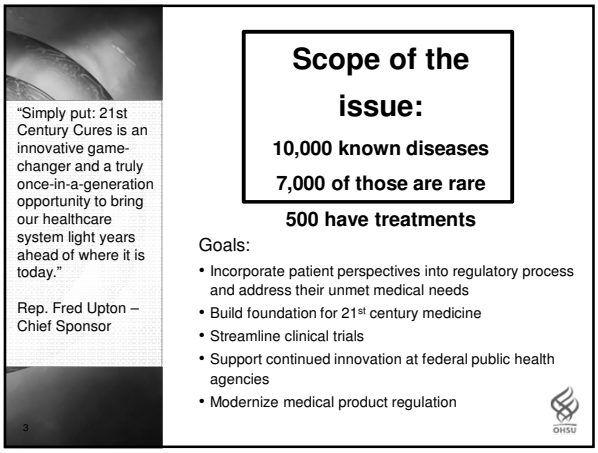
21st Century Cures Act: Impact on Research Compliance

Kathryn Schuh, MD, MCR
IRB Chair
Director, Human Research Protection Program

21st Century Cures Act: Impact on Research Compliance

- Harmonizing the differences between HHS and FDA Human Subject Regulations
- Changes to privacy protections
- The role of IRBs



"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

3

Scope of the issue:

10,000 known diseases

7,000 of those are rare

500 have treatments

Goals:

- Incorporate patient perspectives into regulatory process and address their unmet medical needs
- Build foundation for 21st century medicine
- Streamline clinical trials
- Support continued innovation at federal public health agencies
- Modernize medical product regulation

H. R. 34

One Hundred Fourteenth Congress
of the
United States of America

AT THE SECOND SESSION

Begun and held at the City of Washington on Monday, the fourth day of January, two thousand and sixteen

An Act

To accelerate the discovery, development, and delivery of 21st century cures, and for other purposes.

Be it enacted by the Senate and House of Representatives of the United States of America in Congress assembled,

SECTION 1. SHORT TITLE; TABLE OF CONTENTS.

(a) SHORT TITLE.—This Act may be cited as the "21st Century Cures Act".

OHSU

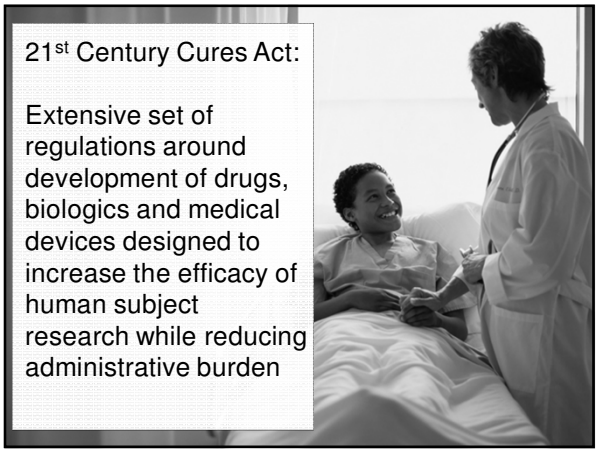
21st Century Cures Act

21st Century Cures Act is signed into law, December 13, 2016

HR 34 Public Law No. 114-255

5

OHSU



21st Century Cures Act:

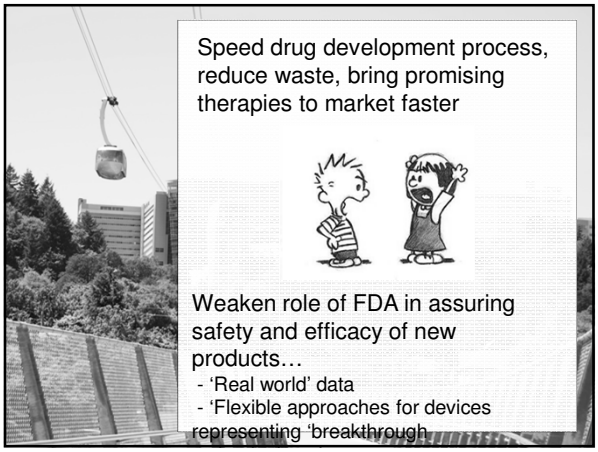
Extensive set of regulations around development of drugs, biologics and medical devices designed to increase the efficacy of human subject research while reducing administrative burden

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

Despite input from multitudes of stakeholders and nearly unanimous vote, the regulation is quite controversial!



