Changes to the Common Rule

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Introduction:

NOTE:

Relative to the Common Rule changes, this presentation does not address requirements for FDA regulated research or other specific HIPAA requirements

Seminar Topics:

- General Discussion of the New Common Rule
- IRBMED implementation and minimizing the impact on researchers
    - Transition period amendments
    - Consent changes/updates
    - Changes to categories for exempt research
    - Informed consent process and documents
    - Scheduled Continuing Review (SCR) Requirements
    - Reporting Requirements
    - Guidance
- FDA Harmonization with the New Common Rule
- Certificates of Confidentiality
- NIH sIRB Requirement
- These changes are NOT currently in effect (except transitions period amendments)

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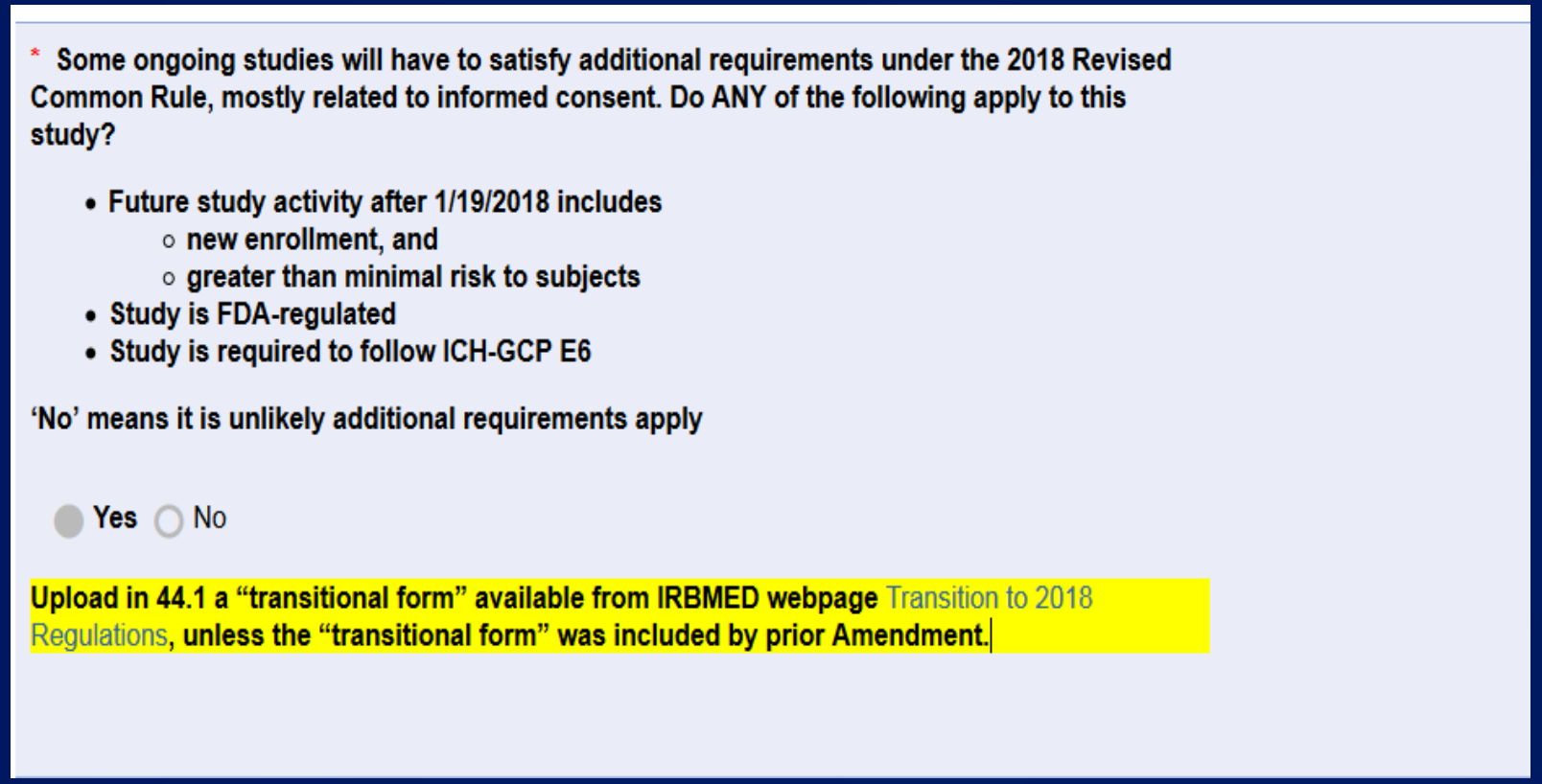
Important Dates and Unknowns

- Current effective/compliance date is **January 19, 2018**
- On October 7, OHRP submitted a request to OIRA (Office of Information and Regulatory Affairs) to delay the general implementation date for one year but permit implementation of three "burden-reducing provisions"
- This is a proposed rule and would require a comment period

New Amendment Cover Sheet:



* Some ongoing studies will have to satisfy additional requirements under the 2018 Revised Common Rule, mostly related to informed consent. Do ANY of the following apply to this study?

