THE COMMON RULE IMPACT ON CLINICAL RESEARCH
Clinical Research Professionals Appreciation and Education Day

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Objectives

- Discuss some but not all changes to the 2018 Common Rule (Title 45 CFR part 46)
- Identify key “Action Items” for Clinical Research Professionals
- Help ensure regulatory compliance
NYS Public Health Article 24A – Protection of Human Subjects

- Some human research MUST be approved by the NYS Commissioner of Health, unless it is subject to and in compliance with federal regulations:
  - Minors
  - Incompetent persons
  - Mentally disabled persons
  - Prisoners
- Most NY Institutions voluntarily apply the Common Rule to ALL research.

Review updated IRB policies as soon as they are available.

Find out if your IRB applies the Common Rule to ALL research or just to federally funded research.

<table>
<thead>
<tr>
<th>IRB Approval Date:</th>
<th>Compliance Dates &amp; Transitioning Provisions §101</th>
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<tbody>
<tr>
<td>Anytime</td>
<td>IRB can adopt more stringent standards provided they are compatible with the Common Rule. (e.g., some or all of the new informed consent or waiver requirements)</td>
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<tr>
<td>7/19/18</td>
<td>3 burden-reducing provisions can be applied; however, the research must be 100% compliant on 1/21/19:</td>
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<td></td>
<td>1) Revised definition of “research,”</td>
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<td>2) Eliminate continuing review of some minimal risk research, &amp;</td>
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<td>3) Elimination of IRB review of grant congruency.</td>
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<tr>
<td>Before 1/21/19</td>
<td>Pre-2018 (2016) Common Rule applies. Note: Studies are grandfathered, if the 2018 Common Rule is not applied later.</td>
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<tr>
<td>1/21/19</td>
<td>2018 Common Rule applies. Note: IRB May transition prior studies.</td>
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<tr>
<td>1/20/20</td>
<td>Single IRB review for federally funded multi-site studies (Cooperative Research). Note: NIH funded multi-center studies require sIRB after 1/25/18.</td>
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**Compliance Dates and Transitioning Provisions §.101**

- Review revised IRB policies.
- Determine if IRB requires more stringent standards before 1/21/19 (e.g., informed consent and/or waiver requirements)
- If beneficial, collaborate with IRB to transition previously approved research to the 2018 Common Rule.
- If the IRB applies the 3-burden reducing provisions to your study, during 6 month transition, ensure the research is in compliance with **ALL** provisions by 1/21/19.
- Confirm with your institution that grant congruency is not required.

**Human Subject Clarified to Include Biospecimens §.102 (e)(1)(i-ii)**

- Biospecimens obtained through an intervention or interaction
- Identifiable biospecimens

Consult with IRB to determine if IRB approval is required.
Clinical Trial Informed Consent Posting Requirement §.102(b) & §.116 (h)

- **Clinical trial** means 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.

Post one IRB-approved informed consent on a Federal Website, no later than 60 days after last study visit:
- ClinicalTrials.gov
- Docket folder on Regulations.gov (Docket ID: HHS-OPHS-2018-0021)

**Note:** FDA and NIH have different definitions for Clinical Trials.

New Exemption Categories §.104

- **Restricted:** Exemption #1
- **Expanded:** Exemption #2, #4, & #5
- **New:** Exemption #3, #7 & #8
- **Unchanged:** Exemption #6 (FDA exemption).
- **Limited IRB review** is a condition of some activities under Exemption 2,3,7&8: (§__.104(d)(2)(iii), (d)(3)(i)(C), (d)(7), and (d)(8)).

Understand applicability of exemption categories and the IRB review process for such research.
### Continuing Review is Not Required in Certain Circumstances §.109(f)(1)

- Research eligible for expedited review, unless IRB justifies why continuing review would enhance protections.
- Research undergoing limited IRB review.
- Research that has progressed and is now limited to:
  - Data analysis (including identifiers) and/or,
  - Access to clinical data from clinical care.

