Below is a summary of the 21st Century Cures Act, which Congress passed on November 25, 2016 and President Obama signed on December 13, 2016. Key regulations in this nearly 1,000-page legislation ease the burden for researchers conducting clinical studies, create new FDA approval pathways for novel and life-saving devices, accelerate the process for regenerative medicines to become FDA approved, and aim to improve medical device classification, testing, safety, and reimbursement.

This legislation also requires the Department of Health and Human Services (HHS) and FDA to prioritize patient experience by making public patient experience data part of an approved new drug application (NDA) or biologics license application (BLA) and set general guidance on the collection of this data. Finally, the law authorized funding for new and existing programs, all of which must then be appropriated each year through the annual appropriations process.

The summary is organized by innovation category, including:

- Regenerative Medicine
- Medical Devices
- Drug Development
- Combination Products
- Antimicrobial Resistance
- Clinical Studies
- FDA Regulatory Changes
- NIH-Funded Research

Regenerative Medicine:

Sec. 3033 – Accelerated Approval for Regenerative Advanced Therapies

Allows the FDA to grant accelerated approval for regenerative therapeutic products and directs the FDA to consider the unique characteristics of such therapies and provide a rationale for when determining whether to grant accelerated approval. This section also defines regenerative medicine to include: “cell therapy, therapeutic tissue engineering products, human cell and tissue products, and combination products using any such therapies or products.”

Sec. 3034 – Devices

Requires no later than 1 year after enactment the FDA to issue guidance on how devices used in regenerative therapy will be evaluated, answering the following questions:

- How the FDA intends to simplify and streamline regulatory requirements for combination device and cell or tissue products;
- What, if any, intended uses or specific attributes would result in a device used with a regenerative therapy product to become classified as a class III device;

- When the FDA considers it is necessary, if ever, for the intended use of a device to be limited to a specific intended use with only one particular type of cell; and
- Application of the least burdensome approach to demonstrate how a device may be used with more than one cell type.

Sec. 3035 – FDA Report on Regenerative Advanced Therapies
Requires the FDA to report each year on the number and type of applications for approval of regenerative advanced therapies filed, approved or licensed as applicable, withdrawn, or denied; and how many of such applications or therapies, as applicable, were granted accelerated approval or priority review.

Sec. 3036 – Standards for Regenerative Medicine and Advanced Therapies
Requires the FDA to consult with stakeholders and the National Institute of Standards and Technology (NIST) to establish standards within two years of enactment of the Cures Act to support the development, evaluation, and review of regenerative medicine and advanced therapies products.

Medical Devices:
Sec. 3051 – Breakthrough Devices
Establishes a breakthrough device pathway for 510(k) applications, de novo petitions and premarket approval (PMA) applications that is an expansion of the current Expedited Access Pathway and is like what already exists for drugs. It will allow for expedited development and priority review of devices intended for unmet needs. Like the drug breakthrough program, it will mean the FDA staffs individuals with appropriate expertise on the review team, adopts an efficient dispute resolution process, and allows early and frequent interactions between the FDA and the sponsor. The FDA will designate a device as breakthrough if it is intended to treat or diagnose life-threatening or irreversibly debilitating diseases or conditions, and meet at *least* one of the following four qualifications:

- The device represents a breakthrough technology that provides a clinically meaningful advantage over existing technology.
- No approved alternative treatment or means of diagnosis exists.
- The device offers significant, clinically meaningful advantages over existing approved alternatives.
- The availability of the device is in the best interest of patients by way of its benefits to a well-defined patient population.

Sec. 3052 – Humanitarian Device Exemption (HDE)
Provides the FDA with the authority to apply the HDE to devices that treat diseases and conditions that affect up to 8,000 individuals in the US. The current cap is 4,000. An HDE is

similar in both form and content to a PMA application, but is exempt from the effectiveness requirements of a PMA.

Sec. 3053 – FDA's Recognition of Standards
Requires FDA to determine within 60 days of a submitted request whether officially to recognize a standard (in whole or in part) issued by a nationally or internationally recognized standard development organization in a response to the requester that explains FDA's rationale, which will be made publicly available. Also, all FDA employees who review premarket device submissions must receive training on recognized standards. Previously, FDA could decide to adopt a standard, but was not required to disclose publicly its rationale and was not obligated to act within a specified time frame.

Sec. 3054 – Certain Class I and Class II Devices
Requires FDA to update lists regarding the appropriate regulation of Class I and Class II devices no more than 120 days after enactment of the act and every 5 years thereafter.