- Future study activity after 1/19/2018 includes
  - new enrollment, and
  - greater than minimal risk to subjects
- Study is FDA-regulated
- Study is required to follow ICH-GCP E6

'No' means it is unlikely additional requirements apply

(•) Yes ( ) No

Upload in 44.1 a "transitional form" available from IRBMED webpage Transition to 2018 Regulations, unless the "transitional form" was included by prior Amendment.

https://research.medicine.umich.edu/office-research/institutional-review-boards-irbmed/guidance/transition-2018-regulations

New Consent Requirements:

- Developing cover page to meet new requirements
- This will be added to existing consents
- Minimize additional work
- No need for re-consent of existing subjects
- Any additional changes may require full update
- Awaiting updated NCI template
- A new IRBMED consent template will be forthcoming

Consent:
Key Information

‘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.

This part of the informed consent must be organized and presented in a way that facilitates comprehension.

§ __.116(5)(i)

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Consent:
Document

"Informed consent as a whole must present information in sufficient detail relating to the research, and must be organized and presented in a way that does not merely provide lists of isolated facts, but rather facilitates the prospective subject's or legally authorized representative's understanding of the reasons why one might or might not want to participate."

§ __.116(5)(il)

Supplemental Consent Cover Page: Example

You may be eligible to take part in a research study. Taking part in this study is *completely voluntary*.

This form contains information that will help you decide whether to take part. All of this information is important, but here are some especially important points to keep in mind:

- It is totally up to you whether to take part in this study.
  - Even if you decide to join the study, you are free to leave at any time if you change your mind.
- This is research; medical scientists do research to learn about diseases and how to treat them.
  - Research is different from regular medical care, which has already been tested in research.
- [Continue this bulleted list with other key points for potential subjects to consider, such as study purpose, risks, benefits, and alternatives to participation.]

- *Optional components*
  - [If your research includes an optional sub-study, briefly summarize here.]
  - [If your research involves optional broad consent to storage, future use, and/or sharing of specimens and/or data, briefly summarize here.

Please take time to read this entire form (or have it read to you). After you have finished, you should talk to us about the study and ask us any questions you have. You may also wish to talk to others (for example, your friends, family, or other doctors) about your participation in this study.

If you decide to take part in the study, you will be asked to sign this form. Before you sign this form, be sure you understand what the study is about.

Consent:
Broad Consent

Broad Consent allows participants to agree to researchers' using their identifiable private information or identifiable biospecimens (collected for other research studies or other purposes such as clinical care) for future, yet-to-be specified research studies.

Broad consent will be an optional alternative that an investigator may choose instead of:

1. obtaining consent for a specific study or
2. having an institutional review board (IRB) waive the requirement for informed consent, or
3. conducting the research on non-identified information and non-identified biospecimens

Consent:
Broad Consent Interpreted

- Participant responses will need to be tracked by the study team
  - Difficult procedurally
  - If declined when sought in the context of an individual study, does it apply to all opportunities - forever?
  - How often can a participant be re-approached?

- If broad consent is declined by the participant, it can't be waived by the IRB

Broad Consent:

⚠ At this time, the U-M HRPP and IRBs will not mandate nor implement the institutional use of Broad Consent, as the tracking requirements may be burdensome.

- Exemption categories 7 and 8, which rely on Broad Consent, will not be available
- U-M will continue to support study teams seeking subject permission for the collection and storage of identifiable private information/biospecimens for future secondary use research through the following processes:
  - Study-specific consent and comprehensive IRB review
  - IRB waiver of consent (as eligible) and comprehensive IRB review
  - Exemption #4
  - De-identification to remove the research activity from Common Rule purview and not require IRB review or consent

Note: For studies designed to collect identifiable data and/or biospecimens **solely** for the purpose of maintaining a repository, the study team may find it useful to employ a specialty informed consent template (e.g., biorepository template).