**NOTE:** Annual review is still required for FDA-regulated research.

### Continuing Review is Not Required in Certain Circumstances §.109(f)(1)

- Follow your IRB’s policy regarding frequency of continuing review.
- Ensure annual review is conducted for grandfathered research approved under the Pre-2018 Common Rule.
- Follow your policies for conflict of interest disclosures and training requirements, as they may no longer be a part of the IRB’s continuing review process.
General Requirements of Informed Consent §.116 (a)(4-5)

- Provide information that a reasonable person would want to have in order to make an informed decision...
- …begin with a concise and focused presentation of key information … to assist… in understanding the reasons why one might or might not want to participate
- …present information in sufficient detail… organized and presented in a way… that facilitates… understanding the reasons why one might or might not want to participate

Basic Elements of Informed Consent §.116 (b)(9)(i-ii)

- If collecting identifiable private information or identifiable biospecimens, include either:
  - A statement that identifiers might be removed…for future research …without additional informed consent…; or
  - A statement that the information or biospecimens … will not be used … for future research …
Additional Elements of Informed Consent §.116 (c)(7-9)

- Three new disclosures, when applicable:
  - Whether biospecimens will be used for commercial profit and whether participants will share profits,
  - Whether and under what conditions clinically relevant research results will be provided, and/or
  - Whether research will (if known) or might include whole genome sequencing.

Screening, Recruitment, & Determining Eligibility §.116(g)

- An IRB may approve a research proposal in which an investigator will obtain information or biospecimens for the purpose of screening, recruiting, or determining the eligibility of prospective subjects without the informed consent of the prospective subject or the subject’s legally authorized representative, if either of the following conditions are met:
  - The investigator will obtain information through oral or written communication with the prospective subject or legally authorized representative, or
  - The investigator will obtain identifiable private information or identifiable biospecimens by accessing records or stored identifiable biospecimens.

Obtain IRB approval for the process of screening, recruitment and determining eligibility without informed consent.
**Documentation of Informed Consent Using Short Form §.117(b)(2)**

- A short form written informed consent form stating that the elements of informed consent required by §__.116 have been presented orally to the subject or the subject’s legally authorized representative, and that the key information required by §__.116(a)(5)(i) was presented first to the subject, before other information, if any, was provided.

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**Action Items Regarding Informed Consent**

- Ensure the informed consent process and the consent forms are compliant with the 2018 Common Rule
- Be prepared to discuss new requirements with Sponsors
- Stay tuned for future changes in the FDA regulations, which under the 21st Century Cures Act must be harmonized with the Common Rule, to the extent practicable.
Summary

- Review and understand new IRB requirements for your institution
- Follow IRB instructions and guidance
- Take necessary actions to ensure compliance

Questions
The following slides are provided for independent review…

Key Historical Events Regarding the Common Rule

1972-2016
- Tuskegee Syphilis Study Exposé
- National Research Act ('74)
- The Belmont Report ('79)
- Original Common Rule ('81)
- Last Revised CR ('16)

2011–2015
- Multiple notices and extensions for comments on proposed changes to the Common Rule
  - 1st notice 7/26/11; last notice for extension through 1/6/16.

2017
- Final Common Rule is published 1/19/17.
- Most provisions were to become effective 1/19/18; however, White House freezes all Obama-era regulations on 1/20/17.

2018
- White House announces 1-year delay with possibility for 3 burden reducing provisions
- 6 month delay in general compliance date.
  - Allows for 3 burden-reducing provisions during the delay, starting 7/19/18.
- Most provisions of the 2018 Common Rule go into effect on 1/21/19.
  - sIRB provisions go into effect 1/19/20.
Legally Authorized Representative (LAR or Surrogate): §.102(i)

- Legally authorized representative means an individual or judicial or other body authorized under applicable law to consent on behalf of a prospective subject to the subject’s participation in the procedure(s) involved in the research. If there is no applicable law addressing this issue, legally authorized representative means an individual recognized by institutional policy as acceptable for providing consent in the nonresearch context on behalf of the prospective subject to the subject’s participation in the procedure(s) involved in the research.

- Consult with your IRB for local policy.