Speed drug development process, reduce waste, bring promising therapies to market faster

Weaken role of FDA in assuring safety and efficacy of new products…
- 'Real world' data
- 'Flexible approaches for devices representing 'breakthrough

Four Key Sections

- Title I: Innovation Projects and State Responses to Opioid Abuse
  - $4.8 billion over 10 years to NIH
  - Precision Medicine Initiative
  - Bolster 'Cancer Moonshot'
  - BRAIN Initiative
  - $1 billion over 2 years for opioid abuse prevention and treatment

All of Us The Precision Medicine Initiative
THE FUTURE OF HEALTH BEGINS WITH you

CANCER MOONSHOT

9

Four Key Sections

- Title II: Discovery
  - Precision Medicine
    - NIH-required data sharing, HS protections: COC, FOIA
  - Supporting young emerging scientists
  - NIH Administration – reduce regulatory burden
    - COI, sub-awards, animal regulations, expense reporting, create 'Research Policy Board' (advisory committee)
  - Advancing NIH research and data access
    - Clinicaltrials.gov
  - Facilitating collaborative research
    - Research use of PHI
    - Minority populations

10

Four Key Sections

- Title III: Development
  - Patient-focused drug development
  - Advancing new drug therapies
    - Review pathway for biomarkers, models
    - Genetically targeted drugs for rare disease
    - Reauthorize Pediatric Rare Disease program
  - Modern trial design and evidence development
    - Novel clinical trial designs
    - Real World Evidence
    - Harmonize with Common Rule, central IRB
  - Patient access to therapies and information
    - Streamline adding new indications
    - Expanded access policies
    - Health Care Economic Information
    - Regenerative medicine
  - Medical Device Innovations
  - Improving FDA scientific expertise and outreach

11

Four Key Sections

- Title IV: Delivery
  - Health IT – Amends HITECH, Medicare-Medicaid 'Meaningful Use' Incentive Program
  - Interoperability
    - 'Trusted exchange framework' – policies, HIT standards, noncompliance
  - Information Blocking
    - Authorizes OIG enforcement
  - Leverage EHR, Education
  - GAO Studies on Patient Matching, Patient Access to EHR

12

Additional Sections

- Title V: Savings (Medicare/Medicaid)

DIVISION B – HELPING FAMILIES IN MENTAL HEALTH CRISIS

- Title VI: Strengthening Leadership and Accountability
- Title VII: Ensuring Mental and Substance Use Programs Keep Pace
- Title VIII: Supporting State Prevention Activities
- Title IX: Promoting Access to Mental Health Care
- Title X: Strenthening Mental and Substance Use Care for Children
- Title XI: Compassionate Communication on HIPAA
- Title XII: Medicaid Mental Health Coverage
- Title XIII: Mental Health Parity
- Title XIV: Mental Health and Safe Communities

13

Additional Sections

DIVISION C – INCREASING CHOICE, ACCESS, AND QUALITY IN HEALTH CARE FOR AMERICANS

- Title XV: Medicare Part A
- Title XVI: Medicare Part B
- Title XVII: Other Medicare Provisions
- Title XVIII: Other Provisions

14

Human Subjects Research (HSR) General Provisions

- HHS required to harmonize OHRP and FDA regulations
- HHS required to modify 'Common Rule' and FDA regulations to:
  - Reduce regulatory duplication and unnecessary delays
  - Modernize and facilitate multisite and cooperative research
  - Protect vulnerable populations, incorporate local considerations and support community engagement
- January 18, 2017: HHS published revisions to 'Common Rule'
- Breaking news: New Common Rule implementation delayed until July 19, 2018 (or later…)