Consent for Screening, Recruiting and Determining Eligibility

- Under the new rule, information or biospecimens can be obtained without individual's consent for the purposes of screening, recruiting or determining eligibility, provided certain conditions are met:
    - Information will be obtained by communicating with prospective subject or LAR, OR
    - The information or biospecimens will be obtained by accessing records or stored biospecimens
- This is not a waiver of the consent requirement but rather an exception to the requirement.
- "Wavier of Consent" in eResearch will not need to be requested for these activities in the scope of the main project
- HIPAA Requirements will still apply!

eResearch Update: Q# 10.1

10.1* **What type of informed consent will be obtained from adults or minors legally able to consent to treatments or procedures involved in the research?**

With signature:

- ☐ Comprehensive written
- ☐ Written assent for cognitively or decisionally impaired adults

Without signature (waiver of documentation):

- ☐ Comprehensive written
- ☐ Comprehensive oral consent script
- ☐ Assent for cognitively or decisionally impaired adults

Waivers of informed consent:

- ☐ Request for waiver of informed consent/parental permission/legally authorized representative consent (Note: no longer required for screening/recruitment)
- ☐ Request for waiver of assent for cognitively or decisionally impaired adults

Other:

- ☐ Short form, comprehensive oral script, and witness
- ☐ Request for alteration of informed consent requirements
- ☐ Pre-existing consent(s) covers this activity
- ☐ Re-consent/assent subjects for use of existing data/records/specimens for a new research purpose

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eResearch Update: Q# 10.2

10.2* **What types of informed assent for children and parental consent/permission will be obtained?**
NOTE "Parent" or "Parental" below refers to parent or guardian. See Help **for important instructions on selecting the appropriate category or categories.**

Children
With signature:

- [ ] Written document

Without signature(waiver of documentation):

- [ ] Written document
- [ ] Oral assent script

Waiver of assent:

- [ ] Request for waiver of informed assent

Other:

- [ ] Pre-existing assent covers this activity

Parents
With signature:

- [ ] Comprehensive written

Without signature (waiver of documentation):

- [ ] Comprehensive written
- [ ] Comprehensive oral consent/permission script

Waiver of parental consent/permission:

- [ ] Request for waiver of parental consent/permission (Note: no longer required for screening/recruitment)

Other:

- [ ] Short form permission, comprehensive oral script, and witness
- [ ] Request to use substitute mechanism for parental permission where research is designed for conditions or for a subject population for which parental or guardian permission is not a reasonable requirement to protect the subjects
- [ ] Request for IRB to appoint an advocate for children who are wards of the state or any other agency, institution or entity –required for studies related to the children's status as wards that are approved under 46.406 or 46.407 (see section 33)
- [ ] Pre-existing consent/permission covers this activity

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Consent:
Posting Consents

- Consent must be posted on a "publicly available Federal Web site"
- Applies only to federally-conducted or supported clinical trials

Consent:
Posting Consents

- Only one IRB-approved version used to enroll subjects is required
  - Even if multiple exist, multisite study, or different subject groups
- Posting can take place any time after recruitment closes but no later than 60 days after the last study visit by any subject
- Federal department or agencies may permit/require redactions to the posted information
  - e.g. confidential commercial information
  - could determine that the very existence of a particular clinical trial should not be publicly disclosed, in which case no posting would be required (rare)

Consent:
Posting Consents - Issues

- The Federal web site has not been announced
  - Many think Clinicaltrials.gov is the likely choice
- Which consent should be posted?
  - Should it harmonize with clinical protocol posted on Clinicaltrials.gov?
- Remembering to post the document

Exemptions:
Introductions

- Revision to 4 of the 6 current categories
- Retention of 1 current category with no change
- Deletion of 1 current category

- Addition of 3 new categories

- Two review standards for exempt research
  - Exempt determination
  - “Limited IRB Review” for privacy and confidentiality of sensitive data

Exemption One: Education

Research, conducted in established or commonly accepted educational settings, **that specifically involves** normal educational **practices that are not likely to adversely impact students' opportunity to learn required educational content or the assessment of educators who provide instruction.** This includes most research on regular or special education instructional strategies, and research on the effectiveness of or the comparison among instructional techniques, curricula, or classroom management methods.

Exemption One: Education

The additional text clarifies that to be exempt, the study is:

“not likely to adversely impact student’s opportunity to learn required educational content or the assessment of educators who provide instruction.”

Exemption Two:
Surveys, Interviews, Observation

Research **that only includes interactions involving** educational tests (cognitive, diagnostic, aptitude, achievement), survey procedures, interview procedures, or observation of public behavior **(including visual or auditory recording) if at least one of the following criteria are met:**

- The information obtained is recorded **by the investigator** in such a manner that the identity of human subjects **cannot readily be ascertained,** directly or through identifiers linked to the subjects;

Exemption Two: Surveys, Interviews, Observation

- Any disclosure of the human subjects' responses outside the research **would not** reasonably place the subjects at risk of criminal or civil liability or be damaging to the subjects' financial standing, employability, educational advancement, or reputation; **or**

- **The information is recorded by the investigator in such a manner that the identity of the human subjects can be readily ascertained, directly or through identifiers linked to the subjects, and an IRB conducts a limited IRB review to make the determination required by §46.111(a)(7).**

NOTE: Research involving children is not exempt under the last bullet.

