Reflecting on the Revised Common Rule

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- 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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Agenda

- Regulatory background –the Common Rule
- Recent publication of final rule revising the Common Rule
  - Brief overview of new requirements and flexibilities
- Implementation considerations
- Harmonization considerations

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COMMON RULE REGULATORY BACKGROUND

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U.S. Federal Protection of Human Subjects regulations

- U.S. Federal Policy for the Protection of Human Subjects – "Common Rule" (1991)
  - Applies to 17 (will be 18) Federal Departments and Agencies
  - FDA has largely congruent IRB and informed consent regulations at 21 CFR parts 50 and 56
- Some Common Rule agencies have adopted additional regulatory protections or requirements
  - e.g., HHS human subjects regulations include Subparts B (pregnant women, fetuses and neonates), C (prisoners), D (children), E (IRB registration)

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Determining Applicability of Common Rule

- **Research involving human subjects conducted or supported by Common Rule department or agency**

- **Non-exempt human subject research covered by a Federalwide Assurance (FWA):**
  - Currently, if research institution voluntarily extends FWA to all research regardless of funding source, OHRP can extend jurisdiction to privately funded research
  - **Final Rule update**: Revised Common Rule preamble states plan to eliminate voluntary extension of FWA **– this has not happened yet! The "box" is still on the FWA and still can be checked.**

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Regulatory Protections

Three basic protections for human subjects:

- Institutional Assurances
  - Each institution engaged in human subject research must provide an assurance to the appropriate Dept/Agency that it will comply with the regulations
- Institutional Review Board (IRB) Review
  - Approval necessary prior to beginning human subjects research
- Informed Consent
  - Prior to involvement of human subjects in research
  - May be waived in certain circumstances

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Common Rule– Applicability

- Applies to research obtaining information or biospecimens through interaction or intervention with an individual
- Applies to secondary research use of identifiable private information or identifiable biospecimens obtained for purposes other than the research
- Not applicable to secondary research use of non-identified information or biospecimens
- Generally not applicable to research funded only by industry (unless also Federal support or if research site voluntarily applies requirements by "checking the box" on its FWA)

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Common Rule vs. FDA Regulations: 45 CFR part 46 vs. 21 CFR parts 50 and 56

- Basic requirements for IRBs and for informed consent are congruent
  - More so now that 21st Century Cures Act allows FDA to implement general waiver of informed consent
- Differences in applicability
  - Common Rule based on U.S. Federal Common Rule agency conducting or supporting human subjects research
  - FDA regulations based on use of FDA regulated product: drugs, devices, or biologics

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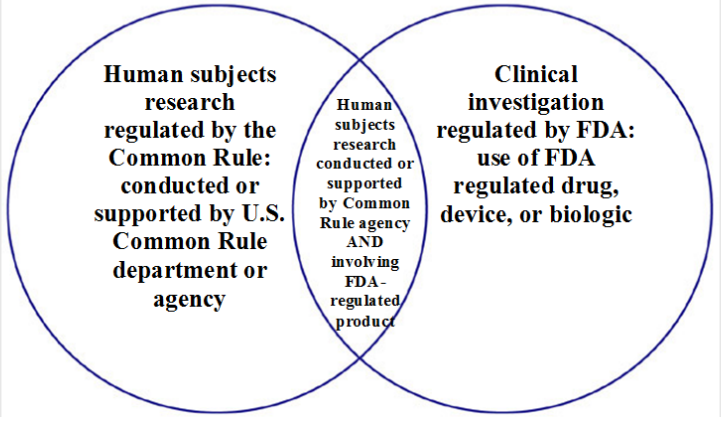
Jurisdiction: Common Rule vs. FDA

- An activity may be regulated under both the Common Rule and FDA informed consent and IRB regulations: e.g., a clinical trial conducted at the NIH Clinical Center that is comparing two FDA-regulated drugs



