Chart Reviews: Exempt 4 vs. Expedited 5

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Office for Human Research Ethics
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THE UNIVERSITY
of NORTH CAROLINA
at CHAPEL HILL

Objectives

- Define exempt and expedited categories for when conducting medical chart reviews
- Provide guidance on level of review required
- Discuss waivers of consent and HIPAA justifications
- OHRE Updates/Next Steps

What is Human Subjects Research?

- **Research**: *a systematic investigation, including research development, testing, and evaluation, designed to develop or contribute to generalizable knowledge.*

- **Human Subjects**: *a living individual about whom an investigator (whether professional or student) conducting research:*

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

  *(ii) **Obtains, uses, studies, analyzes**, or generates identifiable private information or identifiable biospecimens. (*this includes accessing)*

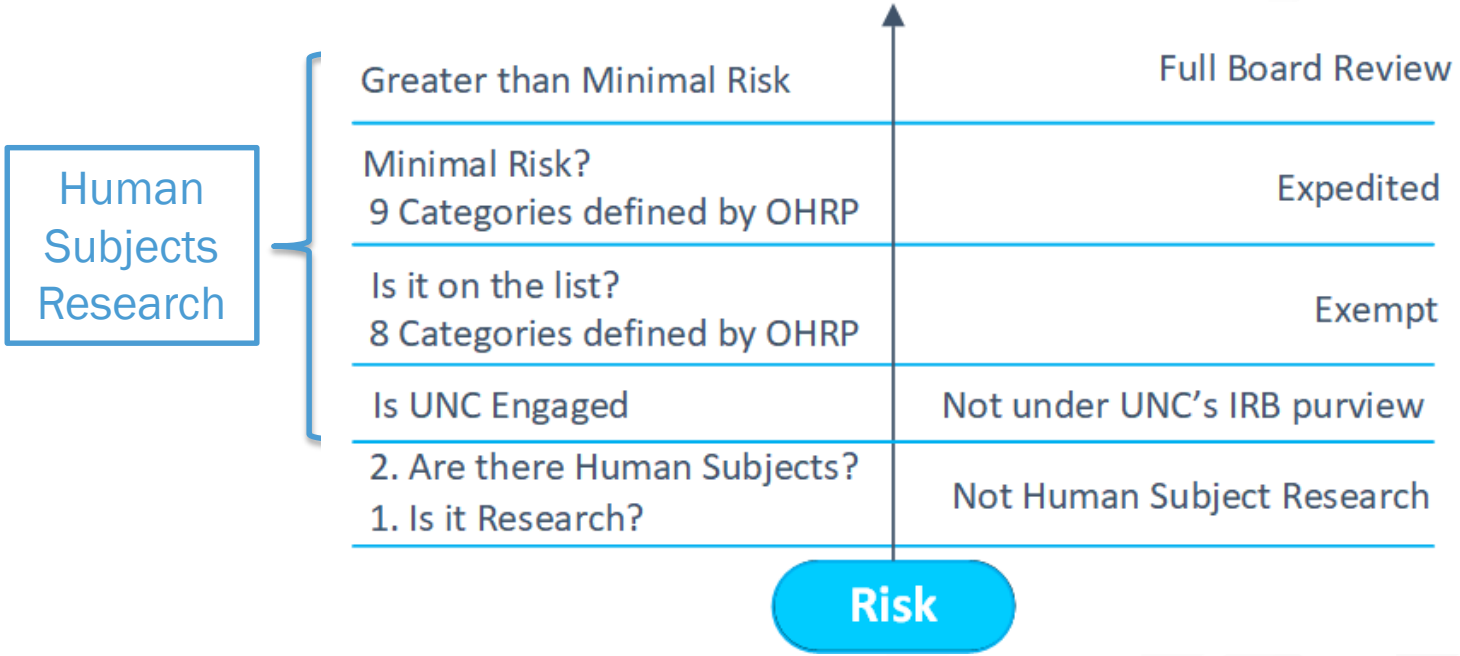
Medical Chart Reviews and HSR

Research: Use of medical charts may or may not be research depending on the aim.

E.g. quality assurance, case studies may not be research as the aim may not be to develop or contribute to generalizable knowledge.

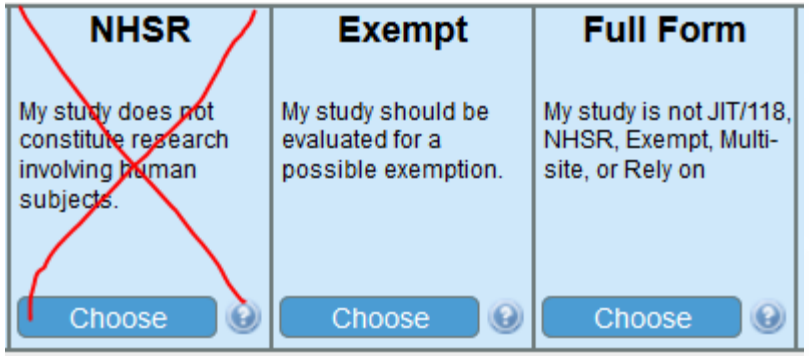
Human Subjects: Medical Charts contain private, identifiable information. Any accessing of medical records, means your project involves human subjects.

Levels of IRB Review



Medical Chart Reviews and HSR

Medical Chart reviews that are designed to develop or contribute to generalizable knowledge are human subjects research.