Sec. 3055 – Classification Panels
Ensures adequate expertise among members of FDA's medical device classification panels by requiring two or more voting members with a specialty or other expertise clinically relevant to the device under review and at least one voting member knowledgeable about the technology of the device. It also allows the sponsor the chance to correct misstatements, clarify information and call on experts to address specific issues. Finally, it provides the opportunity for patients, representatives of patients, and sponsors to recommend individuals to fill voting member positions on such panels.

Sec. 3056 – Flexibility for Institutional Review Board (IRB)
Strikes the requirement that a sponsor of a medical device trial always use a local institutional review board. This change will allow the use of centralized models.

Sec. 3057 – CLIA Waivers
Requires FDA to revise a section of its 2008 guidance document, "Recommendations: Clinical Laboratory Improvement Amendments of 1988 (CLIA) Waiver Applications for Manufacturers of In Vitro Diagnostic Devices" (CLIA Waiver Guidance), which may result in more flexible data standards. A manufacturer of an in vitro diagnostic (IVD) test may label and promote the test for use by CLIA-waived users (e.g., many physicians' offices) if FDA has determined the test is a simple laboratory procedure with insignificant risk of an erroneous result. It requires FDA to revise the CLIA Waiver Guidance to describe the appropriate use of studies that compare the performance of a test by waived users against users in CLIA "moderately complex" laboratory setting.

Sec. 3058 – Least Burdensome Device Review
Requires an audit by the FDA ombudsman and an assessment of the measurements used to track the implementation of the least burdensome requirements, including representatives from the industry to be involved in such process. The audit must be made public no later than one month after it is conducted. It also clarifies that FDA reviewers shall consider the least burdensome appropriate means necessary for demonstrating a reasonable assurance of safety and effectiveness when requesting additional information from manufacturers during the pre-market approval process.

Sec. 3059 – Cleaning Instructions and Validation Data Requirement
Following serious patient issues linked to infections from reusable devices and the release of guidance from 2015, this section encourages and clarifies that FDA requires cleaning and validation data for reusable medical devices.

Sec. 3060 – Medical Software Regulation Exemption
Identifies specific categories of medical software that will not be regulated as a medical device by FDA based on their low level of risk to patients. This list includes software intended to serve as electronic patient records; software for maintaining or encouraging a healthy lifestyle that is unrelated to the diagnosis, cure, mitigation, prevention, or treatment of a disease or condition; software for administrative support of a healthcare facility; and software for transferring, storing, converting formats, or displaying clinical laboratory test or other device data and results.

Sec. 5002 – Medicaid Reimbursement to States for Durable Medical Equipment
Requires that Medicaid reimbursement to states for durable medical equipment (DME) be limited to Medicare rates effective January 1, 2018. Under prior law, the effective date was January 1, 2019.

Pharmaceuticals:
Sec. 3004 – Report on Patient Experience
Requires FDA to report on its review of patient experience data and information on patient-focused drug development tools as part of approved drugs not later than 1st of June 2021, 2028 and 2031.

Sec. 3011 – Drug Development Tools Qualification
Expands FDA's new program known as the Drug Development Tools Qualification Program to validate new biomarkers, clinical outcome assessments, patient reported outcomes and animal models as being useful and appropriate. It establishes a review pathway for biomarkers and other development tools that can be used to help shorten drug development times, aiming to help reduce the high failure rate in drug development. It also

requires the Secretary to consult with the biomedical research consortia and others through a "collaborative public process," to establish a taxonomy for the classification of biomarkers (and related scientific concepts) for use in drug development. FDA is required to make publicly available on at least a biannual basis on its website, the following:

- All drug development tools qualified, including all surrogate endpoints which were the basis of approval or licensure (as applicable) of a drug or biological product;
- Information on each qualification submission under the qualification process;
- Whether external scientific experts were utilized in the development of a qualification plan or the review of a full qualification package;
- Formal written determinations in response to such qualification submissions;
- Summary reviews that document conclusions and recommendations for determinations to qualify drug development tools

Sec. 3012 – Targeted Drugs for Rare Diseases

Clarifies FDA's authority on genetically targeted drugs for rare diseases, allowing sponsors of genetically targeted or variant protein targeted drugs to rely on data for the same or similar technology from previously approved applications by the same sponsor, although the section does not alter the existing approval standards for drugs. Defines the term "genetically targeted drug" by saying that it may result in the modulation (including suppression, up-regulation, or activation) of the function of a gene or its associated gene product; and incorporates or utilizes a genetically targeted technology. The term "genetically targeted technology" means a technology comprising non-replicating nucleic acid or analogous compounds with a common or similar chemistry that is intended to treat one or more patient subgroups, including subgroups of patients with different mutations of a gene, with the same disease or condition, including a disease or condition due to other variants in the same gene.