Exemption Two:
Surveys, Interviews, Observation

- Language updated to be in the affirmative
- Addition of “Limited IRB Review”

“When appropriate, there are adequate provisions to protect the privacy of subjects and to maintain the confidentiality of data.”

Exemption Two:
Surveys, Interviews, Observation

The current Exemption Three has been deleted:

> Research involving the use of educational tests (cognitive, diagnostic, aptitude, achievement), survey procedures, interview procedures, or observation of public behavior that is not exempt under paragraph (b)(2) of this section, if:
> (i) the human subjects are elected or appointed public officials or candidates for public office; or (ii) federal statute(s) require(s) without exception that the confidentiality of the personally identifiable information will be maintained throughout the research and thereafter.

Exemption Three:
Benign Behavioral Interventions

Research involving benign behavioral interventions in conjunction with the collection of information from an adult subject through verbal or written responses (including data entry) or audiovisual recording if the subject prospectively agrees to the intervention and information collection and at least one of following criteria is met:

- The information obtained is recorded by the investigator in such a manner that the identity of the human subjects cannot readily be ascertained, directly or through identifiers linked to the subjects;

Exemption Three:
Benign Behavioral Interventions

- Any disclosure of human subjects' responses outside the research would not reasonably place the subjects at risk of criminal or civil liability or be damaging to the subject's financial standing, employability, educational advancement, or reputation; or

- The information obtained is recorded by the investigator in such a manner that the identity of the human subjects can be readily ascertained, directly or through Identifiers linked to the subjects, and an IRB conducts a limited IRB review to make the determination required by §46.111(a)(7).

Exemption Three:
Benign Behavioral Interventions

For the purpose of this provision, 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.

NOTE: Waiting on guidance for definition of “brief”

Exemption Three:
Benign Behavioral Interventions

Examples:

- Playing an online game
- Having them solve puzzles under various noise conditions
- Having them decide how to allocate a nominal amount of received cash between themselves and someone else.

Exemption Three:
Benign Behavioral Interventions

If the research involves deceiving the subjects regarding the nature or purposes of the research, this exemption is not applicable unless the subject authorizes the deception through a prospective agreement to participate in research in circumstances in which the subject is informed that he or she will be unaware of or misled regarding the nature or purposes of the research.

This is similar to the UM Flexibility Initiative: Exemption 2A

https://research.medicine.umich.edu/sites/default/files/res_irbmed_SP.FlexibilityInitiative.Exemption2A.2015.05.01_0.pdf

Exemption Four:
Secondary Use of Identifiable Data

Previous/current Exemption Four:

Research involving the collection or study of **existing** data, documents, records, pathological specimens, or diagnostic specimens, if these sources are publicly available or if the information is recorded by the investigator in such a manner that subjects cannot be identified, directly or through identifiers linked to the subjects.

Exemption Four:
Secondary Use of Identifiable Data

Secondary research for which consent if not required: Secondary research uses of identifiable private information or identifiable specimens, if at least one of the following criteria is met:

- The identifiable private information or identifiable biospecimens are publicly available;
- Information, which may include information about biospecimens, is recorded by the investigator in such a manner that the identity of human subjects cannot readily be ascertained directly, or through identifiers linked to subjects, the investigator does not contact subjects, and the investigator will not re-identify subjects;

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Exemption Four: Secondary Use of Identifiable Data

- The 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 [HIPAA]; or,

- The research is conducted by, or on behalf of, a Federal department or agency or using government-generated or government-collected information obtained for nonresearch activities.

Exemption Four:
Secondary Use of Identifiable Data

The revised Exemption Four eliminates the requirement that the data exist at the time of the exempt determination; data may be collected prospectively.

New Exemption #4 - Secondary Use Research:

#4 - SECONDARY RESEARCH (IDENTIFIABLE PRIVATE INFORMATION/BIOSPECIMENS)

What's New: The scope of this exemption will be expanded to allow:

- Prospective data review
- Maintenance of identifiers, if **all** study data is protected health information (PHI)
- Research that is conducted by, or on behalf of, a Federal department/agency or using government-generated or government-collected information obtained for non-research activities

Review Path: An **IRB Determination** is required; however, if PHI is used then a **Privacy Board review** (HIPAA) is conducted with the IRB Determination.

