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Navigating New Terrain: Recent Developments in Human Subjects Research Regulation

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Today's Exploration

- Common Rule
- NIH Policies
- Federal substance abuse disorder regulations (Part 2 regulations)
- 21st Century Cures Act: What new developments are ahead?

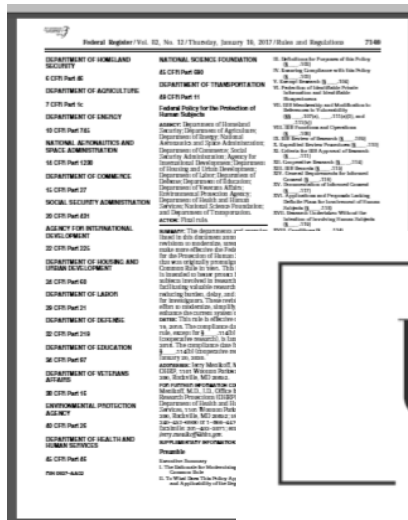
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Disclaimer – Laura Odwazny

- This presentation does not constitute legal advice.
- The views expressed are the presenter’s own and do not bind the U.S. Department of Health and Human Services or its operational components.

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The revised Common Rule



- Published January 19, 2017
- **Not yet effective**
- **NOTE:** Current rule

UPDATED

Interim Final Rule
Displayed 1/17/18

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Legal effect of the Interim Final Rule (displayed 1/17/18, published 1/22/18)

- While the IFR’s “effective date” is July 19, 2018, the IFR had an immediate legal impact upon display in the *Federal Register*:
 - **Legal effect #1:** Delays the effective date of the January 2017 final rule (the revised Common Rule) until July 19, 2018, and
 - **Legal effect #2:** Amends §__.101(l) (transition provision) of the not-yet-effective revised Common Rule so that general compliance date in that provision mirrors the effective date, which amendments will take effect July 19, 2018.
 - “Effective date” of regulatory text amendment made through the IFR has to be delayed to match the delayed “effective date” of the revised Common Rule.

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For now until July 19, 2018

- Status quo: Compliance with current Common Rule required
- Institutions can voluntarily apply provisions of revised Common Rule that do not conflict with current Common Rule
 - E.g., can implement revised Common Rule’s new informed consent disclosures, but not revised Common Rule’s continuing review flexibilities or new exemptions
- So, no compliance with entire revised Common Rule allowed instead of current Common Rule
- **Transition to revised rule after Effective Date**
 - Transition existing studies to revised rule, or keep under prior rule?
 - Consider both new flexibilities (e.g. continuing review) vs. potential application of new requirements (e.g. posting of informed consent)

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Future action?

- Either or both the IFR and the revised Common Rule could be further delayed or rescinded through other rulemaking.
- From IFR: “The federal departments and agencies listed in this document are in the process of developing a proposed rule to further delay implementation of the 2018 Requirements. The limited implementation delay accomplished by this interim final rule both provides additional time to regulated entities for the preparations necessary to implement the 2018 Requirements, and additional time for the departments and agencies listed in this document to seek input from interested stakeholders through a notice and comment rulemaking process that allows for public engagement on the proposal for a further implementation delay.”

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Common Rule Revisions: Informed Consent and Broad Consent

- Changes to informed consent
 - Summary
 - Posting clinical trial consent forms
 - New elements
- What is broad consent?
 - Included in the rule as an *alternative* to traditional study-specific informed consent
 - Never required (but certain exemptions are based on its prior use)
 - Used **only** for storage, maintenance, and secondary use of *identifiable private information or identifiable biospecimens*
 - Alternatives:
 - Informed consent under __.116(a)
 - De-identification
 - Waiver of informed consent (but heed the warning)
 - **Warning!**
 - Tracking, auditing and diligence required!
 - Waiver of consent **not permitted** if subject was asked to provide broad consent and refused

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Pragmatic Implementation Considerations for IRBs

- Revise protocol templates
- Change IRB review forms and train on new exemption categories
- Draft IRB reliance agreements and consider allocation of responsibilities
- Consider need to realign IRB resources
- New flexibilities be fully implemented or will institutional policy add layers?

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Common Rule Revisions

How does the new HIPAA exemption apply?

- Exempts “[s]econdary research uses of identifiable private information or identifiable biospecimens, if . . . [t]he research involves only information collection and analysis involving the investigator’s use of identifiable health information when that use is regulated under 45 CFR parts 160 and 164, subparts A and E, for the purposes of ‘health care operations’ or ‘research’ as those terms are defined at 45 CFR 164.501 or for ‘public health activities and purposes’ as described under 45 CFR 164.512(b).”

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Common Rule Revisions

How does the new HIPAA exemption apply?

- Does it apply to biospecimens?
 - The Secretary’s Advisory Commission on Human Research Protections (“SACHRP”) recently issued a recommendation to OHRP that the exemption should not apply to secondary research use of identifiable biospecimens
 - Why?
 - Literal reading of exemption, which applies only to “identifiable health information” (in contrast to other exemptions that expressly include biospecimens)

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Common Rule Revisions

How does the new HIPAA exemption apply?