Exempt 4 and Expedited 5 Definitions

[See handout]

Exempt 4

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

(i) The identifiable private information or identifiable biospecimens are publicly available

(ii) Information, which may include information about biospecimens, 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, the investigator does not contact the subjects, and the investigator will not re-identify subjects;

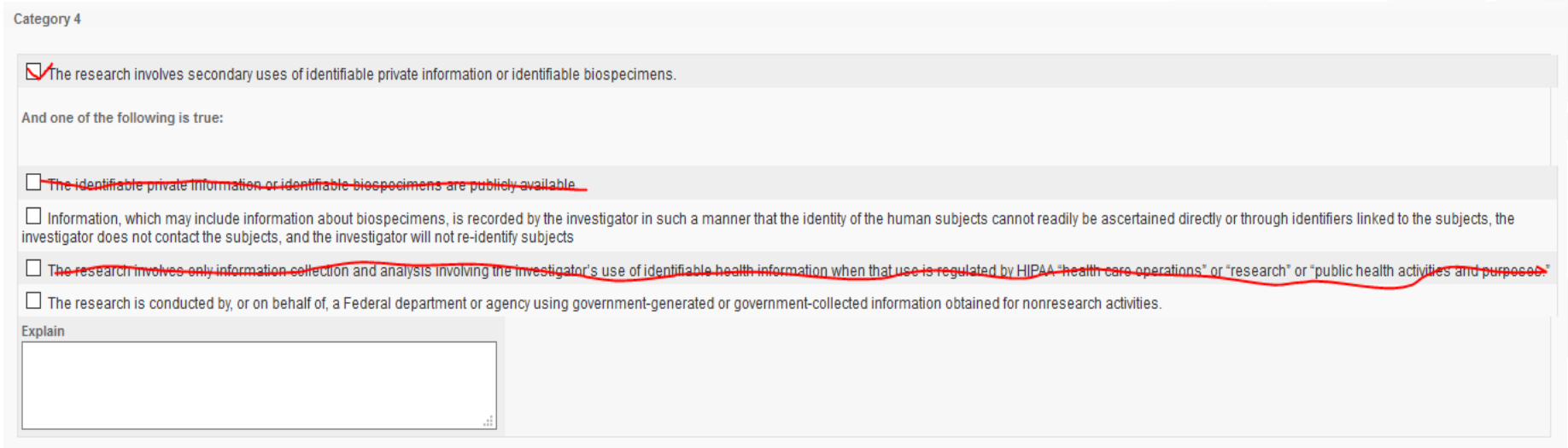
(iii) The research involves only information collection and analysis involving the investigator's use of identifiable health information when that use is regulated under 45 CFR parts 160 and 164, subparts A and E, for the purposes of “health care operations” or “research” as those terms are defined at 45 CFR 164.501 or for “public health activities and purposes” as described under 45 CFR 164.512(b); or

(iv) The research is conducted by, or on behalf of, a Federal department or agency using government-generated or government-collected information obtained for nonresearch activities, if the research generates identifiable private information that is or will be maintained on information technology that is subject to and in compliance with section 208(b) of the E-Government Act of 2002, 44 U.S.C. 3501 note, if all of the identifiable private information collected, used, or generated as part of the activity will be maintained in systems of records subject to the Privacy Act of 1974, 5 U.S.C. 552a, and, if applicable, the information used in the research was collected subject to the Paperwork Reduction Act of 1995, 44 U.S.C. 3501 et seq.

Expedited 5

Research involving materials (data, documents, records, or specimens) that have been collected, or will be collected solely for nonresearch purposes (such as medical treatment or diagnosis).

Exempt 4 – N/A to Chart Review Studies


Category 4

☑ The research involves secondary uses of identifiable private information or identifiable biospecimens.

And one of the following is true:

☐ ~~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 the human subjects cannot readily be ascertained directly or through identifiers linked to the subjects, the investigator does not contact the subjects, and the investigator will not re-identify subjects

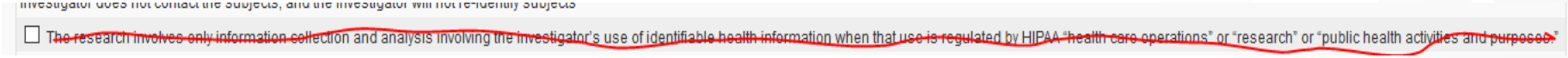
☐ ~~The research involves only information collection and analysis involving the investigator's use of identifiable health information when that use is regulated by HIPAA "health care operations" or "research" or "public health activities and purposes."~~

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

Explain

- (ii) The identifiable private information or identifiable biospecimens are publicly available
- (iii) 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, 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);

Exempt 4 – N/A to Chart Review Studies



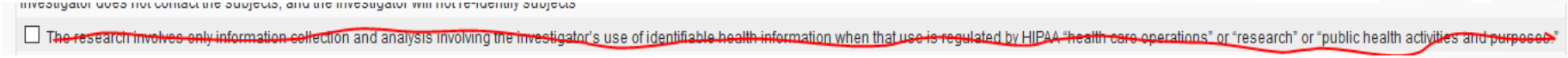
[1]Exemption 4(iii) is only applicable to information collection and analysis involving the investigator's use of identifiable health information when that use is regulated under 45 CFR parts 160 and 164.

Use and disclosure are not the same.

a. Use means, with respect to individually identifiable health information, the sharing, employment, application, utilization, examination, or analysis of such information within an entity that maintains such information.

b. Disclosure means the release, transfer, provision of access to, or divulging in any manner of information outside the entity holding the information.

Exempt 4 – N/A to Chart Review Studies



[1]Under exempt 4(iii), release, transfer, provision of access to, or divulging in any manner of information outside the entity holding the information would not be allowed.

That means no one outside of a covered entity could be on your study team or could conduct analysis on your behalf.

Due to complications and limitations stemming from UNC's hybrid status, 4(iii) will NOT be used at UNC-CH at this time.

