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C10:Compliance Considerations Introduced by the Revised Federal Policy for the Protection of Human Subjects (Common Rule)

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Objectives

- Review the major changes included in the new rule
- Identify areas in IRB Operations & Administration that have been impacted that Internal Auditors should be aware of
- Describe the key research compliance risk areas that internal auditors or others responsible for compliance assurance should focus on when conducting reviews

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History of the Rule Development

- Revisions to Common Rule were initiated in 2011 with an ANPRM
- September 2015 NPRM was released
  - Generated large public response
  - Rule felt to be incomplete and confusing
  - Included provisions thought to have a negative impact on research
- **Final rule: Published January 19, 2017**
  - Planned Effective Date: January 19, 2018
  - Final Effective/Compliance Date: January 21, 2019
    - Select provisions of the revised rule could be used in advance but required a study fully transition to be compliant with the revised rule post effective date
  - Exception: Single IRB review requirement for cooperative research- Compliance Date: January 20, 2020

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Goals of the Revised Common Rule

- Identify opportunities to reduce regulatory burden on investigators
- Change requirements for minimal risk research to allow IRBs to focus on research posing greater risk
- Update the rule to reflect advances in science

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Key Changes outlined in the New Final Rule
Expansion of the definition of research to exclude certain types of activities [e.g. public health surveillance]
Expansion of research activities that qualify for exemption
Introduces concept of "limited IRB review" with certain exempt categories
Eliminates requirements for continuing review in certain cases
Eliminates requirement for grant vs. protocol review by the IRB [Institution must address]
Requires posting of consent forms for clinical trials
Changes to required formatting of consent to require that "key information" be listed first
New required/optional elements of consent
Adds a new required element for consent waivers [when research involves identifiable data or biospecimens]
Allows for new broad consent option but the IRB may not grant a waiver if a participant says "no"

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Changes to the definition of human subjects research

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Revision to the Definition of "Human Subjects Research"

- IRBs have oversight for projects that qualify as human subjects research
- The definition of human subjects research has always had 2 components- The definition of a human subject & the definition of research
- Under the new rule, the definition of research remains unchanged. It is: "*A systematic investigation, including research development, testing, and evaluation, designed to develop or contribute to generalizable knowledge.*"
- The definition of a human subject HAS been revised

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Revised Definition of Human Subjects

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

~~(1) Data through intervention or interaction with the individual,~~

(i) Obtains information or biospecimens through intervention or interaction with the individual, and uses, studies, or analyzes the information or biospecimens; or

~~or (2) Identifiable private information.~~

(ii) Obtains, uses, studies, analyzes, or generates identifiable private information or identifiable biospecimens.

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New Terms

Identifiable private information is private information for which the identity of the subject is or may readily be ascertained by the investigator or associated with the information.

An **identifiable biospecimen** is a biospecimen for which the identity of the subject is or may readily be ascertained by the investigator or associated with the biospecimen.

Definitions must be examined within 1 year and every 4 years after that- A bit of a moving target!

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Activities that do not meet the definition of Human Subjects Research

Clarified the list of activities that are specifically deemed not to be research. *Think about ACTIVITIES, not DISCIPLINES*. The Common Rule does not exclude whole academic fields.

"…the following activities are deemed not to be research:"*

(1) Scholarly and journalistic activities

(2) Public health surveillance activities

(3) Collection and analysis of information, biospecimens, or records by or for a criminal justice agency

(4) Authorized operational activities in support of homeland security, defense other national security missions

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Compliance Considerations

- Organizations must be aware of and adapt policies to reflect the changing concept of identifiability
- Where previously determinations of "Not Human Subjects Research" may have been more streamlined, now a more robust assessment may be required
- Investigators may be unaware when their project becomes human subjects research

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Changes to the Categories of Exemption & the Introduction of Limited IRB Review

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What does "EXEMPTION" mean?