- Does it apply to biospecimens?
 - Why?
 - Would “subvert the greater protection afforded to identifiable biospecimens under the modernized Common Rule infrastructure” (new requirements for informed consent)
 - Of limited utility because of state law restrictions on genetic testing
 - But sequencing information derived from biospecimens would be eligible for the exemption?

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Common Rule Revisions

How does the new HIPAA exemption apply?

- Does it apply to disclosure (or just internal use)?
 - SACHRP recommends application to disclosure (although uses restrictive example of collaborative research)
 - Common Rule doesn't make the same distinction between "use" and "disclosure" as HIPAA
 - Intent is to exempt research that is regulated by HIPAA

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Common Rule Revisions

How does the new HIPAA exemption apply?

- How does it apply in the hybrid entity setting?
 - Only HIPAA "covered components" are regulated by HIPAA (which often exclude non-provider research functions within the AMC)
- Does it apply to business associates?
 - Yes, but use by BA must be within the scope of services provided to the covered entity

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Common Rule Revisions

How does the new HIPAA exemption apply?

- IRB review may still be required to comply with HIPAA
 - IRB will review patient authorization if folded into the informed consent document (or if IRB review required by institutional policy)
 - IRB waiver of consent/HIPAA authorization

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New framework to assess 'identifiability'

- Same "identifiable" language: Identity of subject is or may be readily ascertained by the investigator or associated with the information
- New: reexamination of meaning of identifiable private information and identifiable biospecimens
- Assessment of whether there are analytic technologies or techniques that should be considered to generate identifiable private information or identifiable biospecimens
- For each:
 - Consultation with appropriate experts
 - Within 1 year and regularly thereafter (at least every 4 years)
 - Collaboration by Common Rule departments and agencies
 - Interpretation of terms may be changed; or any identified technologies/techniques will be included on list published after notice and comment

How will this intersect with other Federal laws/policies relating to “identifiability”?

- **HIPAA Privacy Rule: PHI**
 - “Individually identifiable” health information: Information that identifies individual, or reasonable basis to believe information can be used to identify individual

- **NIH CoC Policy: Identifiable sensitive information**
 - Information where individual is identified; or for which there is at least a very small risk, that some combination of the information, a request for the information, and other available data sources could be used to deduce the identity of an individual.

- **Privacy Act (and Federal policies): PII**
 - Information that can be used to distinguish or trace an individual’s identity, either alone or when combined with other personal or identifying information that is linked or linkable to a specific individual.

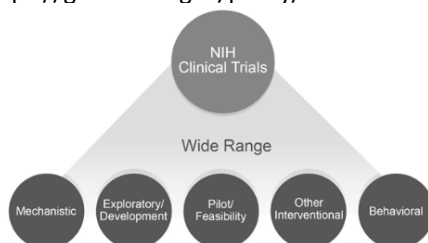
NIH Clinical Trial Policies

2014 Definition of a Clinical Trial

- A research study¹ in which one or more human subjects² are prospectively assigned³ to one or more interventions⁴ (which may include placebo or other control) to evaluate the effects of those interventions on health-related biomedical or behavioral outcomes.⁵
- <https://grants.nih.gov/policy/clinical-trials/definition.htm>

New interpretation, significant consequences

- Case studies: <https://grants.nih.gov/policy/clinical-trials/case-studies.htm>



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NIH Clinical Trial Policies

- New policies bring new requirements:
 - GCP Training (1/1/17)
 - Registration and results reporting at clinicaltrials.gov (1/18/17)
 - Clinical Trial-Specific Review Criteria (1/25/18)
 - Grant applications limited to clinical trial specific funding opportunity announcements (FOAs) 1/25/18

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NIH Policies

NIH Single IRB Policy (January 25, 2018)

- All sites in NIH-funded multi-site human subjects research studies must use a single Institutional Review Board (sIRB)
- Policy is “intended to enhance and streamline the process of IRB review and reduce inefficiencies so that research can proceed as expeditiously as possible without compromising ethical principles and protections for human research participants.”
- **Applicability**
 - Domestic sites where each site is conducting the same protocol
 - Doesn’t apply to career development, research training or fellowship awards.
- Plans for the sIRB must be included with grant application

<https://grants.nih.gov/policy/clinical-trials/single-irb-policy-multi-site-research.htm>

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NIH Policies

NIH Certificates of Confidentiality (October 1, 2017)

- Applies to research starting or ongoing after December 13, 2016
- Issued automatically as term and condition of NIH award
- Prohibits recipient from disclosing the name of research subject or “or any such information, document, or biospecimen that contains identifiable, sensitive information about the individual and that was created or compiled for purposes of the research” (unless with consent):
 - In any Federal, State, or local civil, criminal, administrative, legislative, or other proceeding, or
 - To any other person not connected with the research
- Some exceptions (consent, required by certain laws, necessary for medical treatment of the individual, disclosure for other research)
- Institutions must establish and maintain effective internal controls (e.g., policies and procedures) “that provide reasonable assurance that the award is managed in compliance with Federal statutes, regulations, and the terms and conditions of award.”
- Required by Section 2012 of 21st Century Cures Act