HIPAA Identifiers

2 HIPAA Identifiers

- Name
- Address (all geographic subdivisions smaller than state, including street address, *city, *county, and *zip code)
- *All elements (except years) of dates related to an individual (including birthdate, admission date, discharge date, date of death, and exact age if over 89)
- Telephone numbers
- Fax number
- Email address
- Social Security Number
- Medical record number
- Health plan beneficiary number
- Account number
- Certificate or license number
- Any vehicle or other device serial number
- Web URL
- Internet Protocol (IP) Address
- Finger or voice print
- Photographic image - Photographic images are not limited to images of the face.
- Any other characteristic that could uniquely identify the individual

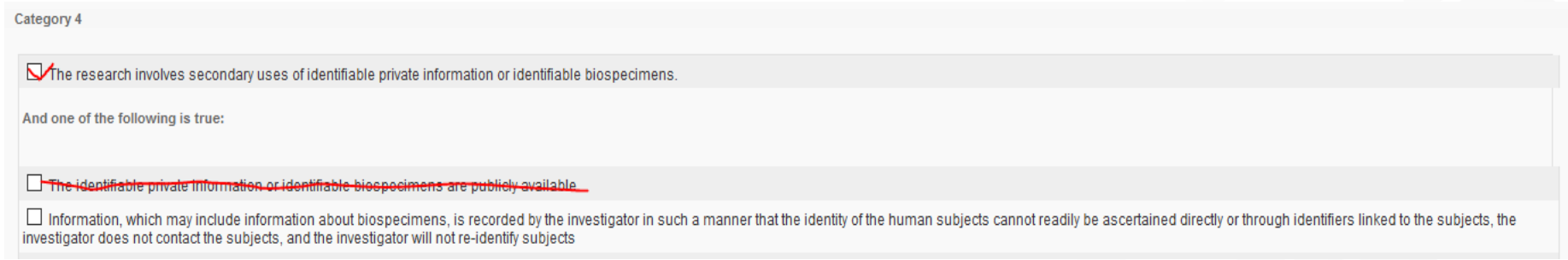
*Allowed under Limited Dataset: All elements of dates, city, county, state, ZIP code

These variables are also listed in A.9.1. of the IRBIS application

HIPAA Identifiers - Codes

- Any other characteristic that could uniquely identify the individual.
  - IDs created from other identifiable information.
    - E.g. S43mm – derived from last two of SSN and initials
  - IDs that are linked to other identifying information.
    - E.g. Dataset 1 includes: code (S1,S2, S3…), age, diagnosis, medications. Dataset 2 includes: S1 = MRN 1234, S2 = MRN 4567, etc.

Exempt 4(ii) – Most Commonly Used



Category 4

☑ The research involves secondary uses of identifiable private information or identifiable biospecimens.

And one of the following is true:

☐ ~~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 the human subjects cannot readily be ascertained directly or through identifiers linked to the subjects, the investigator does not contact the subjects, and the investigator will not re-identify subjects

- Can access medical records, see all IDs, but cannot abstract IDs
- Must create a research dataset with no IDs (or limited data set)
- May not interact with subjects
- May not attempt to re-identify
- Cannot retain link to IDs

Exempt 4(ii) – Example – No Identifiers

A researcher contracts the CDW-H to access medical records on their behalf.
An analyst at the CDW-H abstracts data from 500 patients and provides it to the investigator.
Data received by the investigator includes diagnosis, prescriptions, test results, age. Without any of the 18 identifiers, and no link to any identifying information, the investigator, nor anyone, should be able to match the data back to an individual.

No one on the investigative team has plans to contact patients (and couldn't) nor will they use this or any other data in combination to attempt to re-identify patients.

Exempt 4(ii) – Example – Limited Data Set

Indirect identifiers allowed under Limited Dataset: All elements of dates, city, county, state, ZIP code

A researcher contracts the CDW-H to access medical records on their behalf.
An analyst at the CDW-H abstracts data from 500 patients that includes *appointment dates*, *date of birth, zip code*, diagnosis, prescriptions, test results. With the limited indirect identifiers and no other link/code to any identifying information, it would be very difficult for the investigator, or anyone, to match the data back to an individual.

No one on the investigative team will contact patients nor will they use this or any other data in combination to attempt to re-identify patients.

Expedited 5 – Use of Identifiers

A researcher contracts the CDW-H to access medical records on their behalf.
An analyst at the CDW-H abstracts data from 500 patients that includes appointment dates, date of birth, zip code, diagnosis, prescriptions, test results, and a *randomly generated code*. The code created allows the investigator to match the data back to an individual so that they can later ask the CDW-H to pull future data on patients if those patients have any other follow-up visits.

Because the code is linked to identifiers, expedited 5 is required.

