacists Association, are more cautious citing concerns over whether patient copays will be adjusted for partial fills and other potential costs. This bill has yet to be reintroduced; however, if reintroduced and passed, it might serve as another safeguard to help curb the nation's sweeping opioid addiction crisis.

## Did You Know? FDA Advisory Committees

The FDA relies on advisory committees to provide independent advice from external experts. It has over 15 separate drug advisory committees grouped primarily by disease area or product type and also has advisory committees for blood, vaccines, biologics, medical devices, and other non-drug products.

While a variety of legislation affects the role of the advisory committees, the Federal Advisory Committee Act of 1972 established the key laws for the advisory panels. Each advisory committee consists of a chairperson, several subject matter experts (SMEs), a consumer, industry representation, and, on occasion, patient representatives. Additional experts or key stakeholders may be consulted for select meetings when needed. Suitable panel members offer significant technical expertise, provide a diverse perspective, and have minimal conflicts of interest.

Advisory committees meetings can occur at any stage of a product's development or following marketing. In some cases, the FDA is required to consult an advisory committee, such as for pediatric labeling changes or postmarket safety analyses, but in others, the FDA may choose whether or not to summon a committee. Announcements for advisory committee meetings are published at least 15 days in advance via the *Federal Register* and on the FDA's Advisory Committee Calendar. Those who wish to present during the Open Public Hearing portion of the meeting may contact the Designated Federal Officer for the committee. Background materials and the itinerary are generally published at least 2 business days prior to the meeting, and some meetings are available via a free webcast. Transcripts from the meetings are usually available 30 days following the meeting.

***"Key information presented at advisory committees for drugs include pharmacology, pharmacokinetics, safety, efficacy, and any relevant public health concerns, such as an opioid's potential for abuse."***

Key information presented at advisory committees for drugs include pharmacology, pharmacokinetics, safety, efficacy, and any relevant public health concerns, such as an opioid's potential for abuse. Most commonly, both the FDA and the manufacturer present their interpreted data to the committee. In addition, there is time appropriated for additional stakeholders, such as patient and/or community representatives. During each meeting, the advisory panel votes on various prespecified questions posed by the FDA. For instance, they may vote "yes" or "no" regarding whether a drug is safe, effective, and/or whether or not it should be approved. While this vote plays a role in advising the agency, the FDA is not required to follow the committee conclusions, although it generally does.

## Pipeline Report: 2nd/3rd Quarter 2017

| Drug/Manufacturer | Clinical Use | Anticipated Date | Projected Market Impact |
|---|---|---|---|
| **Select Branded Pipeline Agents: Potential New Emerging Expenses for Health Plans** | | | |
| betrixaban maleate<br>Portola | Venous thromboembolism (VTE) prevention | June 24, 2017 | Factor Xa inhibitor; oral; may be first novel oral anticoagulant to gain approval for extended-duration prevention of VTE in acutely ill patients; Fast Track/Priority Review |
| sofosbuvir/velpatasvir/ voxilaprevir<br>Gilead | Chronic hepatitis C virus (pangenotypic) | August 8, 2017 | Once-daily, single-tablet combination of an NS5B nucleotide polymerase inhibitor, an NS5A inhibitor, and an NS3/4A protease inhibitor; offers alternative pangenotypic therapy; studied as salvage therapy; Breakthrough Therapy (genotype 1 with prior NS5A inhibitor therapy) |
| glecaprevir/ pibrentasvir<br>Abbvie | Chronic hepatitis C virus (pangenotypic) | August 18, 2017 | Oral multi-pill combination of an NS3/4A protease inhibitor and an NS5A inhibitor; offers alternative pangenotypic therapy; studied as an 8-week regimen across all genotypes in non-cirrhotic patients; Breakthrough Therapy (genotype 1 with prior direct acting antiviral therapy)/Priority Review |
| **Select New Generics/Patent Expirations** | | | |
| eletriptan HBr tablets generic for Pfizer's Relpax® | Migraine | 1H 2017 | Settlement agreement with Apotex; appears to be eligible for 180-day exclusivity but only through 8/29/17; U.S. sales of $371 million in 2016 |
| trientine HCl capsules generic for Valeant's Syprine® | Wilson's disease | 2Q 2017 | No longer protected by patent; ANDAs submitted by more than one manufacturer; U.S. sales of $143 million in 2016 |
| moxifloxacin HCl ophthalmic solution generic for Alcon's Vigamox® | Bacterial conjunctivitis | July 2017 | Settlement agreement with Lupin and Teva; no filer will receive 180-day exclusivity; U.S. sales of $276 million in 2016 |
| prasugrel HCl tablets generic for Eli Lilly's Effient® | Acute coronary syndrome | August 15, 2017 | Settlement agreement with Mylan; U.S. sales of $662 million in 2016 |
| **Select Biosimilars** | | | |
| epoetin zeta (Retacrit) – biosimilar to Amgen's Epogen® and Janssen's Procrit®<br>Hospira/Pfizer | Anemia due to chronic kidney disease, zidovudine, and myelosuppressive chemotherapy; to reduce need for allogeneic red blood cell transfusions | June 2017 | Intravenous and subcutaneous erythropoiesis-stimulating agent; product launch likely to be delayed due to regulatory hurdles; Epogen had $1.48 billion and Procrit had $876 million in U.S. sales in 2016 |