Specific HSR Provisions - IRB

Waiver of consent - FDA

- Waive/alter consent for minimal risk research
  - Where consent not feasible
  - If consent contrary to the best interests of human beings
  - Poses no more than minimal risk, and
  - Includes appropriate safeguards to protect rights, safety and welfare of subjects
  - Examples: retrospective reviews, anonymized data
  - First of FDA-Common Rule harmonization

Specific HSR Provisions - IRB

Central IRB

- Encourages use of central IRBs
- Removes FDA requirement for local IRB review of device studies

NIH Single IRB policy: All multi-site research submitted after January 25, 2018 must use single IRB.

Revised Common Rule: All US-based federally funded research approved after January 20, 2020 must use single IRB.



Specific HSR Provisions - Privacy

Certificates of Confidentiality

- Expands protection of research subject privacy
  - Require Certificates of Confidentiality for all federally funded research involving identifiable sensitive information (ISI)
  - Expands ISI definition to include any information for which there is a risk of identification, even if only 'a very small risk'
  - Disclosure still allowable when required by law, consented, for other scientific research…
- NIH policy issued October 2017, reto-effective 12/13/2016:
  - CoCs will automatically be in place for:
    - Human research
    - Research involving identifiable biospecimens
    - Research using or generating individual level genomic data
  - New grants on 'identifiable, sensitive data' - part of the grant application
  - Existing research:
    - Identify federally funded projects, flag EHR, reconsent subjects

Specific HSR Provisions - Privacy

Freedom of Information Disclosures

- HHS can exempt HS research data from FOI disclosures if individual is identified or 'there is at least a very small risk that some combination of the information and other available data sources could be used to deduce the identity'
- In practice, much of this data excluded already (PHI)

Specific HSR Provisions - Privacy

Research Use of PHI under HIPAA – Guidance 12/18/2017

- Remote access for preparatory to research allowed if:
  - Privacy and security safeguards of Privacy Rule
  - Researcher does not copy or retain the PHI
  - Recommends risk analysis and reasonable assurances re: technical safeguards and lack of retention
- 'Future research' authorizations – referred to HIPAA Final Rule preamble, still exploring this issue
- Authorizations may be 'broad' (e.g., all providers in last year)

Specific HSR Provisions - Privacy

Research Use of PHI under HIPAA – Guidance 12/18/2017

- Revocation of authorization affirmed:
  - May continue to use/disclose PHI obtained prior to revocation to maintain integrity of research (e.g., report adverse events)
  - Revocations effective when received
  - May provide reminders to subjects regarding the right to revoke authorization
  - Mechanism for revoking should be generally available to all subjects
  - Although required to be in writing, entities may cease using and disclosing PHI based on oral request
- HHS must convene a working group to study uses and disclosure of PHI for research purposes – we are actively awaiting the findings of the working group…

Specific HSR Provisions - Privacy

Data Sharing by NIH Grant Recipients

- Allows NIH to require grant recipients to share data 'to extent feasible' and in 'manner consistent with applicable laws and regulations, including protection of research participants and grant recipients' proprietary interests, confidential commercial information and intellectual property rights.'

Specific Provisions – ClinicalTrials.gov

ClinicalTrials.gov

- Encourage compliance
- Update policies to improve data
- Consultation regarding enhancements to usability, functionality and search capability

Specific Provisions - COI

Conflict of Interest (COI)

- HHS to review all research funding agencies and harmonize policies to reduce administrative burden related to COI:
  - Thresholds for reporting COIs
  - Timelines for reporting requirements
  - Appropriateness and relevance of reporting requirements to research funding awards
- Review for updating training modules related to disclosures