Expedited 5 – Use of Identifiers

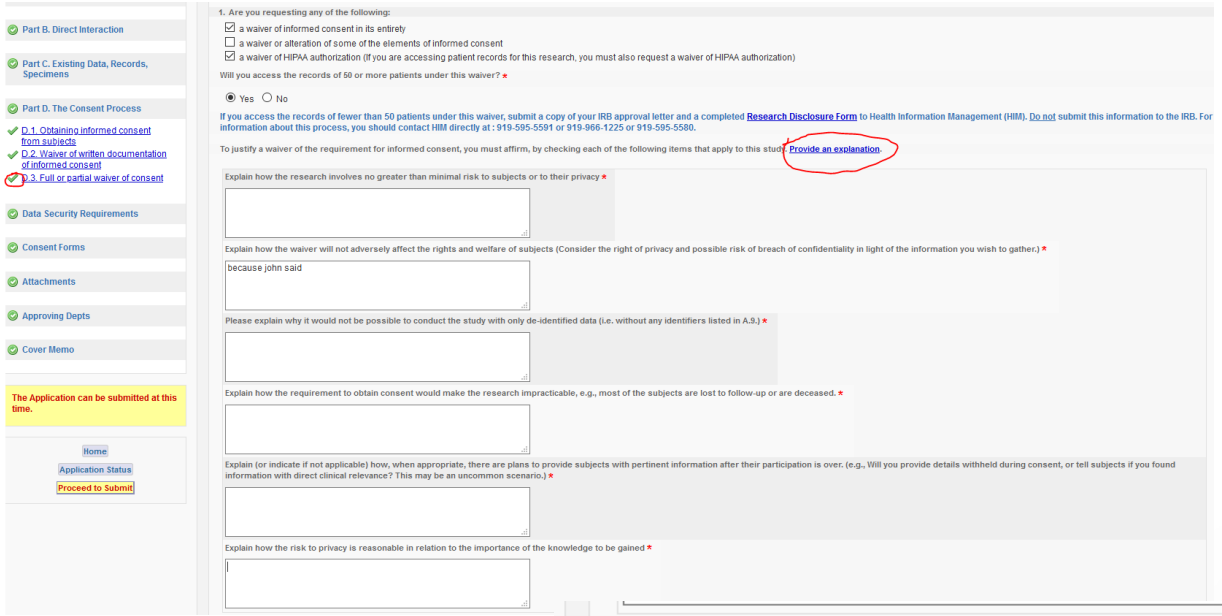
A researcher accesses medical records for research purposes.
The researcher abstracts medical record numbers (MRN), appointment dates, date of birth, zip code, diagnosis, prescriptions, and test results. MRN is recorded to avoid duplicate entries into the research dataset. Prior to data analysis, MRN is destroyed.

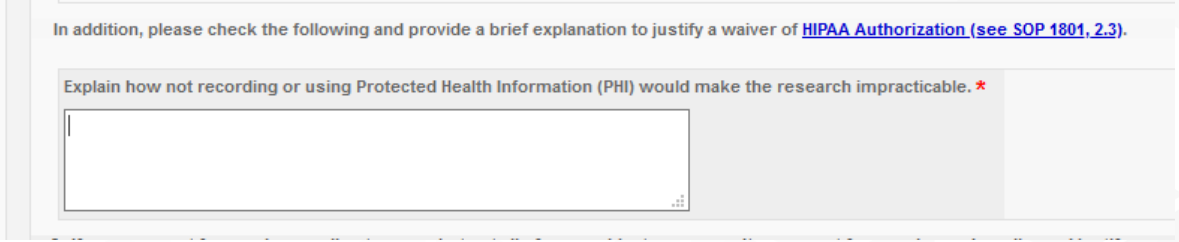
Even though the MRN was destroyed, it allowed for re-identification so expedited 5 is required.

[1]HIPAA Waivers

Review Category	HIPAA Waiver
Exempt 4(ii) - No PHI	Access of PHI may be approved without a HIPAA Authorization or waiver.
Exempt 4(ii) – Limited Dataset	Use of limited dataset PHI may be approved without a HIPAA Authorization or waiver. Requires a data use agreement.
Expedited 5	Must meet criteria for a full waiver of HIPAA Authorization or obtain HIPAA Authorization from patients/subjects

Expedited 5 – HIPAA Waiver Request – D.3.1.





Expedited 5 – HIPAA Waiver Guidance

https://research.unc.edu/files/2018/04/EXTERNAL-Waiver_of_Consent_Secondary_Data_Use_ver_4-19-18.pdf

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

a. Explain why the waiver will not adversely affect subjects' rights. Patients have a right to privacy regarding their medical records. The impact of the research on this right must be minimized to the extent possible. Minimizing the impact can be achieved through the use of an honest broker (such as the CDW) that extracts the data, or by placing clear limitations on individuals within the research team who will engage in data extraction from the medical records. The latter option requires the investigator making the request to clearly identify the steps and/or strategies that will be used to limit exposure of the patient's *entire* medical record during the data extraction process (for example, what training has the data extractor completed that will reduce the likelihood of unintended exposure of elements of the record that are not essential to the research? What methods will be used to record the data without creating and maintaining additional hard copies of PHI?).

b. Explain how the waiver will not adversely affect subjects' welfare. Regarding the concept of welfare, the investigator must consider several factors depending on the original source of the data.

   i. For medical record review: Consider the impact of record review on a patient's ongoing clinical care; in addition, consider the psychological, physical, social, economic, and legal implications of a breach that would result if the private information placed in the research record became known outside the research team. The waiver request should identify any specific data that is considered sensitive in nature and address specific concerns about a breach of confidentiality regarding those sensitive data.

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

Carefully consider the principle of Respect for Persons within the context of the proposed study. Is the study entirely retrospective or does it involve prospective data collection that might offer an opportunity to consent subjects and obtain HIPAA authorization? Describe the real (not presumed) barriers to obtaining consent, understanding that having limited financial resources to support the consent process does not justify the waiver. Answer the following questions:

a. Is contact information of potential subjects readily available?

b. Is the contact information likely reliable? Consider the age of the records and the likelihood that the contact information is outdated.

c. Are potential subjects likely to be deceased or lost to follow-up?

d. How many records are required to review? Would the resources required to obtain consent from all subjects exceed reasonable expectations of any research team? (For example, the study is a case-control cohort design involving hospitalized patients, and the sample size estimate indicates 200,000 cases are needed to answer the research question.)

e. Are subjects geographically dispersed? Consider the feasibility of the research team obtaining consent from individuals located outside the local catchment area.

f. Will subjects be burdened? Consider whether the consent process:

   i. Necessitates an unreasonable time burden on subjects.

   ii. Creates additional risk to subjects in the form of the collection of unnecessary identifiable information (i.e. name, phone number, signature on a consent or HIPAA form).

