IRB SUBMISSIONS FOR CHART REVIEWS

AND SECONDARY ANALYSES

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LEARNING OBJECTIVES AND SCOPE

Objectives:

1. understand which regulatory determinations likely apply to your study
2. choose the correct review pathway
3. use correct terminology to support your review pathway
4. know what responses we're looking for

What we won't cover:

- Chart review/ secondary analyses paired with other activities
- Anything greater than minimal risk
- Change requests and amendments
- Continuing Review
- Multi-site research requiring reliance agreements

The INSPIR system has been designed (and is constantly being updated) to ask the questions we need answers to AND to prompt you to think of and do certain things.

READ THE INSTRUCTIONS & USE THE HELP TEXT

CHART REVIEW VS. SECONDARY ANALYSES

The main differentiator between the two is why the data was originally collected

- **Chart/Lab Review: Clinical data collected for treatment purposes; now analyzed for research**
  - Review pathways: Can be NHSR, Exempt 4, Exempt 9, Expedited 5
- **Secondary Analyses: Collected for research purposes (generally); analyzed for new research questions**
  - Review pathways: Usually NHSR. Can be Exempt 4 if funder wants it. Expedited 5 for FHS. Could theoretically be Exempt 9 but this is not common. Can be Exempt 10.

REVIEW PATH DETERMINATION?

- There are 4 regulatory determinations for these types of studies, corresponding to 4 INSPIR "review paths":
  - NHSR or "Not Human Subjects Research" → NO ACCESS to **direct** identifiers
  - Exempt Category 4 (Exempt Review Path) → Will NOT use master code or RECORD direct identifiers
  - Exempt Category 9 (Chart Review Path or Exempt Review Path) → WILL use master code or record direct identifiers, internal funding only, other restrictions
  - Expedited Category 5 (Chart Review Path or Expedited Review Path) → WILL use master code or record direct identifiers AND has external funding or accesses sensitive populations (ie, prisoners or Part 2).
    - Framingham Heart Study requires Expedited review of ALL secondary analyses using their data!

Chart Review is not a regulatory determination. It is a procedural review path built for PI convenience which the IRB will then determine to be under Exempt 9, or Expedited 5.

NO ACCESS TO IDENTIFIABLE INFORMATION

NHSR

ACCESS TO IDENTIFIABLE INFORMATION – OHRP REGS

- **45 CFR 46.102 (e): (1) *Human subject*** means 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.
- **(2) *Intervention*** includes both physical procedures by which information or biospecimens are gathered (*e.g.,* venipuncture) and manipulations of the subject or the subject's environment that are performed for research purposes.
- **(3) *Interaction*** includes communication or interpersonal contact between investigator and subject.
- **(4) *Private information*** includes information about behavior that occurs in a context in which an individual can reasonably expect that no observation or recording is taking place, and information that has been provided for specific purposes by an individual and that the individual can reasonably expect will not be made public (*e.g.,* a medical record).
- **(5) *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.
- **(6) *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.

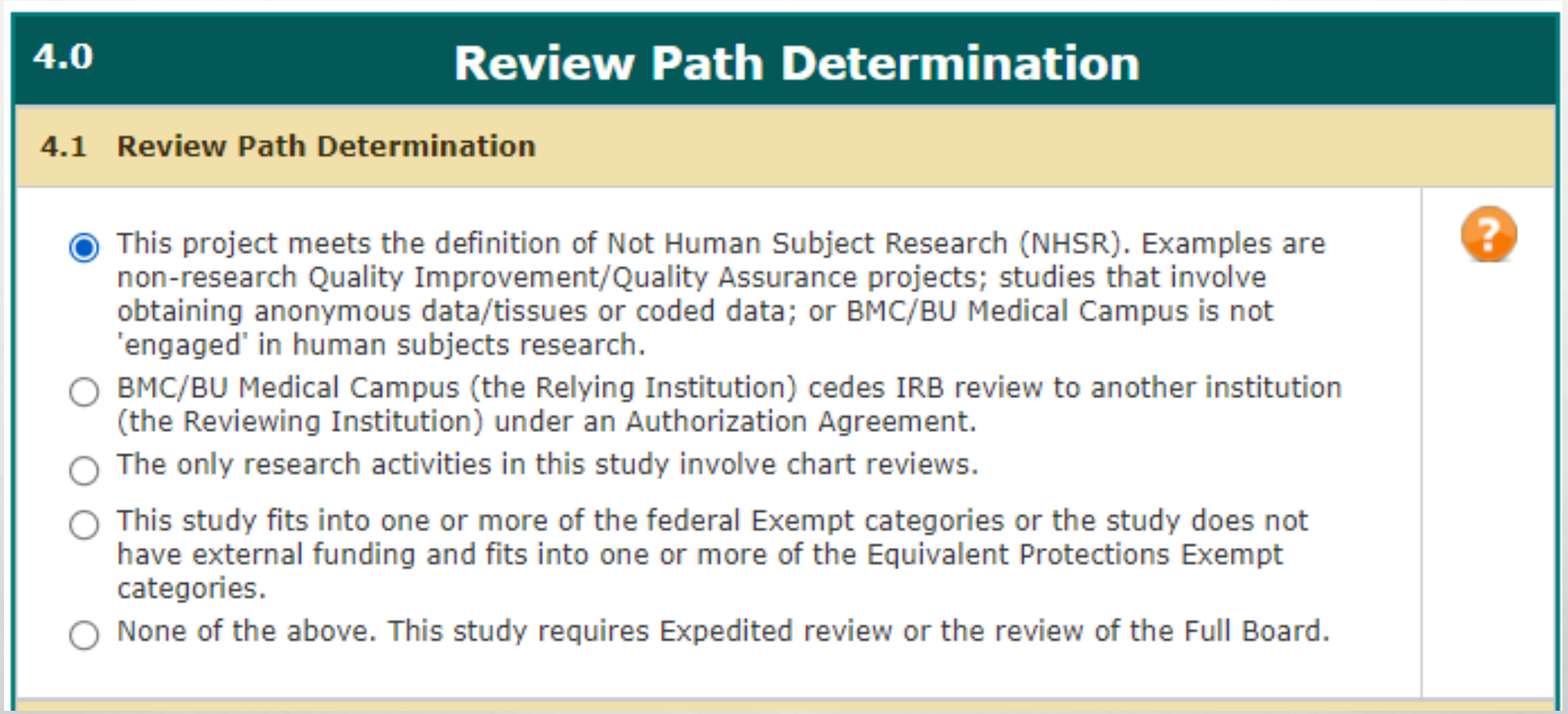
If you do not access identifiers, you are not doing research with "human subjects." This is referred to as "Not Human Subjects Research."