Sec. 3013 – Rare Pediatric Diseases

Reauthorizes a program to encourage treatments for rare pediatric diseases and extends the authorization of the Rare Pediatric Disease Priority Review Voucher program that allows a drug designated for a rare pediatric disease prior to September 30, 2020 to receive a priority review voucher upon approval of an NDA or BLA through September 20, 2022.

Section 3014 – GAO Study of Priority Review Voucher Programs

Requires GAO to conduct a study and issue a report by January 31, 2020 that evaluates all three priority review voucher programs: tropical disease, rare pediatric disease, and medical countermeasure focusing on whether the voucher impacted the sponsor's decision to develop the drug, value of the voucher, the resource burden on FDA to review drugs for which vouchers use, whether any improvements to programs are needed to incentivize drugs that would not otherwise be developed, and the impact of the sunset of rare pediatric disease and medical countermeasure programs.

Sec. 3015 – Orphan Drug Grants
Expands this program so prospectively planned and designed observational studies and other natural history analysis can qualify for grants so long as the studies are used to develop or validate a drug development tool or understand the full spectrum of disease manifestations.

Sec. 3016 – Drug Manufacturing
Authorizes HHS to award grants to academic institutions and nonprofit organizations to study and recommend improvements to the continuous manufacturing process of drugs and biologics.

Sec. 3032 – Compassionate Use
Requires that pharmaceutical companies have publicly accessible compassionate use policies for drugs treating serious or life-threatening conditions. FDA is required to include a statement regarding any patient experience data that was used at the time of a drug's approval and the bill defines patient experience data as "data collected by any persons (including patients, family members and caregivers of patients, patient advocacy organizations, disease research foundations, researchers, and drug manufacturers)."

Combination Products:
Sec. 3038 – Combination Product Innovation
This section aims to improve the regulation of medical products that contain both a drug or biologic and a device, known as combination products by requiring that FDA meet with sponsors and agree early in development how to best study the combination product to meet the standard for approval. Within 4 years of the enactment of this Act, the FDA must submit an official guidance explaining the structured process of managing pre-submission interactions with sponsors developing combination products, best practices for ensuring that feedback in the pre-submission interactions represents the Agency's best advice, and information on meetings between the sponsor and FDA. It also clarifies how dispute resolutions work when the different centers of FDA do not agree, and it includes provisions for reporting on combo product regulations.

Antimicrobial Resistance:
Sec. 3042 – Limited Population Pathway
Provides FDA with the flexibility to approve antimicrobial drugs based on a limited population if the drug treats a life-threatening infection. If FDA approves a drug based on a limited population, the labeling and advertising of an antimicrobial drug shall contain "Limited Population" along with a proprietary name of the drug. Gives FDA the authority to review and approve promotional materials of a drug approved based on a limited population at least 30 days prior to drug dissemination.

Sec. 3044 – Susceptibility Test Interpretive Criteria for Microorganisms
Requires the Secretary to clear/classify/approve antimicrobial susceptibility testing devices using updated, recognized susceptibility test interpretive criteria to characterize the in vitro susceptibility of certain bacteria, fungi, or other microorganisms, as applicable, to antimicrobial drugs. No later than one year after enactment, the Secretary must establish and maintain on FDA's website a dedicated website that contains a list of any appropriate new or updated susceptibility test interpretive criteria standards and interpretive criteria.

Clinical Studies:
Sec. 2034 – Reducing Administrative Burden for Researchers
Requires the Secretary to review the agency's financial conflict of interest policies and regulations and to harmonize existing policies to reduce administrative burden; evaluate financial expenditure reporting procedures and requirements for recipients of NIH grants, and take appropriate actions to avoid duplications; and clarify the applicability of certain Office of Management and Budget requirements related to documentation of personal expenses for recipients of HHS-funded grants. It also requires the NIH Director, the Secretary of Agriculture, and the Commissioner of the FDA to review and revise as appropriate laboratory animal regulations and policies to reduce administration burden on investigators. The review shall eliminate or reduce inconsistencies and duplication across the board.

Sec. 2051 – Technical Updates to Clinical Trials Database
Makes technical updates to the clinical trials data base requirements to allow information from device clinical trials to be posted prior to clearance or approval if the manufacturer requests that the information be posted earlier. It also makes technical updates to the clinical trials database to clarify whether combination products are considered drug clinical trials or device clinical trials for purposes of the database, using the primary mode of action of the combination product to inform whether it will be listed under device or drug/biologic.