Summary

OHRP Review Category	Allowed under Determination or Approval	Examples	HIPAA Authorization	Restrictions
Exempt 4(ii)	Can access medical records, see all IDs, but cannot abstract Must create a research dataset with no IDs	A researcher contracts the CDW-H to access medical records on their behalf. An analyst at the CDW abstracts data that includes none of the 18 HIPAA identifiers and provides it to the investigator. Without any of the 18 identifiers, and no link to any identifying information, the investigator, nor anyone, should be able to match the data back to an individual.	Access of PHI may be approved without a HIPAA Authorization	• May not interact with subjects • May not attempt to re-identify • Cannot retain link to IDs
Exempt 4(ii)	Can access medical records, see all IDs but must create a research dataset with only indirect IDs allowed under a limited dataset (i.e. dates related to an individual, location information)	A researcher contracts the CDW-H to access medical records on their behalf. An analyst at the CDW abstracts data that includes only date of birth and zip codes of patients and provides it to the investigator. With the limited indirect identifiers and no link to any identifying information, it would be very difficult for the investigator, or anyone, to match the data back to an individual.	Use of limited dataset PHI may be approved without a HIPAA Authorization	• May not interact with subjects • May not attempt to re-identify • Cannot retain link to IDs
Exempt 4(iii)	Allows full use of identifiers Abstracting, recording, retaining	**NOT BEING USED AT UNC DUE TO COMPLICATIONS STEMMING FROM HIPAA HYBRID ENTITY STATUS**	Must meet criteria for a full waiver of HIPAA Authorization or obtain HIPAA Authorization from patients/subjects	• PHI must remain under covered entity • May not be shared with any personnel outside of covered entity
Expedited 5	Allows full use of identifiers Abstracting, recording, retaining		Must meet criteria for a full waiver of HIPAA Authorization or obtain HIPAA Authorization from patients/subjects	

Chart Reviews and FDA Regulations

- Chart Reviews can be FDA regulated
- If you are evaluating the safety and/or effectiveness of a drug or device, you may be asked to complete and IND Exemption or Investigational Device Worksheet.
- If FDA regulated, the study will require Expedited 5 review there is no exempt category that includes IND and IDE exemptions

Sources Cited

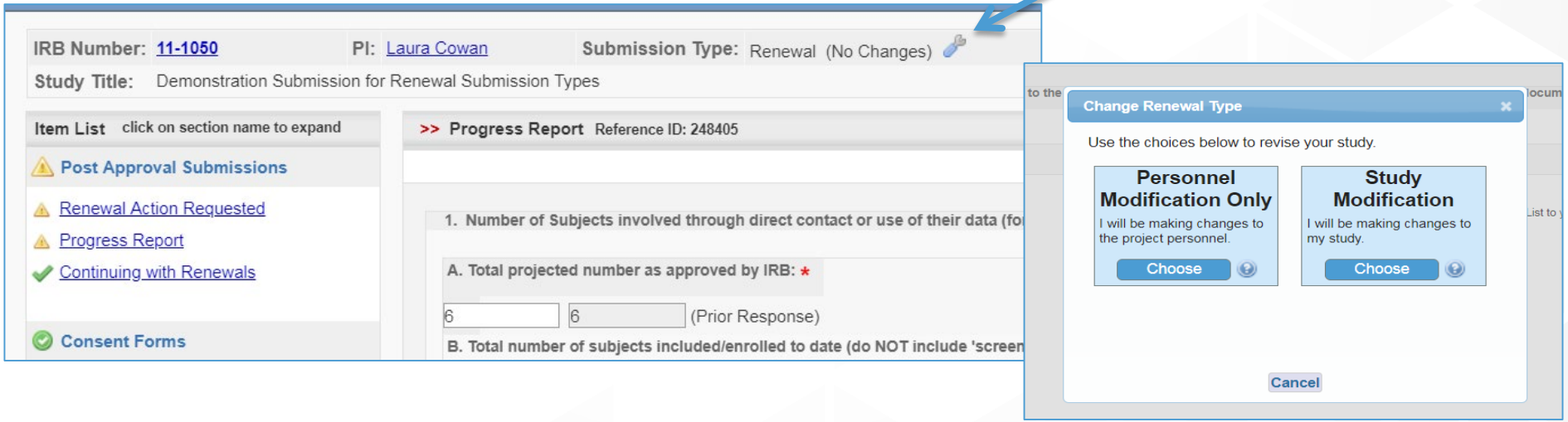
1. U.S. Department of Health and Human Services, National Institutes of Health. (2007, February 2). HIPAA Privacy Rule and Its Impacts on Research. https://privacyruleandresearch.nih.gov/pr_08.asp

2. McFarland, M. (2019, November 17). Regulatory Requirements of Exemption Category 4(iii) and Transitioning Ongoing Research Activities [PowerPoint slides].