Simplifying "Application Type" for Secondary Use

1-1.1* Select the appropriate application type:

	Application Type	Description
☐	Human Subjects research **involving interaction or intervention** *(formerly Standard, non-exempt research project - or - Exempt)*	Studies that involve either or both of the following: • Interaction, including communication or interpersonal contact between investigator and subject • Intervention, including both physical procedures by which information or biospecimens are gathered (e.g., venipuncture) and manipulations of the subject or subject's environment that are performed for research purposes Interaction/Intervention studies may also have a "secondary research" component.
☐	**Secondary research** uses of private information or biospecimens	**"Secondary research"** are studies that involve ONLY re-using private information and/or biospecimens that are collected for some other "primary" or "initial" activity, such as other earlier research studies, a biorepository holding specimens obtained with "broad consent," clinical care, educational records. **Do NOT use this application type for:** • Studies that **also** have an interaction/intervention component, such as primary collection of information or biospecimens for the purposes of the study. (Choose instead "Human subjects research involving **interaction or intervention**.") • Projects involving secondary use of information/biospecimens for **only non-research purposes**, such as QA/QI, case studies on one or two individuals, or use in a class to teach research methods. (Choose instead "Activities **not regulated** as human subjects research.")

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Exemption Five: Demonstration Projects

Research and demonstration projects which are conducted by or subject to the approval of department or agency heads, and which are designed to study, evaluate, or otherwise examine:

1. Public benefit or service programs;
2. Procedures for obtaining benefits or services under those programs;
3. Possible changes in or alternatives to those programs or procedures; or,
4. Possible changes in methods or levels of payment for benefits or services under those programs.

New requirement for agency to maintain public list of such projects and to publish the list before project is conducted.

Exemption Six:
Taste and Food Quality

Taste and food quality evaluation and consumer acceptance studies:

- If wholesome foods without additives are consumed, or

- If a food is consumed that contains a food ingredient at or below the level and for a use found to be safe, or agricultural chemical or environmental contaminant at or below the level found to be safe, by the Food and Drug Administration or approved by the Environmental Protection Agency or the Food Safety and Inspection Service of the U.S. Department of Agriculture

No change.

(Exemption Seven:
Storage and Maintenance of Identifiable Information or Biospecimens)

Storage or maintenance for secondary research for which broad consent is required: Storage or maintenance of identifiable private information or identifiable biospecimens for potential secondary research use if an IRB conducts a limited IRB review and makes the determinations required by §46.111(a)(8).

(Exemption Eight: Secondary Research for Which Broad Consent is Required)

Secondary research for which broad consent is required: Research involving the use of identifiable private information or identifiable biospecimens for secondary research use, if the following criteria are met:

- Broad consent for the storage, maintenance, and secondary research use of the identifiable private information or identifiable biospecimens was obtained;
- Documentation of informed consent or waiver of documentation of consent was obtained;

(Exemption Eight: Secondary Research for Which Broad Consent is Required)

- An IRB conducts a limited IRB review and makes the determination required by §46.111(a)(7) and makes the determination that the research to be conducted is within the scope of the broad consent referenced in paragraph (d)(8)(i) of this section;
- The investigator does not include returning individual research results to subjects as part of the study plan. This provision does not prevent an investigator from abiding by any legal requirements to return individual research results.

Continuing Review:
New Terms

Continuing IRB review will not be required for:

- Research eligible for expedited review
- Research that progressed so that it only involves one or both of the following:

    1. Data analysis, including analysis of identifiable private information or identifiable biospecimens, or
    2. Access to follow-up clinical data from standard clinical care procedures

- Exempt research even if it received limited IRB review

No Continuing Review Requirements:

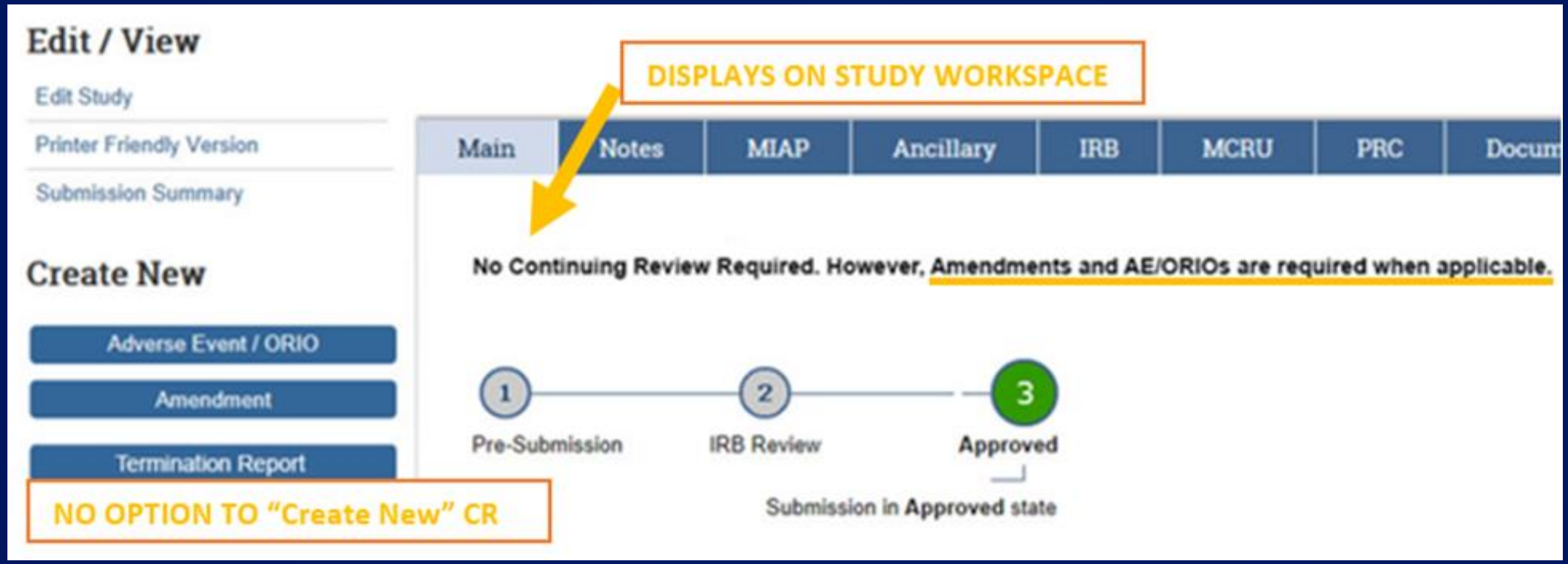
Even when continuing review is not required for a project, the study team must still:

- Submit amendments for project changes
- Report AEs/ORIOs
- Terminate the project once it ends, or when personal identifiers are removed from the data/biospecimens and all codes and keys are destroyed

- U-M will implement an automated annual email in eResearch
- The system email will be sent prior to the anniversary approval date for the study

U-M IRBs may re-evaluate its CR/No CR decision for a project depending on the type of change(s) proposed in an amendment (e.g., protocol change that increases subject risk), or as an outcome of the IRB's review of Adverse Events or ORIOs.

No Continuing Review Requirements:



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Single IRBs (sIRB):
Defining

…each institution is responsible for safeguarding the rights and welfare of human subjects and for complying with this policy.

- This is existing language but takes on new meaning

sIRB Requirements:
Federal

Use of a single IRB in multi-site research is now a requirement

- NIH sponsored
  - January 25, 2018
- Common Rule: federally sponsored
  - January 20, 2020

Single IRB:
Naming Conventions

Agreements

- IRB Authorization Agreements
- Reliance Agreements
- Cooperative Agreement
- IRB of Record Agreements
- Master Service Agreements
- “Smart IRB” National Agreement

IRBs

- Commercial
- Independent
- External
- Central

Single IRB:
How do they work?

- Collaborating institutions complete the agreement document
  - These are not signed by the PI or the IRB
- Roles and responsibilities are apportioned between IRBs and the institution
- Assure all internal institutional documents are in alignment with the arrangements
  - Standard Operating Procedures
- Does not require OHRP or FDA signature or approval

Single IRB:
Parameters

relying on a single IRB, only IRB regulatory oversight is ceded to the single IRB – many of the study team obligations remain in-house such as:

- All ancillary committee reviews
  - Research Pharmacy, Radiation Safety
- Conflict of Interest review and management plans
- Monitoring
- Maintaining compliance with educational requirements

Single IRB:
Intended Benefits

- Reduces duplicative review across sites
- Reduces variability of the study design across sites
- Decreases cumulative review time
- Decreases burdens on local IRBs
- Costs are reduced locally and for the study as a whole

Single IRB Requirement:
Common Rule

- Implementation date of January 20, 2020
  - Applies to all federally supported multi-site studies
  - This is not limited to clinical research

- Final rule seems to allow agencies or departments to exclude certain broad types of research from the requirement
  - No other information available

NIH Single IRB:
Requirement

***Implementation date of January 25, 2018

- Applies to all NIH sponsored multi-site studies
- This is not limited to clinical research
- Applies only to domestic research sites conducting the same protocol

- Not subject to the requirement
  - Requests for exceptions that are not based on a legal, regulatory, or policy requirement will be considered if there is a compelling justification for the exception. The NIH will determine whether to grant an exception following an assessment of the need.