Sec. 3001 – Patient Experience Data
This section of the bill builds on FDA's progress in integrating patient perspectives into its decision-making processes for drugs and devices. Patient experience data are collected by any persons (including patients, family members and caregivers of patients, patient advocacy organizations, disease research foundations, researchers, and drug manufacturers); and "are intended to provide information about patients' experiences with a disease or condition, including the impact of such disease or condition, or a related therapy, on patients' lives; and patient preferences with respect to treatment of such disease or condition."

Sec. 3002 – Patient-focused Drug Development Guidance
Requires the FDA, over the course of 5 years, to issue guidance regarding how to collect such patient experience data, with guidance documents addressing:

- Appropriate ways to collect data for use in regulatory decisions;
- How patients wishing to propose draft guidance to FDA may submit such documents;
- How FDA will respond to patient experience data submissions to FDA;
- The format and content for patient experience data submissions;
- How FDA plans to use relevant patient experience data and related information when evaluating the risks and benefits of a drug

Section 3004 – Report on Patient Experience Drug Development
Requires the FDA to issue a report assessing the use of patient experience data in regulatory decision-making, with respect to the review of patient experience data and information on patient-focused drug development tools as part of approved drugs no later than June 1 of 2021, 2026, and 2031.

Sec. 3021 – Novel Clinical Trial Designs
Following the release of draft guidance from February 2010, it requires FDA to hold a public meeting and issue additional guidance that addresses the use of complex adaptive and other novel trial designs for the development and regulatory review of NDAs and BLAs. It will assist sponsors in incorporating adaptive designs and novel statistical modeling into new drug applications.

Sec. 3022 – Real World Evidence
In July, FDA released draft guidance with plans to use real world evidence or data in making medical device regulatory decisions. The law requires FDA to evaluate the use of real world evidence to help support the approval of a new indication for a previously approved drug and to help support or satisfy post-approval study requirements, issuing an official guidance no more than 2 years after the enactment of this Act.

Sec. 3023 – Protection of Human Research Subjects
Requires the Secretary of HHS to harmonize differences between the human subject regulations under the Common Rule and the FDCA. Modification made must aim to protect vulnerable populations, incorporate local considerations, and support community engagement through mechanisms such as consultation with local researchers and human research protection programs.

Sec. 3024 – Informed Consent Waiver or Alteration for Clinical Investigations
Provides FDA with the flexibility to waive or alter informed consent requirements for clinical trials with minimal risk, similar to existing flexibility for HHS and NIH under the Common Rule.

Sec. 3031 – Summary Level Review
Allows FDA to rely upon qualified data summaries to support the approval of an application for a new indication of an already approved drug. However, the law states, "Sponsors of the application still must submit all information to FDA."

Sec. 3057 – CLIA Waiver Improvements
Requires that the FDA update its existing regulatory guidance by November 2018 to clarify the criteria for waiving Clinical Laboratory Improvement Amendment (CLIA) requirements, which aims to expand patient access to point-of-care diagnostics, no later than one year after enactment.

NIH-Funded Research:
Sec. 2012 – Privacy Protection for Human Research Subjects
Directs the Secretary of HHS to issue certificates of confidentiality to researchers that receive federal funding. Allows the Secretary of HHS to also issue certificates to privately funded researchers. Prohibits researchers to whom certificates are issued from disclosing the name of participants or any other identifiable data gathered during research, except when required by law, consented to by the participant, necessary to treat the patient, or in compliance with other privacy laws.

Sec. 2013 – Protection of Identifiable and Sensitive Information
Allows the Secretary of HHS to exempt individual biomedical research data from being disclosed if the data is identifiable, or could be used for identification. Requires the Secretary of HHS to submit written basis for each disclosure exemption, made available to the public upon request to the Chief Freedom of Information Act Officer at HHS.

Sec. 2014 – Data Sharing
Allows the Director of the NIH to require grant recipients to share the data that is generated from the NIH-funded research. Requires the data to be shared in a manner that is consistent with Federal laws and regulations, including laws and regulations for protection of human research participants, proprietary data, and national security interest
Funding Authorization:

- $4.8 billion total over 10 years to the National Institutes of Health (NIH) for i
- $1.51 billion for the Brain Research through Advancing Innovative Neurotechnologies Initiative (BRAIN)
- $1.8 billion for cancer research
- $30 million for regenerative medicine using adult stem cells
- $500 million for FDA to move drugs and medical devices to patients more quickly
- $1 billion over 2 years for grants to states to supplement opioid abuse prevention and treatment activities

- $14 million for fiscal years 2018-2020 for National Mental Health and Substance Use Policy Laboratory (NMHSUPL) within SAMHSA to solicit related grants