

21st Century Cures Overview and Implications

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The 21st Century Cures Act

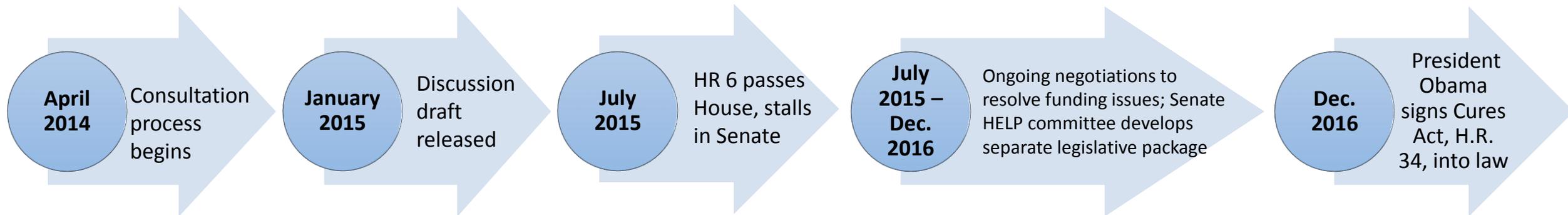
The 21st Century Cures Act of 2016 was signed into law on December 13, 2016, and *is aimed at improving and accelerating the discovery, development, and delivery of new biomedical products.*

“Simply put: 21st Century Cures is an innovative game-changer and a truly once-in-a-generation opportunity to bring our healthcare system light years ahead of where it is today.”

Rep. Fred Upton – Chief Sponsor

21st Century Cures: Timeline to Passage

The passage of 21st Century Cures was three years in the making



Legislative Timeline:

- **July 10, 2015** – House approves H.R. 6, the 21st Century Cures Act, by a vote of 344-77
- **November 30, 2016** – House approves new version of 21st Century Cures Act, H.R. 34, by a vote of 392-26
- **December 7, 2016** – Senate approves 21st Century Cures Act by vote of 94-5
- **December 13, 2016** – President Obama signs 21st Century Cures Act into law

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Breakdown of 21st Century Cures Act

The legislation includes four key sections that have important implications for clinical research and drug development:

Title I: Special
Innovation
Projects

Title II:
Discovery

Title III:
Development

Title IV:
Delivery

21st Century Cures: Innovation Projects (Title I)

Provides over \$4.8 billion over 10 years to the National Institutes of Health (NIH) to:

Advance the **Precision Medicine Initiative** to drive research into the genetic, lifestyle and environmental variations of disease
(\$1.45 billion)

Bolster Vice President Biden's "**Cancer Moonshot**" to speed research
(\$1.8 billion)

Invest in the **BRAIN Initiative** to improve our understanding of diseases like Alzheimer's (\$1.5 billion)

Provides \$500 million over 10 years to the Food and Drug Administration to fund activities listed in Title III: Development

Provides \$1 billion over 2 years for grants to states to supplement opioid abuse prevention and treatment activities

21st Century Cures: Discovery (Title II)

In addition to funding specific initiatives, there are a number of sections of Cures that are directly relevant to NIH's mission — measures that will provide the agency with tools and resources to advance biomedical research:

1

**ADVANCING PRECISION
MEDICINE**

2

**SUPPORTING YOUNG
EMERGING SCIENTISTS**

3

**NIH PLANNING AND
ADMINISTRATION**

4

**ADVANCEMENT OF NIH
RESEARCH AND DATA ACCESS**

5

**FACILITATING COLLABORATIVE
RESEARCH**

21st Century Cures: Discovery (Title II)

1 Advancing Precision Medicine (Sec. 2011-2014)

- Encourages HHS to carry out a “Precision Medicine Initiative” to augment efforts to address disease prevention, diagnosis, and treatment
- Increases privacy protection for research volunteers by issuing certificates of confidentiality and by prohibiting researchers from being compelled to disclose identifiable, sensitive information
- Enhances data sharing by requiring grant recipients to share data that is generated from NIH funded research