Single IRB:
Challenges

- What do you know about the Reviewing IRB?
- Consideration of local context
- Apportionment of institutional liability
- Managing ‘shared’ control and accountability
- Developing/agreeing to different standardized procedures

FDA – New Guidance on Waivers of Consent

- Guidance issued July 2017
- Towards Common Rule Harmonization
- Guidance currently in effect

FDA does not intend to object to the initiation or conduct of certain minimal risk clinical investigations for which an IRB waives or alters the informed consent requirements in 21 CFR 50.25

FDA Waiver of Informed Consent Criteria:

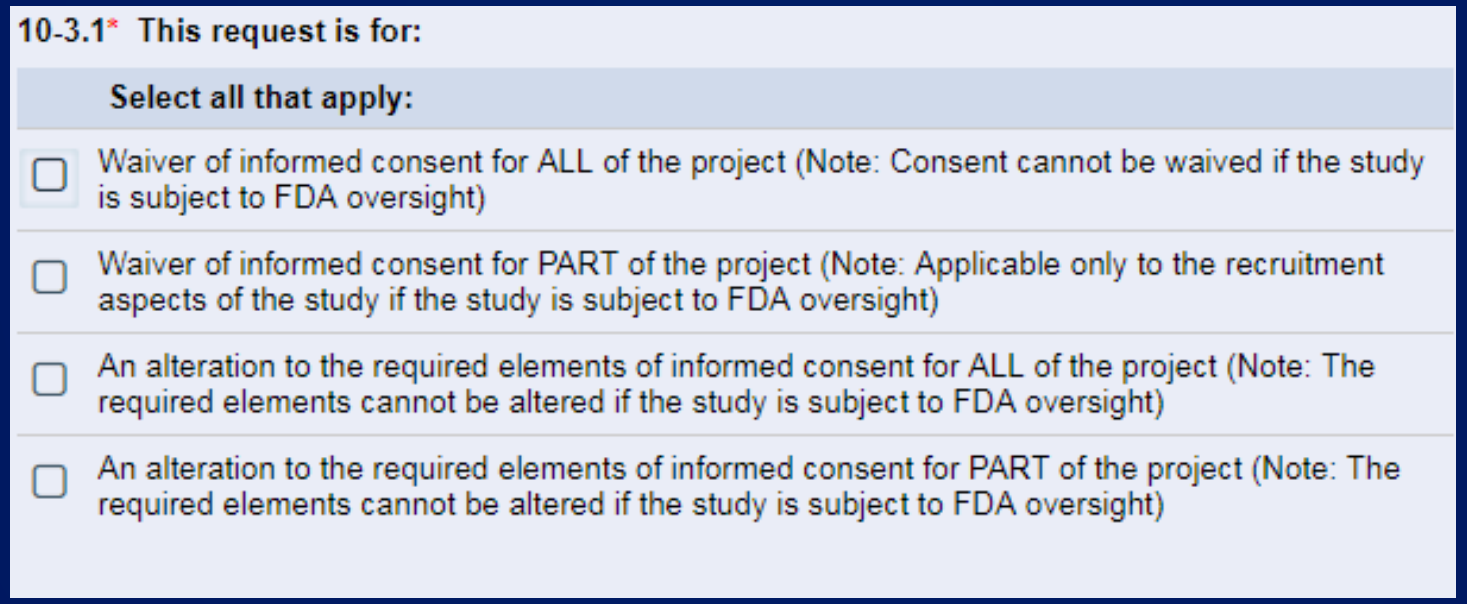
1. The clinical investigation involves no more than minimal risk (as defined in 21 CFR 50.3(k) or 56.102(i)) to the subjects

2. The waiver or alteration will not adversely affect the rights and welfare of the subjects

3. The clinical investigation could not practicably be carried out without the waiver or alteration

4. Whenever appropriate, the subjects will be provided with additional pertinent information after participation

Waiver of Informed Consent:
Current in eResearch



10-3.1* **This request is for:**

	Select all that apply:
☐	Waiver of informed consent for ALL of the project (Note: Consent cannot be waived if the study is subject to FDA oversight)
☐	Waiver of informed consent for PART of the project (Note: Applicable only to the recruitment aspects of the study if the study is subject to FDA oversight)
☐	An alteration to the required elements of informed consent for ALL of the project (Note: The required elements cannot be altered if the study is subject to FDA oversight)
☐	An alteration to the required elements of informed consent for PART of the project (Note: The required elements cannot be altered if the study is subject to FDA oversight)