- "Exempt Categories" identify different types of research thought to pose low risk to participants
- IRB's make an "exempt determination" by evaluating whether the proposed research falls into one of the categories defined in the regulations
- Consequence: Research is "exempt" from other Common Rule regulatory requirements including ongoing oversight
- Exempt research should still meet general ethical principles
  - Ethical recruitment and consent processes
  - Voluntary participation of target population
  - Personal privacy and data confidentiality protections

**Just because a project is EXEMPT from the Common Rule regulatory requirements does NOT mean it is Exempt from HIPAA requirements

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Key Changes to Exemptions under the New Rule

- Increases Exemptions from 6 Categories to 8;
  - Surveys, interviews etc. that may include sensitive information
  - Review of data/biospecimens, including those with protected health information
  - Certain behavioral interventions if these interventions are not thought to pose a risk of harm [Benign Behavioral Interventions]
- Introduces the requirement for "Limited IRB Review"
  - "Limited IRB Review" requires verification of adequate provisions to protect privacy and data confidentiality – no specific criteria are provided for assessment
  - "Limited IRB Review" must be completed by an IRB member

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Compliance Considerations

- More projects will now qualify for exemption and will not be subject to ongoing oversight by the IRB
- Organizations still need to be knowledgeable about the research activities that are active at their organization
- Application of the new exempt categories is challenging especially in the absence of concrete guidance

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Changes to the Requirements for Continuing Review

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Changes to the Requirements for Continuing Review

Continuing Review is not required by regulation for;

- Exempt research that requires limited IRB review
- Research eligible for expedited review (defined by regulations);
- Research that has progressed to the point that it involves only one or both of the following:
  - (A) Data analysis, including analysis of identifiable private information or identifiable biospecimens, or
  - (B) Accessing follow-up clinical data from procedures that subjects would undergo as part of clinical care.

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Compliance Considerations

Organizations maintain a broader responsibility to oversee human subjects research, ensure it is conducted properly and ensure risks to subjects continue to be minimized even if continuing review is not required by law.

- An IRB may require a continuing review [If not required by regulation, the IRB must document the reason why it has elected to require continuing review]
- An organization may also require a different type of check-in [e.g. an institutional progress report] or increase its monitoring or auditing to compensate for reduced IRB oversight

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Changes to the Requirements for Informed Consent and Consent Waivers

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New Required Element for Consent Waivers

Requirements for waiver and alteration. *In order for an IRB to waive or alter consent the IRB must find and document that:*

(i) The research involves no more than minimal risk to the subjects;

(ii) The research could not practicably be carried out without the requested waiver or alteration;

(iii) If the research involves using identifiable private information or identifiable biospecimens, the research could not practicably be carried out without using such information or biospecimens in an identifiable format;

(iv) The waiver or alteration will not adversely affect the rights and welfare of the subjects; and

(v) Whenever appropriate, the subjects or legally authorized representatives will be provided with additional pertinent information after participation.

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New Required Consent Elements: Research with Identifiable Data or Biospecimens

(i) A statement that identifiers might be removed from the identifiable private information or identifiable biospecimens and that, after such removal, the information or biospecimens could be used for future research studies or distributed to another investigator for future research studies without additional informed consent from the subject or the legally authorized representative, if this might be a possibility;

OR

(ii) A statement that the 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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New Optional Consent Elements

- A statement that 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;
- A statement regarding whether clinically relevant research results, including individual research results, will be disclosed to subjects, and if so, under what conditions; and
- For research involving biospecimens, whether the research will (if known) or might include whole genome sequencing (i.e., sequencing of a human germline or somatic specimen with the intent to generate the genome or exome sequence of that specimen)

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"Key Information"

- Informed consent* must begin with a concise and focused presentation of the key information that is **most likely to assist a prospective subject or legally authorized representative in understanding the reasons why one might or might not want to participate in the research.**
- Must be organized and presented in a way that does not merely provide lists of isolated facts
- Adopts new standard of what a reasonable person wants to know
- Limited early OHRP guidance suggests this is to be an "Executive Summary" not a copy and paste of information presented in other sections.