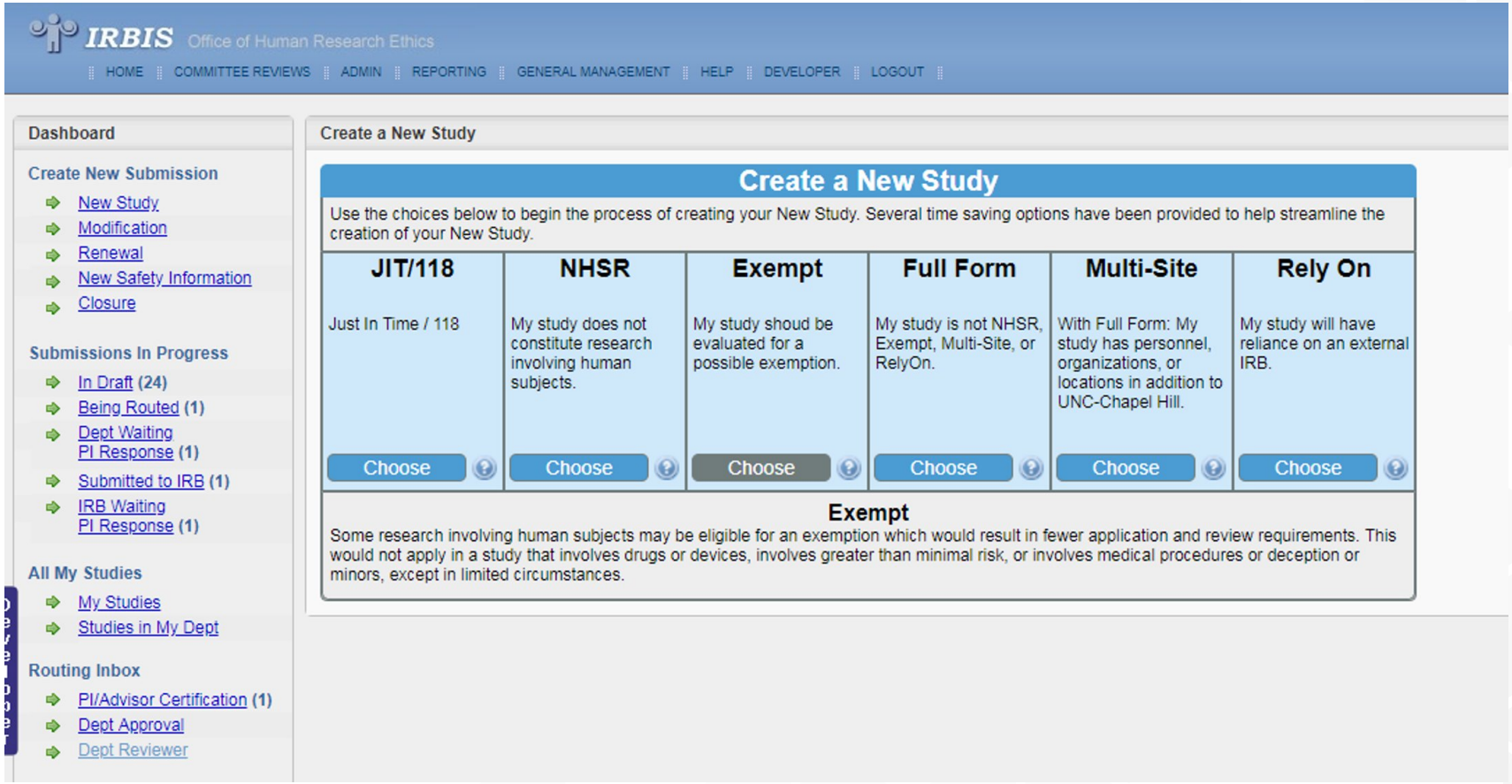
IRBIS and OHRE Updates

Wrench – Completed 7/16/2019

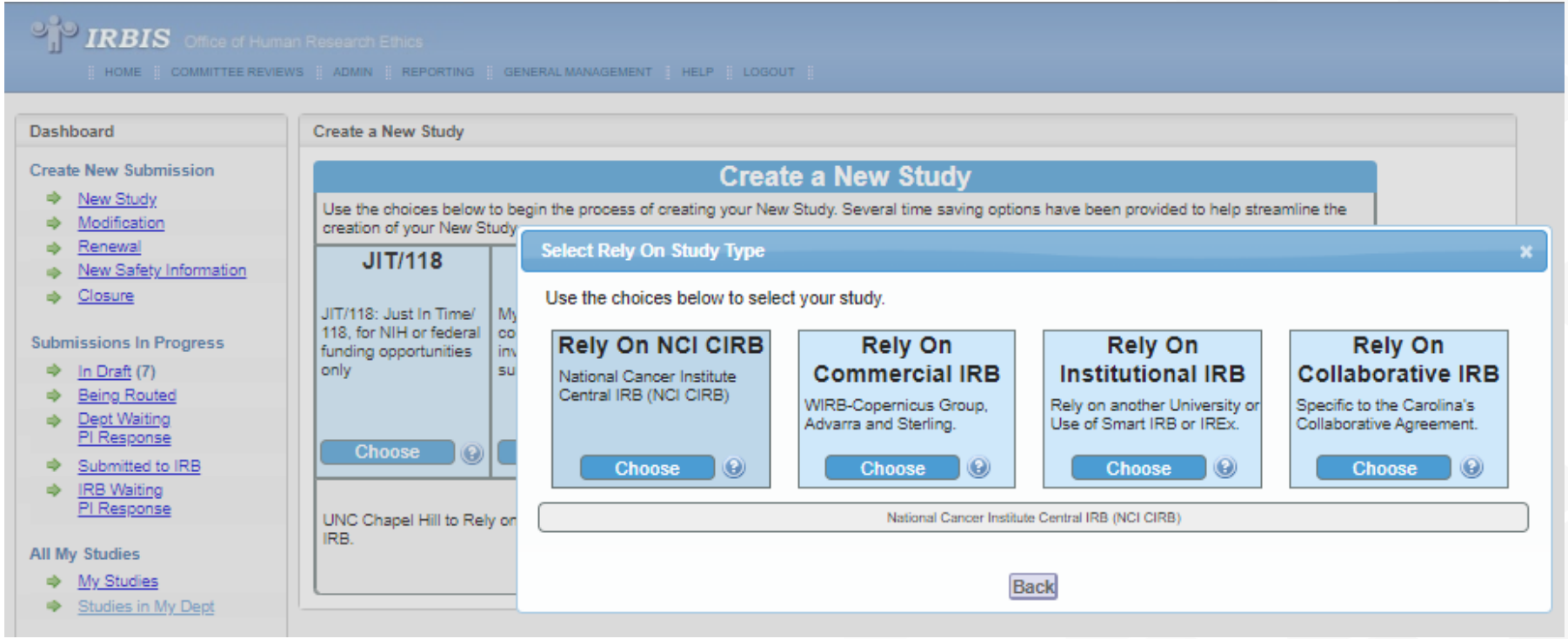
- The “Wrench” feature will be very important for submissions going forward as additional updates are done.
- Allows for a submission change “type” (e.g., Renewal with no changes to personnel modification, or exempt to full submission)