2 Supporting Young Emerging Scientists (Sec. 2021-2022)

- Creates a “Next Generation of Researchers Initiative” to coordinate and develop policies and programs to improve opportunities for new researchers, including improving the loan repayment program

21st Century Cures: Discovery (Title II)

3 NIH Planning and Administration (Sec. 2031-2044)

- Requires NIH to take several steps to improve strategic planning, grantmaking, collaboration, and reporting processes
- Requires NIH to reduce key administrative burdens for researchers and exempts agency from certain Paperwork Reduction Act requirements

4 Advancement of NIH Research and Data Access (Sec. 2051-2054)

- Makes technical updates to the ClinicalTrials.gov database and requires HHS to consult with stakeholders to receive recommendations related to enhancements to the clinical trial registry

5 Facilitating Collaborative Research (Sec. 2061-2063)

- Requires HHS to issue two guidances that clarify the access, sharing, and use of health data for research purposes

21st Century Cures: Development (Title III)

Provides \$500 million to the FDA over 10 years to move drugs and medical devices to patients more quickly, while maintaining the same standard for safety and effectiveness with an emphasis on:

1

**PATIENT-FOCUSED
DRUG DEVELOPMENT**

2

**ADVANCING NEW
DRUG THERAPIES**

3

**MODERN TRIAL DESIGN AND
EVIDENCE DEVELOPMENT**

4

**PATIENT ACCESS TO
THERAPIES AND
INFORMATION**

5

**ANTIMICROBIAL
INNOVATION AND
STEWARDSHIP**

6

**IMPROVING SCIENTIFIC
EXPERTISE AND OUTREACH
AT FDA**

1 Patient-Focused Drug Development

Patient Experience Data Use (Sec. 3001)

- Requires the FDA to report any patient experience data that was used to support a drug's approval, and to provide aggregate reports on agency use of this data at 5-yr intervals
- Patient experience data includes data 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*

Patient-Focused Drug Development Guidance (Sec. 3002)

- Requires the FDA to issue guidance regarding how to collect patient experience data
- Such guidance documents should address:
 - Appropriate ways to collect such data for use by FDA
 - How patients may submit draft guidance documents to FDA
 - How FDA will respond to patient experience data submissions
 - The format and content for patient experience data submissions
 - How the FDA plans to use relevant patient experience data and related information when evaluating the risks and benefits of a drug

2 Advancing New Drug Therapies

Qualification of Drug Development Tools (Sec. 3011)

- Formalizes the review pathway at FDA for biomarkers and other drug development tools (COAs, animal models) that can be used to help shorten drug development time and reduce the failure rate in drug development

Targeted Drugs for Rare Diseases (Sec. 3012)

- Expedites the development and review of genetically targeted drugs and variant protein targeted drugs for rare disease subgroups in areas of high unmet need by allowing sponsors to resubmit data already used in previous applications or approvals for drugs using the same genetic targeting technology

Reauthorization for Pediatric Rare Disease Program (Sec. 3013)

- Reauthorizes the pediatric rare disease priority review voucher program to encourage treatment for rare diseases until 2020

3 Modern Trial Design and Evidence Development

Novel Clinical Trial Designs (Sec. 3021)

- Requires FDA to hold a public meeting and issue guidance documents that would assist sponsors in incorporating adaptive designs and novel statistical modeling into new drug applications
- Such guidance should include:
 - Use of such clinical trial designs, including how these designs can satisfy the substantial evidence of effectiveness standard
 - How sponsors can obtain feedback from FDA on technical issues related to modeling and simulations
 - The types of qualitative and quantitative information that should be submitted for review
 - Recommended analysis methodologies

Real World Evidence (Sec. 3022)

- Requires FDA to establish a program to evaluate the potential use of real world evidence to:
 - Help support the approval of new indications for an approved drug
 - Help support or satisfy post approval study requirements

Cures definition of RWE: “Data regarding the usage, or the potential benefits or risks, of a drug derived from sources other than clinical trials. May also include ongoing safety surveillance, observational studies, registries, claims data, and patient-centered outcomes research activities.”