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Broad Consent

- New type of consent introduced that allows organizations to obtain broad consent up front for the storage, maintenance, and secondary research use of identifiable private information or identifiable biospecimens (collected for either research studies other than the proposed research or nonresearch purposes)
- This is an alternative to traditional consent
- If broad consent is used, the IRB may not approve a subsequent consent waiver to allow use of data/biospecimens for individuals who say "no"
- Tracking requirements thought to be prohibitive

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Compliance Considerations

- Very little guidance exists about the section on "key information"
- While organizations may wish to take one approach and update consent templates to comply with the revised common rule, these changes are not required for FDA-regulated research
- Industry partners may push back

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Posting of Clinical Trial Consent Forms

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Posting of Consent Forms for Federally-Funded Clinical Trials

Requirement: An informed consent form used to enroll subjects must be posted on a publicly available website.

Goal: Increase transparency for federally-funded clinical trials and simultaneously create a repository of sample consent forms that may be used as a reference for future research.

What studies are subject to this new requirement?

The requirement applies to all federally-funded clinical trials including social, behavioral or educational (SBER) research studies that meet the definition of a clinical trial.

A clinical trial is defined as a research study in which one or more human subjects are prospectively assigned to one or more interventions (which may include placebo or other control) to evaluate the effects of the interventions on biomedical or behavioral health-related outcomes.

Who is responsible for posting?

Adherence to the posting requirement is the responsibility of the awardee. For multi-site research, generally the prime awardee is considered the responsible party and must ensure compliance with the posting requirement.

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Posting of Consent Forms for Federally-Funded Clinical Trials

Where must the consent form be posted?

The consent form must be posted on a publicly available website approved for such posting. On 8/28/2018, the Office of Human Research Protections issued guidance that two publicly available federal websites have been identified that will satisfy the consent form posting requirement. These include:

- ClinicalTrials.gov
- A docket folder on Regulations.gov (Docket ID: HHS-OPHS-2018-0021).

When must the posting occur?

The informed consent form must be posted on the Federal Web site after the clinical trial is closed to recruitment, and no later than 60 days after the last study visit by any subject, as required by the protocol.

Which consent version must be posted?

The Revised Common Rule requires that the version of the consent document that is posted must a) be IRB-approved and b) have been used to enroll a participant in the clinical trial. The version of the consent that should be posted is the most recent IRB-approved version that was used to enroll a participant.

Can any information be redacted from the consent form prior to posting?

Any requests to redact certain information prior to posting must be submitted to the Federal department or agency supporting the clinical trial. Only the Federal agency supporting the clinical trial may permit or require redactions to the information posted.

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Compliance Considerations

- Organizational responsibility to post
- Tracking the exact time frame for posting and ensuring this occurs may be challenging

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Requirement for single IRB [sIRB] review of cooperative research

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NIH policy: Use of a single IRB for multi-site research

June 21, 2016: New policy requires single IRB (sIRB) review for **multi-site NIH-funded research**

Effective Date: January 25, 2018

What types of studies does this policy apply to?

- NIH-funded **multi-site studies** that involve non-exempt research
  - **Multi-site Studies**: The same protocol is being conducted at more than one site and the study is being funded wholly or in part by NIH
- New applications or competitive renewals submitted on or after the effective date

https://grants.nih.gov/grants/guide/notice-files/NOT-OD-16-094.html

Exceptions:

- Does not apply to Exempt research
- International sites [Policy applies to Domestic Sites only]
- Does not apply to studies conducted under career development, research training or fellowship awards
- Exceptions to this policy will be made where sIRB review would be prohibited by a federal, tribal, or state law, regulation, or policy.
- Requests for exceptions that are not based on a legal, regulatory, or policy requirement may be considered by NIH
  - Compelling justification required

sIRB is the selected IRB of record that conducts the ethical review for participating sites of the multi-site study.

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Additional Regulatory Requirements for sIRB Review under the Revised Common Rule

❖The Revised Common Rule extends the Single IRB review requirement to all "cooperative research" [Research involving one or more institutions]

❖Required compliance date for this provision: **January 20, 2020**

All research funded by any *federal agency that is a signatory to the Common Rule must comply

* Federal agencies that are signed onto the Common Rule: https://www.hhs.gov/ohrp/regulations-and-policy/regulations/common-rule/index.html

Under the 21st Century Cures Act the FDA is required to harmonize its applicable regulations for human subjects protections to align with Common Rule changes to the extent possible by December 2019. [May include requirements for sIRB review].