Certain Activities Are Not Research: §.102(l)(1-4)

- Scholarly and journalistic activities… that focus directly on the specific individuals about whom the information is collected.
- Public health surveillance activities…
- … criminal justice… activities authorized… for criminal investigative purposes
- Authorized operational activities…
- Consult with IRB to determine if IRB approval is required.
New Exemption Categories
§.104

- Exemptions can be applied to research with pregnant women, fetuses, neonates, and research to involve a broader population that only incidentally includes prisoners and to research with Children, except as noted below:
  - Exemption 2 [(d)(2)(i) and (ii)] only may apply to research with Children involving educational tests or the observation of public behavior when the investigator(s) do not participate in the activities being observed.
  - Exemption 2 [(d)(2)(iii)] may not be applied to research with Children. (e.g., when identifiers are recorded).
  - Exemption 3.

New Exemption Categories
§.104

- **Restricted:** Exemption #1: Added “not likely to adversely impact student’s opportunity to learn required educational content or assessment of educator who provides instructions.
  - Some previously approved research would now not qualify
- **Expanded:**
  - Exemption #2: Research participants can be identified
  - Exemption #4: Research can be prospective
  - Exemption #5: Project must be published on a federal website
New Exemption Categories §.104

- **New:**
  - Exemption 3: Some benign behavioral interventions.
  - Exemption 7: Storage and maintenance of identifiable data/specimens.
  - Exemption 8: Secondary research for which broad consent is required.
- **Unchanged:** Exemption #6 (FDA exemption).
- Limited IRB review is a condition of some activities under Exemption 2,3,7&8: (§__.104(d)(2)(iii), (d)(3)(i)(C), (d)(7), and (d)(8)).

New Exemption for Benign Behavioral Interventions §.104 (d)(3)(ii)

- …benign behavioral interventions are brief in duration, harmless, painless, not physically invasive, not likely to have a significant adverse lasting impact on the subjects, and the investigator has no reason to think the subjects will find the interventions offensive or embarrassing.
- …examples…include…online game…solve puzzles under various noise conditions…how to allocate a nominal amount of received cash between themselves and someone else
Action Items Regarding: Changes in Exemption Categories

- Consult with IRB to determine applicability of exemptions and whether vulnerable populations can be included.
- Check with IRB to see if there is a new application form.
- Follow your IRB’s Limited IRB review process for research that qualifies for Exemptions 2, 3, 7, & 8.
- Determine if some research previously approved under expedited review is now exempt.

Expedited Review: §.110(a)

- … HHS… will evaluate the list (of expedited review categories) at least every 8 years and amend it, as appropriate…
- Stay tuned for future changes in the list of expedited review categories
Provisions for Broad Consent

§.116(d)(1-7)

- Broad consent may be obtained in lieu of informed consent only with respect to storage, maintenance, and secondary uses of identifiable private information and identifiable biospecimens.
- New Exemption categories #7 & #8, use a Broad Consent process.

Questions:
- Will your institution implement a Broad Consent process?
- Does your IRB have a template available for Broad Consent?
- How will your institution track Broad Consent?
- What does it meant to decline Broad Consent?
- Understand that the IRB can not apply other waivers, when Broad Consent is declined.

New Criterion for General Waiver of Informed Consent §.116(f)(3)(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”

- Ensure waivers satisfy the 5 criteria for approval under the 2018 Common Rule, including research that will transition from the 2016 Common Rule.
References (Links)

- NYS Article 24A
- FDA Guidance: Impact of Revised Common Rule on Clinical Investigations
- OHRP Unofficial Revised Common Rule Regulatory Text
- OHRP Official Version of the 2018 Rule
- OHRP DRAFT Guidance for 2018 Common Rule
- OHRP Videos
- PRIM&R Focus on the Common Rule
- SACHRP Recommendations

About The Presenter

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- Prior to Downstate, Kevin was the Director of Human Research Protections at Maimonides Medical Center. He served in the federal government in various positions, such as the U.S. Veterans Affairs, Office of Research & Development, Program for Research Integrity Development and Education (VA Central IRB), the U.S. Department of Health and Human Services, Office for Human Research Protections (OHRP), and the National Cancer Institute, Laboratory of Pathology.
- Certified IRB Professional (CIP) by the Council for Certification of IRB Professionals (CCIP)
- Certified Medical Technologist (MT), by the American Society of Clinical Pathologists (ASCP).
- Master of Science in Applied Management, from the University of Maryland, University College
- Bachelor of Science in Medical Technology from the University of Texas Health Science Center at San Antonio.
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