<https://grants.nih.gov/grants/guide/notice-files/NOT-OD-15-015.html>

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Part 2 Regulations

- 42 C.F.R. Part 2 amended on 1/17/11 (effective 3/21/17) and on 1/3/18 (effective 2/2/18)
- Part 2 regulations apply to (1) “federally assisted” substance use disorder “programs”; and (2) “lawful holders” that receive Part 2-protected data under the regulations (providers with consent and a re-disclosure notice, health plans with consent and researchers without consent)
- Part 2 –protected data
 - Identifies a patient as having (or having had) a substance use disorder
 - Was obtained by a “federally assisted” Part 2 “program”

AHILA**Part 2 Regulations**

- 2017 amendments changed the old rule requiring approval by the program director
- Now may use or disclose Part 2 data if determination that the recipient:
 - Is a HIPAA covered entity or business associate and has HIPAA authorization or waiver of authorization;
 - Is subject to the Common Rule and has informed consent or waiver of informed consent or is exempt;
 - If both HIPAA covered entity and subject to Common Rule, complies with both

AHILA**Part 2 Regulations**

- If not a HIPAA covered entity or business associate, and not subject to the Common Rule, requires patient consent
- Part 2 consent requirements are problematic for research (see discussion in paper)
 - Consent form could permit disclosure to: (1) a research institution with a treating relationship with the patient; (2) to a research institution without a treating relationship if re-discloses only to treating providers; or (3) to specific named individuals
 - Other requirements not consistent with HIPAA or the Common Rule

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Part 2 Regulations

- An individual or entity that receives Part 2 for research:
 - Is fully bound by the Part 2 Regulations and must resist in judicial proceedings any efforts to obtain access to patient records except as permitted by the Part 2 Regulations;
 - Must not re-disclose patient identifying information except back to the individual or entity from whom that patient identifying information was obtained or as permitted under the data linkage provisions;
 - May include Part 2 data in research reports only in aggregate form in which patient identifying information has been rendered non-identifiable such that the information cannot be re-identified and serve as an unauthorized means to identify a patient, directly or indirectly, as having or having had a substance use disorder;
 - Must maintain and destroy patient identifying information in accordance with the security policies and procedures; and
 - Must retain records in compliance with applicable federal, state, and local record retention laws

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Part 2 Regulations

- Researchers may request linkages to data sets from data repositories:
 - Obtain IRB review by OHRP-registered IRB to ensure patient privacy is considered and the need for identifiable data is justified;
 - Upon request, provide evidence of the IRB approval of the research project that contains the data linkage component; and
 - Ensure that patient identifying information obtained is not provided to law enforcement agencies or officials

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Part 2 Regulations

- Data repository that receives Part 2 data is fully bound by the Part 2 regulations and:
 - After providing the researcher with the linked data, must destroy or delete the linked data from its records, including sanitizing any associated hard copy or electronic media, to render the patient identifying information non-retrievable; and
 - Ensure that the patient identifying information is not provided to law enforcement agencies or officials

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21st Century Cures Act Implementation

- 21st Century Cures Act enacted December 13, 2016
- Provisions to reduce regulatory burden adapted from National Academies report: *Optimizing the Nation's Investment in Academic Research: A New Regulatory Framework for the 21st Century*
- Requirements Include:
 - Review all conflict of interest regulations and policies of funding agencies (§2034(a))
 - Reduce Burdens Related to Monitoring Subrecipients of NIH Funding (§2034(b))
 - Evaluate Required Reporting to NIH of Financial Expenditures (§2034(c))
 - Review and revise NIH, FDA, USDA regulations and policies related to the care and use of laboratory animals (§2034(d))
 - See FASEB, AAMC, COGR, NABR Report "Reforming Animal Research Regulations: Workshop Recommendations to Reduce Regulatory Burden"
 - <https://www.aamc.org/download/484068/data/reforming-animalresearchregulationsworkshoprecommendationstoredu.pdf>
 - Establish a Research Policy Board (§2034(f))

21st Century Cures Act Implementation

Research Policy Board

- Tasked with making recommendations for modifying and harmonizing policies and regulations across research funding agencies to minimize administrative burden.
- Activities could include analyzing existing policies for possible improvements, creating a forum for discussion of regulatory gaps and overlaps, and assessing regulatory burden through the development of metrics
- Statutory deadline: December 13th, 2017 - the anniversary of 21st Century Cures
 - Process for identifying non-federal members has not begun
- Members:
 - 10 Federal: the OIRA administrator from OMB, OSTP Director, HHS Secretary, NSF Director, and 6 other departments or agencies that fund or regulate research as chosen by OMB.
 - 9-12 Non-federal: “representatives of academic research institutions, other private, nonprofit research institutions, or other nonprofit organizations with relevant expertise.”

Further Questions and Discussion