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Transitioning Studies/Request to OHRP

- Current OHRP interpretation is that this requirement applies to:
  - All studies that have "active" federal funding as of January 20th 2020
  - This would mean studies that were reviewed under a local IRB model would need to transition to a single IRB model by January 20, 2020.
- AAMC/COGR pushed back requesting OHRP re-consider as transitioning studies to a sIRB model would be nearly impossible.
  - No funding to support this
  - Not clear who would serve as the reviewing IRB
  - No response to date

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Single IRB Review ≠ Single Institutional Review

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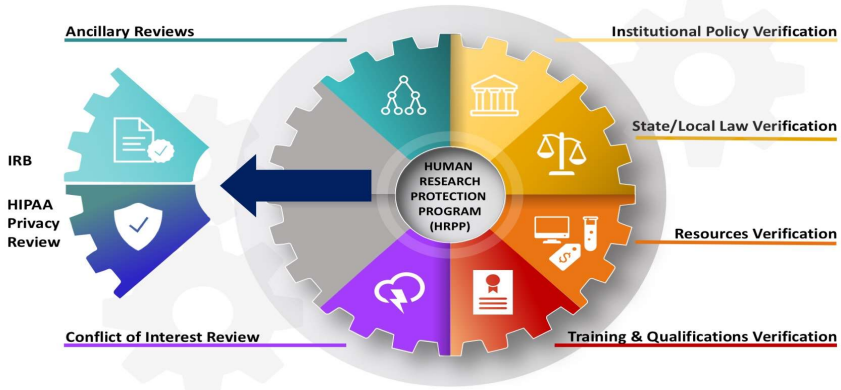
Which Components is the Reviewing IRB responsible for?



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What is a Relying Organization's Responsibility?

Each Relying Institution will… Communicate to the Reviewing IRB the requirements of any applicable state or local laws, regulations, institutional policies, standards, or other local factors, including local ancillary reviews, ***relevant to the Research*** *("Local Considerations") that would affect the conduct or approval of the Research at the Relying Institution. Such communication may be made through the Reviewing IRB's designee, as determined by the Participating Institutions* ***in connection with the specific Research***. [SMART IRB Agreement]

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What types of things do relying sites remain responsible for?

- **Education/Training/Qualifications**. Ensuring that its Research Personnel have adequate education, training, and qualifications to perform the research and safeguard the rights and welfare of participants. This includes ensuring personnel are credentialed to perform the research procedures.
- **Compliance**: Ensuring research personnel comply with determinations of the reviewing IRB and all applicable laws/institutional requirements
- **Institutional Reviews**: Ensuring all applicable institutional reviews required for the research to be conducted at that site are performed [e.g. radiation safety review, COI review, etc.]
- **Perform local context review**: Communicate to the reviewing IRB the requirements of any local laws, ancillary reviews, etc. and provide any required site-specific information for the consent form, where applicable.

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Compliance Considerations

- Disjointed process
- Loss of organizational "gatekeeper" in the IRB
- Other organizations may be evaluating your investigator noncompliance
- New responsibilities as a reviewing IRB in providing oversight for external entities
- sIRB review fees may be charged to federal grants as direct costs- need to carefully set up fee structures

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Additional Compliance Considerations

- Transition of older studies to the new rule is permitted
  - Must be careful to follow transition instructions
- Many organizations now have to operate with 2 versions of the Common Rule & distinct FDA regulations + organizational carve-outs for non-federally funded research [if applicable]
- FDA has not yet harmonized with the Revised Common Rule
  - 21st Century Cures Act requires the FDA to harmonize to the extent possible by Dec 2019
  - More change forthcoming!
- Investigator/IRB Member/IRB staff education
- IRB Staff Burn-Out/Turnover

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Questions/Discussion

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