Specific Submission Type-Completed 9/10/2019
Reduced Swim lanes from 1.77 on average to 1.17



Rely On External IRB Submission types – 9/10/2019
50-60% Reduction in Questions



Administrative Review 12/17/2019 Final Update

Administrative Review ≠ Continuing Annual Review

- Over 1800+ studies given administrative review since 1/21/2019

What is Administrative Review?

Administrative review is a limited review that is administratively approved and does not require a rostered member of the OHRE. An administrative review includes:

- COI Review (Administered by UNC's COI Department)
- Confirmation that the study remains open and in good standing:
  - No unreported NSI's
  - No unsubmitted modifications
  - Enrollment status
  - **Failure to submit the Administrative Review Submission is considered noncompliance.**

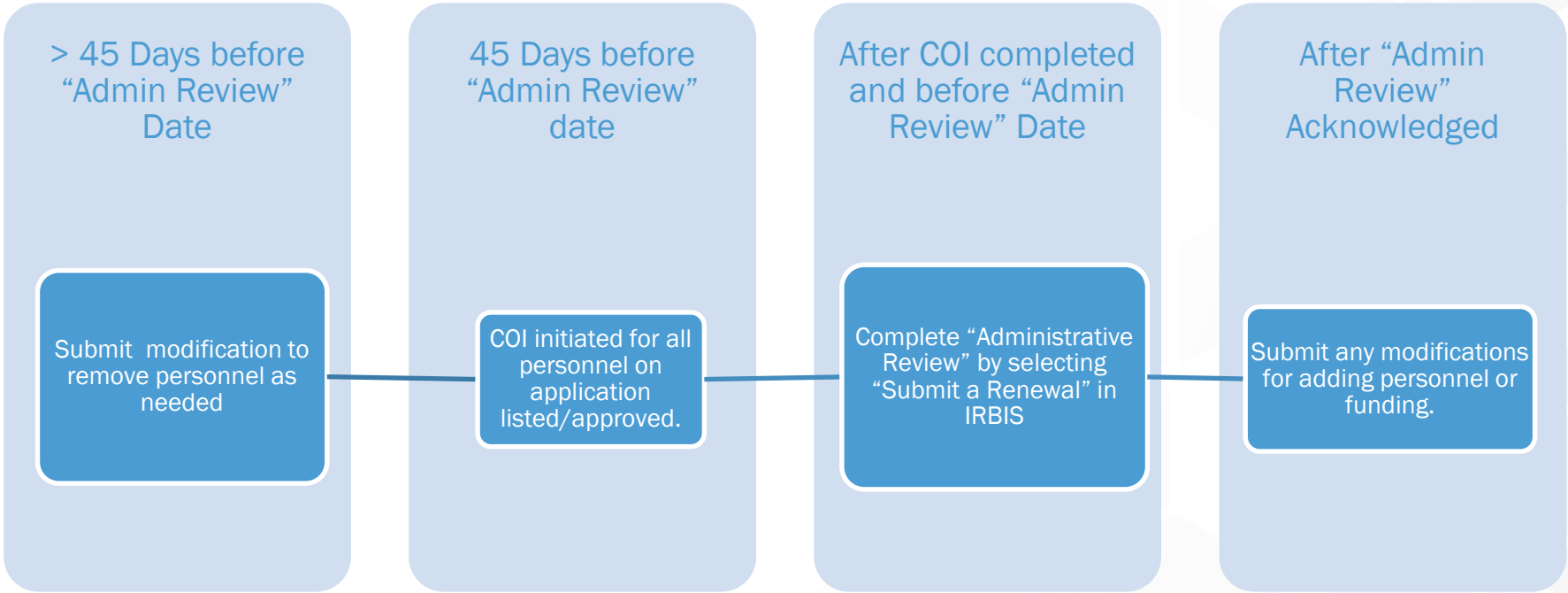
What will happen next?

Issues or concerns that will not receive an “automatic acknowledgement” and will go through a comparable process to the continuing review/renewal submission, include;

- COI Not Completed
- COI Management Plan
- Use of Short Form Consent
- Over-enrollment

Timeline Reminder

*Due Date Reminder- 60-day letter will be sent.