Specific Provisions - Grants

Grant Administrative Burden

- Implement measures to reduce burden related to monitoring subrecipients of NIH grants
  - Exempt from monitoring if meet certain requirements
  - Explore new grant models (such as multiple prime awardees)
- Evaluate required reporting on Financial Expenditures to reduce duplicative or burdensome expenditure reporting requirements
- Clarify Uniform Guidance Requirements for Grant Awardee Documentation of Personnel Expenses

Specific Provisions – Animal Care

Animal Care and Use

- Review and revise NIH, FDA and USDA regulations and policies related to the care and use of laboratory animals
  - Reduce administrative burden, eliminate duplicative, inconsistent, overlapping policies
  - Continue to ensure 'integrity and credibility of research findings and protection of research animals'

Specific HSR Provisions

Pregnant and Lactating Women

- Establish a taskforce on research specific to pregnant women and lactating women
  - Provide guidance on gaps in knowledge and research regarding safe and effective therapies for pregnant women and lactating women

Increased Inclusion of Underrepresented Populations

- Encourages National Institute on Minority Health and Health Disparities to include ways to increase participation of underrepresented populations in clinical trials in its strategic plan.

Awaiting HHS guidance…

Specific HSR Provisions – FDA Device Regulations

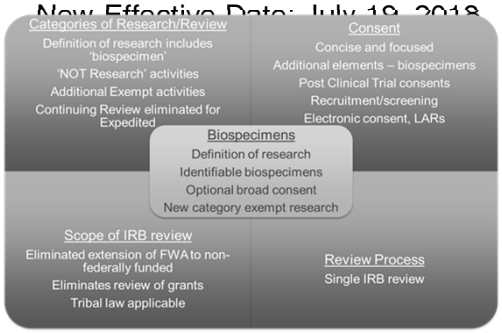
- Exempts 5 categories of software from medical device reg
  - Administrative support of healthcare facility
  - Maintaining healthy lifestyle (not related to dx, cure, mitigation, prevention or treatment of disease)
  - Management of certain electronic medical records, lab tests
  - Clinical Decision Support applications
- Expanding size of patient population that may be served by a 'Humanitarian Use Device'
- Breakthrough Device designation program
  - Expedite development of and review of devices
  - No approved or cleared alternatives
  - Significant advantage over existing or in best interest of patients
- Requires FDA to issue guidance on devices used in regenerative advanced therapies

Specific HSR Provisions – FDA Drug Regulations

- Patient experience data and real world data
- 'Summary level review' – new indications for approved drugs
- Provide new 'limited population' approval pathway for antibiotic and antifungal drugs
- Revise combination product regulation
- Require manufacturers to post expanded access policy at phase 2 stage of development
- FDA revisions: SPIND Chair Review

Impact on IRBs: Common Rule Changes

New, Effective Date: July 19, 2018



30

Common Rule Changes

Implementation Delayed until 7/19/2018

Definition of Human Subject research:

Human subject means a **living individual** about whom an investigator (whether professional or student) conducting research:

- Obtains information or biospecimens through intervention or interaction with the individual, and uses, studies or analyzes the information or biospecimens; OR
- Obtains, uses, studies, analyzes, or generates identifiable biospecimens.

- Definition of 'identifiable' and analytic technologies will be reexamined at least every four years

Common Rule Changes

Implementation Delayed until 7/19/2018

Categories of Research

- Levels of Review of Research
  - Full Committee – above minimal risk research
  - Expedited Review – Performed by 'designated members' for minimal risk research
  - Limited Review – for privacy protections
  - Exempt – Very low risk research exempt from review (but may be required to have limited review)
- Revised and new Exempt categories

Common Rule Changes

Implementation Delayed until 7/19/2018

Revised and New Exempt Categories of Research

- Research in routine educational settings
  - Not likely to adversely impact students' opportunity to learn
  - Not likely to adversely impact assessment of educators
- Educational tests, surveys, interviews, public observations including audio/video recording IF:
  - Recorded nonidentifiable fashion without a code, OR
  - No potential risk of criminal, financial employability or reputation (note: medical info always has risk of reputational harm), OR
  - IRB does a limited review for privacy protection (expedited)