NOT HUMAN SUBJECTS RESEARCH

Study examples of NHSR pathway:

- Publicly available datasets (NHANES)
- CDW delivers dataset with no direct identifiers (dates / zip / advanced age may be included).
- Data from state agency (MA-CHIA), national group (NSQIP), or other group where a data use agreement precludes transfer of direct identifiers (per HIPAA).
- Lab samples without any code tied to identifiers OR coded samples and study team has no access to code.
- BU SPH investigator serves as biostatistician to analyze coded data (BUMC is "not engaged" in HSR)

REVIEW PATH DETERMINATION SECTION



4.0 Review Path Determination

4.1 Review Path Determination

- (●) This project meets the definition of Not Human Subject Research (NHSR). Examples are non-research Quality Improvement/Quality Assurance projects; studies that involve obtaining anonymous data/tissues or coded data; or BMC/BU Medical Campus is not 'engaged' in human subjects research.
- ( ) BMC/BU Medical Campus (the Relying Institution) cedes IRB review to another institution (the Reviewing Institution) under an Authorization Agreement.
- ( ) The only research activities in this study involve chart reviews.
- ( ) This study fits into one or more of the federal Exempt categories or the study does not have external funding and fits into one or more of the Equivalent Protections Exempt categories.
- ( ) None of the above. This study requires Expedited review or the review of the Full Board.

CDW delivers a patient data set to the study team with no direct identifiers – no MRN, name, address, phone #, email address, SSN, driver's license #, etc. CHECK THE FIRST BOX in the Review Path Determination!

NHSR – EXAMPLE STUDY

5.1 Some studies may not need further IRB review because they do NOT meet the definition of HUMAN SUBJECTS or RESEARCH, or because BMC and BU Medical Campus are not "ENGAGED" in human subjects research. Please check the boxes below that apply t this project. Please only answer in regards to study activities occurring at BMC/BU Medical Campus, and/or being done by the BMC/BU Medical Campus investigators. (Starting at question 1, select either "Yes" or "No;" if the instructions provided in the selected option state that this IS human subjects research, follow the instructions to go back to Section 4 and select a different option):

1. Does this project qualify as research? You should answer "Yes" unless this is a non-research QI/QA project or a case se with three or fewer patients. In order to qualify as a QI/QA project, the data cannot be analyzed for research purposes, an the activities in this project must meet *all* of the required Quality Improvement/Quality Assurance criteria as-defined in HRPP Policies and Procedures: https://www.bumc.bu.edu/ohra/hrpp-policies/hrpp-policies-procedures/#10.2.5.2.2

- ○ No
- ◉ Yes

2. Will this research involve any intervention or interaction with living individuals in order to obtain data about the individuals or in order to actively obtain biospecimens directly from the individual?

- ○ Yes. (This IS human subjects research and must be reviewed by the IRB. Please go back to Section 4 and select a different option)
- ◉ No.

3. Will this research involve using data and/or specimens (even if the data and/or specimens are anonymous) about living individuals?

- ○ No.
- ◉ Yes.

4. Will this research only involve obtaining information that is publicly-available? (Will no specimens be obtained, and will all the information that is obtained be readily accessible to everyone?)

- ○ Yes.
- ◉ No.

5. Will anyone on the BMC/BU Medical Campus research team be able to identify who gave any of the specimens or information? (Could the identity of any individual who gave the specimens or information be directly or indirectly deduced?)

- ○ Yes. (This IS human subjects research and must be reviewed by the IRB. Please go back to Section 4 and select a different option)
- ◉ No.