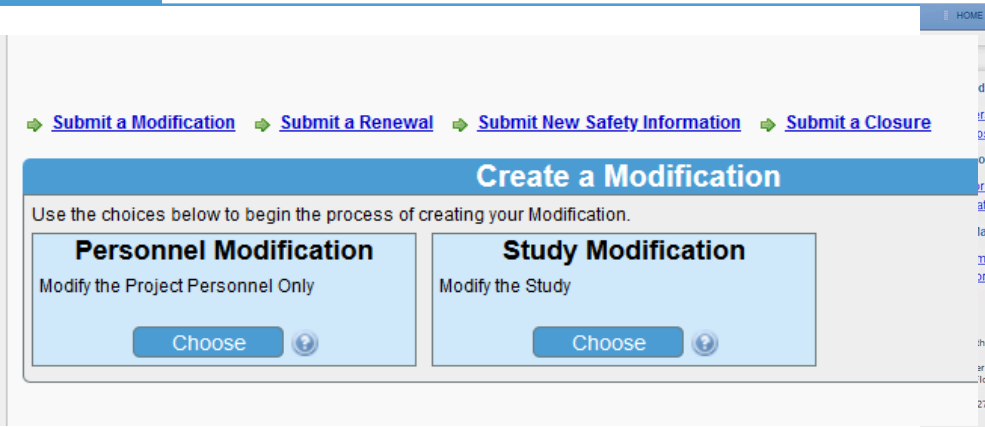


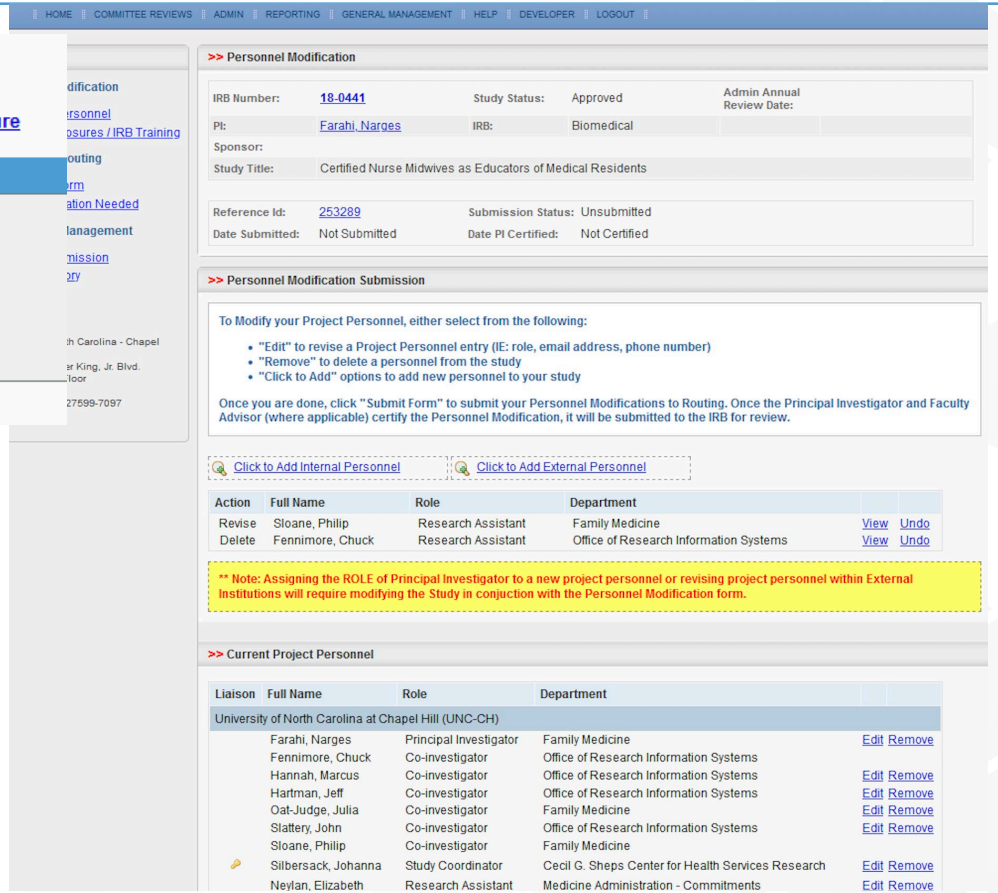
Analyst Assigned– Completed 01/29/2020

If analyst has been assigned

As a reminder the OHRE reviews on a first-in first-out basis and to avoid a bottle neck we assign as an analyst is available.

Next Steps- Personnel Only Modifications





Next Steps - Application Updates

- Similar to the Rely on External IRB applications where ~50% of questions were removed or pre-answered we will be going through the following application types in order to evaluate areas for improvement

  - 118/JIT (Winter/Spring 2020)
  - NHSR (Winter/Spring 2020)
  - Exempt (Summer 2020)
  - Full Form (Fall-Spring 2021)
    - Protocol based submissions

OHRE Updates

CITI - Human Subject Training Requirements

As of March 5, 2020, a core refresher for CITI Human Subjects Training is available to anyone whose training is more than three years old. Users will not be told by the IRB they have "expired" until June 1, 2020.

*CITI Email should match IRBIS email: e.g., cassandra.myers@unc.edu (IRBIS)≠ cmyers1@unc.edu (CITI)

CITI - Human Subject Training Requirements

- These changes are needed to align with the current research landscape and ensure compliance with this requirement

- Renewals
  - This will occur on a rolling calendar utilizing the month you originally took the training so that everyone doesn't expire 6/1/2020.
  - Example, Cassie took her training originally in June 2012, and Mike in September 2005, our renewal comes up in July, Cassie will be required to complete before renewal is complete, Mike will have until the following renewal.

- Initials
  - Starting June 1, 2020 if last CITI human subject training is more than three years old and refresher has not been completed, final approval will not be able to be given.

- GCP trainings previously managed by OCT will be managed by the IRB moving forward, also will be managed via IRBIS/CITI feed

- Refresher has been set to a base level regardless of previous designations/groups enrolled.

UNC OHRE Contacts

- ***General Questions 919-966-3113***

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