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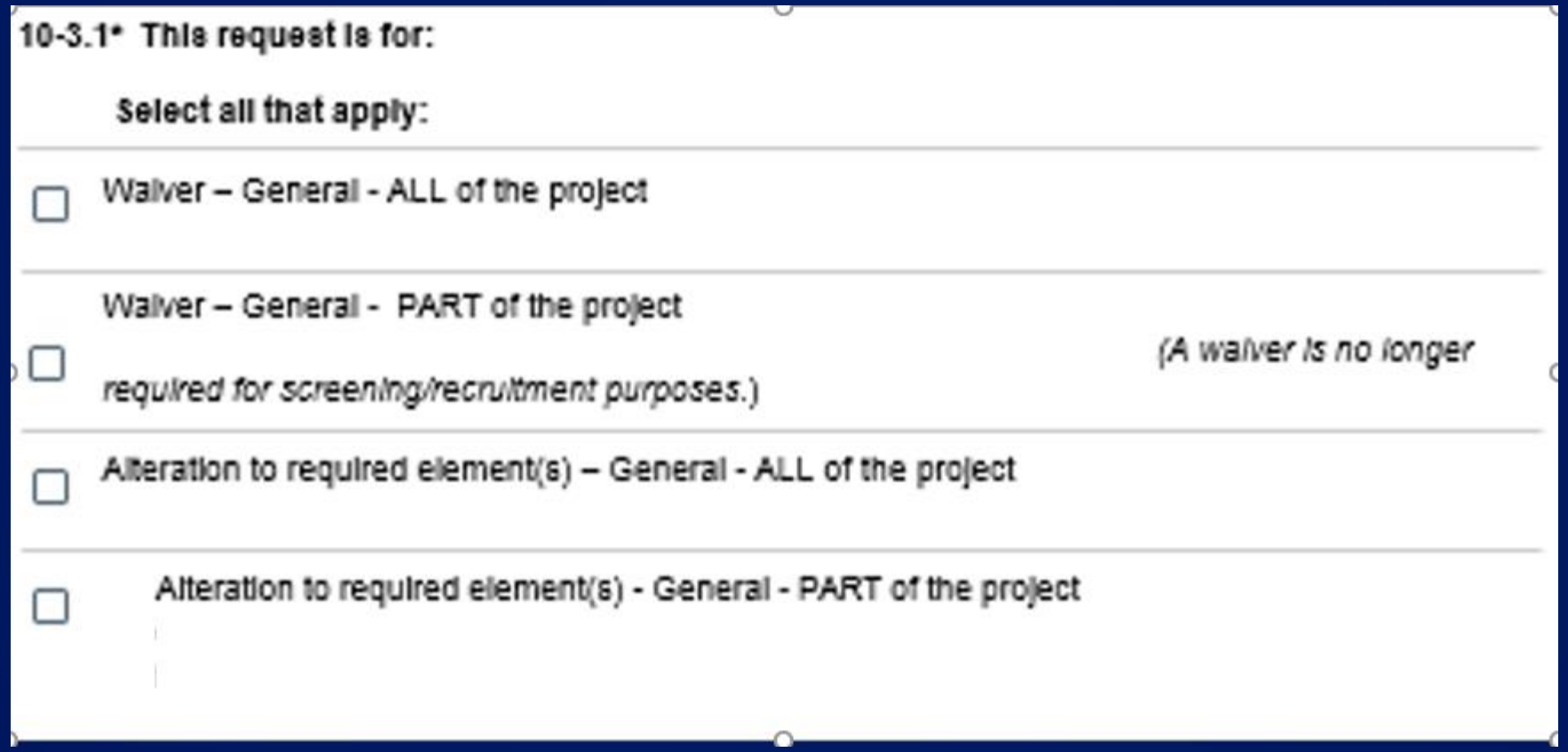
Waiver of Informed Consent:
Future State in eResearch



10-3.1* This request is for:

Select all that apply:

- ☐ Waiver – General - ALL of the project
- ☐ Waiver – General - PART of the project *(A waiver is no longer required for screening/recruitment purposes.)*
- ☐ Alteration to required element(s) – General - ALL of the project
- ☐ Alteration to required element(s) - General - PART of the project

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NIH Certificates of Confidentiality:

- Effective October 1, 2017, all human subjects research funded by NIH will be automatically be issued certificates of confidentiality as part of the terms and conditions of the award
- Applicable to research commenced or ongoing after December 13, 2016
- Part of the 21st Century Cures Act
- NIH will not provide a document, the award itself is confirmation
- The regular application process for certificates of confidentiality will be available for research that is not NIH funded

Common Rule :
Current Status

- (Anxiously) awaiting additional guidance and templates from federal government
- Relying on SACHRP for interpretive guidance

Resources:

- Common Rule
  - https://www.hhs.gov/ohrp/regulations-and-policy/regulations/finalized-revisions-common-rule/index.html
- University of Michigan web-site
  - http://research-compliance.umich.edu/human-subjects

Questions?