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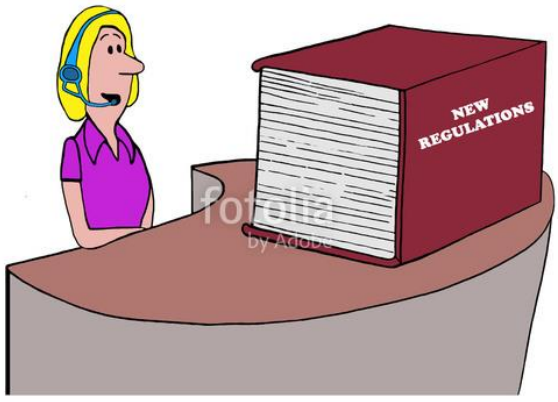

"Give me a couple years, and I can answer your simple question about the new regulations."

#134970409

THE REVISED COMMON RULE

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Why Revise the Common Rule?

- Changes in volume and landscape of research
- Revisit the appropriate protections for human subjects, while facilitating valuable research
- Consideration of how to better triage the level of regulatory protections to the risks of particular research activities
- Reduce burden, delay, and ambiguity for investigators
- Alleviate pressure on institutions' human subject protection programs by streamlining IRB review and reducing administrative burden

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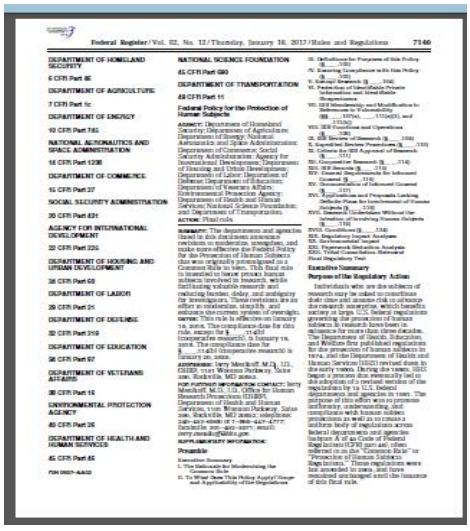
The revised Common Rule



- Published January 19, 2017
- Legally effective as of January 19, 2018
- **Compliance required as of January 21, 2019**
- **NOTE:** Research approved under old Common Rule can follow that version for the study's lifetime, unless voluntarily transitioned to follow the revised Rule

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STREAMLINING IRB OVERSIGHT

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IN EFFECT: New Jurisdiction Over Independent IRBs (.101(a))

- "Institutions that are engaged in research . . . **and institutional review boards (IRBs) reviewing research that is subject to this policy** must comply with this policy"
  - Provides Common Rule agencies authority to enforce compliance directly against IRBs not operated by FWA
  - Anticipated to reassure institutions using independent IRB because compliance actions can be directed against the IRB responsible for regulatory noncompliance, rather than against the relying institution

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COMPLIANCE NOT YET REQUIRED: New Mandated Single IRB Review: §.114(b)

- **On and after January 20, 2020:** U.S. institution engaged in cooperative research must rely on a single IRB approval for the portion of the research conducted in U.S.
  - Cooperative research = research involving more than 1 institution
- Two exceptions :
  - Research for which more than single IRB review required by law (including tribal law); **or**
  - Research for which Federal department or agency supporting or conducting the research determines and documents use of single IRB not appropriate for the particular context

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ALLOWABLE FLEXIBILITY: Changes to Continuing Review (.109(f)(1))

- *Unless IRB determines otherwise*, **continuing review of research is not required in the following circumstances**:
  - Research eligible for expedited review;
  - Research progressed to the point that it involves only:
    - Data analysis, including analysis of identifiable private information or identifiable biospecimens *OR*
    - Accessing follow-up clinical data from procedures subjects would undergo as part of clinical care

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Changes to Expedited Review (.110)

- **No change in concept of expedited review procedure**
  - Performed by IRB Chair or experienced IRB member designated by Chair
  - Reviewers have all authorities of IRB except disapproval of research
- **Retains expedited review list**: list of categories of research that may be reviewed through expedited review procedure, published by Secretary of HHS
  - Prior rule: research has to be included in category on list *and* reviewer had to determine involved no more than minimal risk;
  - Revised rule: research has to be included in category on list, *unless* reviewer determines involved more than minimal risk