3 Modern Trial Design and Evidence Development

Protection of Human Research Subjects (Sec. 3023)

- Requires the Secretary of HHS to harmonize differences between the human subject regulations under the Common Rule and the Federal Food Drug and Cosmetic Act.
- Directs HHS to identify ways to streamline the institutional review board process to avoid duplication of effort
 - For example: using joint or shared review for trials being conducted at multiple sites

Informed Consent Waiver (Sec. 3024)

- Provides FDA the flexibility to waive or alter informed consent requirements for clinical trials as long as:
 - the proposed clinical testing poses no more than minimal risk to human subjects, and
 - includes appropriate safeguards to protect subjects' rights, safety, and welfare
- This is similar to existing flexibility for HHS and NIH under the Common Rule

4 Patient Access to Therapies and Information

Summary Level Review (Sec. 3031)

- Allows FDA to rely upon “qualified data summaries” to support the approval of a new indication for an already approved drug
- Applicable in cases where there is robust, acceptable safety data on the already approved drug
- Still requires sponsor to submit full data sets used to create the data summary
- Subject to FDA and sponsor agreement that the new indication is suitable for summary review

Expanded Access (Sec. 3032)

- Requires the manufacturer of an investigational drug for a serious or life-threatening disease to make available (e.g., on its website) its policy regarding evaluating and responding to requests for expanded access

Health Care Economic Information (Sec. 3037)

- Clarifies the scope of permissible manufacturer communications regarding health care economic information (alters FDAMA 114)
- Broadens the definition of the payer groups that can receive this information beyond formulary committees
- Changes how closely the HCEI must be related to approved indications

Regenerative Medicine (Sec. 3033-3036)

- Allows FDA to grant accelerated approval for regenerative therapeutic products
- Requires FDA to establish standards to support the development, evaluation, and review of regenerative medicine and advanced therapies products

5 Antimicrobial Innovation and Stewardship

Antimicrobial Resistance Monitoring (Sec. 3041)

- Requires reporting from CDC and FDA on information and data regarding human resistance to antimicrobial drugs
- Requires CDC to distribute educational materials related to antimicrobial stewardship programs or practices
- Requires CDC to provide a mechanism where health care facilities can report antimicrobial data that will be made available to the public

Limited Population Pathway (Sec. 3042)

- Provides FDA with the flexibility to approve antimicrobial drugs based on a limited population if the drug treats a life-threatening infection

6 Improving Scientific Expertise and Outreach at FDA

FDA Staffing and Hiring (Sec. 3071-3072)

- Increases the number of positions in the Silvio O. Conte Senior Biomedical research service, allows increased salary, and changes the qualifications to include engineers
- Provides FDA with the authority to appoint candidates to certain positions that support the development, review, and regulation of medical products.
- Allows for the FDA commissioner to determine and fix the annual pay rate up to a limit to help attract and retain qualified employees

Establishment of FDA Intercenter Institutes (Sec. 3073)

- Requires FDA to pilot one or more intercenter institutes to help develop and implement processes for coordination of activities in major disease areas between the drug, biologics, and device centers

Scientific Engagement (Sec. 3074)

- Improves FDA and NIH scientists' ability to attend scientific conferences, ensuring that they stay abreast of the newest advancements in science and are better able to collaborate widely

21st Century Cures: Delivery (Title IV)

The development of new drugs and devices is meaningless unless they are delivered to the right patients at the right time. Cures will help improve delivery by helping fully realize the benefits of a learning health care system through:

- 1** **INTEROPERABILITY**
(Sec. 4003)
- 2** **INFORMATION BLOCKING**
(Sec. 4004)
- 3** **LEVERAGE EHR RECORDS TO IMPROVE PATIENT CARE AND IMPROVE PATIENT ACCESS TO THEIR EHR INFORMATION**
(Sec. 4005-4006)
- 4** **GAO STUDIES ON PATIENT MATCHING AND ON PATIENT ACCESS TO HEALTH INFORMATION**
(Sec. 4007-4008)

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Cures Supports Better Evidence Development

Provides or reinforces important policies for NIH and FDA to improve evidence development

- Aligned with previously stated agency priorities and complementary to existing collaborative activities

Increases the rigor and transparency of a truly 21st Century research and drug development enterprise

- Provides for strong, nimble regulatory science that keeps pace with scientific and methodological advancements

Rather than lowering standards, this provides a path to filling in critical gaps in available evidence

Example: Regulatory use of RWE

Timely:

- Nation's growing electronic health information infrastructure has enabled routine and increasingly robust collection of digital data at the point of patient care

Part of a Bigger Puzzle:

- Drug discovery and development is longer and more costly, with growing public attention on resultant prices
- Providers and payers are moving toward payment and reimbursement models focused on value over volume
- Patients are more involved than ever before in their own care decisions and the push for more personalized treatments

Reinforcing of a Learning Health Care System:

- Doesn't change approval standards, rather it better supports and enables use of data and evidence on outcomes that are hard to get from traditional RCTs (e.g., outcomes that are too costly, too small populations with particular clinical features, too long follow-up needed, diff impact in diff clinical settings, etc.)
- Learning from real-world patient experiences can support better informed health care decision-making by a range of stakeholders

Priority areas for improving RWE

Progress in the development and use of RWE for regulatory purposes will require collaborative stakeholder efforts in the following areas

- 1 Better defining RWD and RWE** – terms are not one-size-fits-all and are context dependent
- 2 Improving methods for pragmatic clinical trials** – capable of harnessing randomization within the clinical setting
- 3 Improving the credibility of observational studies** – to support regulatory decision-making (e.g., indication expansion)
- 4 Establishing a vision for regulatory use** – mapping data sources and research methods with appropriate regulatory use cases
- 5 Building a robust national evidence development infrastructure** – that incentivizes and reinforces evidence generation activities

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Key Implications for Clinical Research and Drug Development

Data Sharing

- Contains numerous provisions aimed at improving data sharing (broadly defined):
 - To support specific projects (e.g., Precision Medicine Initiative, National Neurological Conditions Surveillance System)
 - To improve quality and comprehensiveness of existing data sharing platforms
 - To support EHR interoperability and health information exchange

Evidence Development

- Seeks to expand and improve sources of reliable evidence to support stakeholder decision-making that better reflects real-world care and outcomes

Human Research Subject Protection

- Aims to minimize administrative and regulatory burdens for researchers subject to both the Common Rule and *FDCA* by harmonizing these regulations
- Seeks to ensure that research and data sharing are conducted appropriately and with adequate safeguards to protect privacy

Patient-Centered Medicine

- Aims to advance the science of patient input through development of rigorous approaches to patient experience data collection
- Will formalize and expand processes within FDA for patient engagement, in order to better inform risk-benefit decisions

Moving Forward...

Broader political and policy-related efforts may impact implementation of the legislation in several ways. Uncertainties remain regarding:

Impact of leadership changes

- A new presidential administration will be appointing senior leadership at HHS, which will impact policy priorities at Cures-related agencies

Funding allocations

- Increased funding levels for NIH and FDA are subject to yearly reauthorization by Congress—progress may be slowed if agencies do not have resources to carry out mandates

Upcoming legislative activities

- Additional FDA and NIH legislative proposals may be enacted through 2017's user fee acts; the current draft of PDUFA VI provisions broadly mirrors Cures provisions

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Thank You!

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