Common Rule Changes

Implementation Delayed until 7/19/2018

Revised and New Exempt Categories of Research

- Benign behavioral interventions in adults with prospective consent, IF:
  - Recorded nonidentifiable fashion without a code, OR
  - No potential risk of criminal, financial employability or reputation (note: medical info always has risk of reputational harm), OR
  - IRB does a limited review for privacy protection (expedited)
- Benign means: brief, harmless, painless, not physically invasive, not likely to have significant adverse lasting impact, not offensive, embarrassing
- If involves deception, subject prospectively authorizes the deception

Common Rule Changes

Implementation Delayed until 7/19/2018

Revised and New Exempt Categories of Research

- Secondary research use of identifiable private information or biospecimens that are:
  - Publicly available, OR
  - Recorded in deidentified fashion (no code), OR
  - Health information regulated under HIPAA, OR
- Public service program evaluations
- Taste and food quality evaluation, consumer acceptance studies
- Storage or use for secondary research under broad consent

Common Rule Changes

Implementation Delayed until 7/19/2018

Broad Consent

- Introduces use of 'broad consent' as a permitted alternative to specific consent for the storage, maintenance and secondary research use of identifiable private information or identifiable biospecimens
- Limited list of required elements of consent
- Prohibits waiver of consent if subject refused broad consent
- Allows this type of research to be considered 'exempt' and undergo only limited IRB review
- Major infrastructure required by institution to implement and track subjects who have given/refused broad consent

Common Rule Changes

Implementation Delayed until 7/19/2018

Continuing Review of Research

- Continuing review (CR) is required at intervals appropriate to the degree of risk, but not less than once per year.
- Not required for research eligible for expedited review or limited IRB review, included above minimal risk studies in data analysis or standard of care procedures only

Common Rule Changes

Implementation Delayed until 7/19/2018

Scope of IRB Review

- Eliminated the extension of FWA to non-federally funded research
- Removed requirement for review of grants
- Noted applicability of tribal law

Common Rule Changes

Implementation Delayed until 7/19/2018

Informed Consent – General Requirements

- Information that a reasonable person…. to make an informed decision… and opportunity to discuss …
- Begin with a concise and focused presentation of the key information that is most likely to assist… must be organized and presented in a way that facilitates comprehension.
- As a whole must present information in sufficient detail, and must be organized and presented in a way that does not merely provide lists of isolated facts, but rather facilitates the subjects' understanding…
- Consent forms must be posted on public website within six months of last subject visit

Common Rule Changes

Implementation Delayed until 7/19/2018

Informed Consent – New Elements

- Statement whether identifiers will be removed from identifiable private information or biospecimens
- Statement whether identifiable private information or biospecimens could or will not be used for future research studies
- Whether biospecimens will be used for commercial profit and whether subject will share in this profit
- Whether results will be disclosed to the subject
- Whether research might include whole genome sequencing

Common Rule Changes

Implementation Delayed until 7/19/2018

Informed Consent – Process

- Allows use of identifiable information or biospecimens for screening, recruiting or determining the eligibility of subjects without consent if obtained orally or accessing records or stored biospeciments
- Allows electronic signatures
- Allows consent forms to be read to the subject
- Allows waiver of 'signed' consent for minimal risk research if that is not the cultural norm

Summary

- 21st Century Cures Act is omnibus regulation comprising many broad, far-reaching initiatives
- Major impact on FDA – mandates change in approach/plans/guidance to accommodate modern technologies/approaches and patient experience
  - Guidance documents released
  - Regulatory changes
    - Waiver of consent
    - IRB Chair review of SPIND
    - Allow central IRB review of devices)
- Privacy: Expanded CoC, FOI, remote access for prep
  - HIPAA reexamination to come
- Revised Common Rule – effective 7/19/2018 (or later)
  - Central IRB
  - Broad Consent
  - New exempt categories, removal of minimal risk CR
- Grant administrative burden?

We shall prevail…

Thank you!