  IMPLEMENTATION CONSIDERATION: expedited review list has not been revised

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Related changes to IRB recordkeeping (.115)

- Must document rationale for conducting continuing review when not otherwise required
- Must document rationale for expedited reviewer's determination that research on expedited review list is more than minimal risk
- Must document, for cooperative research, responsibilities an institution and an organization operating external IRB each will undertake to ensure compliance
  - IMPLEMENTATION CONSIDERATION: assignment of liability

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REVISED INFORMED CONSENT REQUIREMENTS

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COMPLIANCE REQUIRED: Revisions to Study-Specific Informed Consent: §.116

- Begin with key information most likely to assist subject in understanding why or why not to participate; organized and presented to facilitate comprehension
- Overall, present information in sufficient detail, organization, and presentation to facilitate understanding of why or why not participate
- Must include either statement:
  - Identifiers might be removed from IPI or identifiable biospecimens and stripped information or biospecimens could be used for future research studies or given to another investigator for future research studies without additional informed consent; **OR**
  - Subject's information or biospecimens collected as part of the research, even if identifiers are removed, will not be used or distributed for future research studies

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COMPLIANCE REQUIRED: Revisions to Study-Specific Informed Consent: Additional Disclosures

When appropriate, informed consent must include the following statements:

- The subject's biospecimens (even if identifiers are removed) may be used for commercial profit and whether the subject will or will not share in this commercial profit
- Whether clinically relevant research results will be disclosed to subjects, and if so, under what conditions
- For research involving biospecimens, whether the research will (if known) or might include whole genome sequencing

IMPLEMENTATION CONSIDERATION: Guidance on "key information"

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ALLOWABLE FLEXIBILITY: New Allowance for Broad Informed Consent: §.116(d)

- New regulatory allowance for broad consent for storage, maintenance, and secondary research use of identifiable private information or identifiable biospecimens
  - Not study specific, but not "brief" either: 10-12 required elements discussing the unspecified future research use
- A regulatory flexibility, not an independent requirement
- Alternatives to broad consent include:
  - Study specific informed consent
  - Waiver of informed consent

IMPLEMENTATION CONSIDERATION: tracking refusals of broad consent

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COMPLIANCE REQUIRED: Required Posting of Clinical Trial Consent Forms (.116(h))

- Posting of clinical trial consent forms
  - For each clinical trial conducted or supported by Common Rule department or agency, 1 IRB-approved consent form used to enroll subjects must be posted on publicly available federal website
  - Timeline of posting: after clinical trial closed to recruitment and no later than 60 days after last study visit by any subject
  - Federal department/agency may permit/require redactions

IMPLEMENTATION CONSIDERATION: posting window

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IMPACT OF THE REVISED COMMON RULE -- HARMONIZATION

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Harmonization Considerations

What will happen to FDA informed consent and IRB regulations (generally and under the 21st Century Cures Act)?

Preamble to revised Common Rule states:

"Finally, it is important to note that, to the extent appropriate, the intent is to …**consider the need for updates to FDA regulations** and other relevant federal departmental or agency regulations with overlapping scope."

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Spring 2019 Unified Agenda (June 2019): FDA entries

- Harmonize, to the extent practicable and consistent with other statutory provisions, certain provisions of FDA IRB and informed consent regulations with revised Common Rule (NPRM anticipated 9/19)

- Codify waiver of informed consent for minimal risk clinical investigations, harmonized with the Common Rule waiver provision (NPRM published 11/18, final rule anticipated 4/20)
  - Does not include new 5th criterion (if research uses IPI or identifiable biospecimens, could not practicably be carried out without identifiers), public comment sought

- Proposal to require sIRB review of multisite research conducted in the U.S., with exceptions, and establishes IRB recordkeeping requirements when reviewing IRB is not the institutional IRB (NPRM anticipated 8/19)

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Is this the end…?

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