6. Will a key exist anywhere linking the specimens or information to the identity of the people who gave them?

- ○ No.
- ◉ Yes.

7. Is there written documentation that the holder of the key will not disclose the key to the research team under any circumstances?

- ○ No. (This IS human subjects research and must be reviewed by the IRB. Please go back to Section 4 and select a different option)
- ◉ Yes.

Example: CDW delivers a patient data set to the study team with no direct identifiers – no MRN, name, address, phone #, email address, SSN, driver's license #, etc.

NHSR – EXAMPLE STUDY

5.3 Provide an explanation of the project and the study activities that are occurring at BMC/BU Medical Campus. Please explain the following as applicable:

- **Where and how will you obtain the data or specimens?**
- **Will the BMC/BU Medical Campus study team receive any of the following identifiers?**
  - **Dates such as admission, discharge, service, DOB, DOD;**
  - **Town or city, State, and zip code.**

Is this really necessary to answer study question? Reframe question as 'age and other factors'

Click here to access the text editor.

This study is a chart review to determine how patient age is related to COVID-19 mortality rates. As we have a large population of COVID patients of all ages, BMC has plenty of data to assess the question. From March 1, 2020-August 31, 2021, BMC saw a total of over 5,000 COVID patients, one-fifth of whom were intubated due to serious illness.

We will obtain a limited dataset from the CDW that will contain dates of COVID diagnosis, dates of admission, and dates of discharge or death. We will also record individual ages >89 as this population is important to analysis of our study question. The dataset will contain all individuals in the timeframe mentioned above who were hospitalized at BMC due to COVID-19 (this had to be the primary ICD code), their ages, and their entire comorbidity list.

We will not obtain town, city, or zip code. We will not obtain any direct identifier including name, MRN, SSN, license #. We will not obtain a master code as the CDW will be able to provide a full dataset.

Example: CDW delivers a patient data set to the study team with no direct identifiers – no MRN, name, address, phone #, email address, SSN, driver's license #, etc.

HIPAA IDENTIFIERS

- **Health Information Identifiers** are any of the following of an individual or of relatives, employers, or household members of the individual:
  - Names; or
  - **All geographic subdivisions smaller than a state, including street address, city, county, precinct, ZIP code, and their equivalent geocodes, except for the initial three digits of the ZIP code if, according to the current publicly available data from the Bureau of the Census:**
    - The geographic unit formed by combining all ZIP codes with the same three initial digits contains more than 20,000 people; and
    - The initial three digits of a ZIP code for all such geographic units containing 20,000 or fewer people is changed to 000; or
  - **All elements of dates (except year) for dates that are directly related to an individual, including birth date, admission date, discharge date, death date, and all ages over 89 and all elements of dates (including year) indicative of such age, except that such ages and elements may be aggregated into a single category of age 90 or older; or**
  - Telephone numbers; or
  - Fax numbers; or
  - Email addresses; or
  - Social security numbers; or
  - Medical record numbers; or
  - Health plan beneficiary numbers; or
  - Account numbers; or
  - Certificate/license numbers; or
  - Vehicle identifiers and serial numbers, including license plate numbers; or
  - Device identifiers and serial numbers; or
  - Web Universal Resource Locators (URLs); or
  - Internet Protocol (IP) addresses; or
  - Biometric identifiers, including finger and voice prints; or
  - Full-face photographs and any comparable images; or
  - Any other unique identifying number, characteristic, or code, including any code that includes or is derived from any of the identifiers on this list.

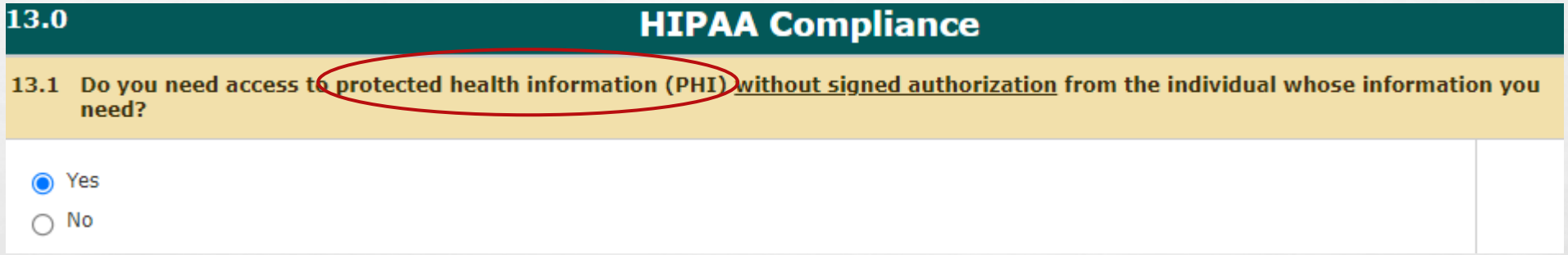
These are "indirect identifiers" under a "Limited Dataset" or LDS

Be careful! "First three letters of mother's last name + last four of phone number" could be identifying!

HIPAA identifiers are crucial and apply to ANY review path and ANY study subject to HIPAA.

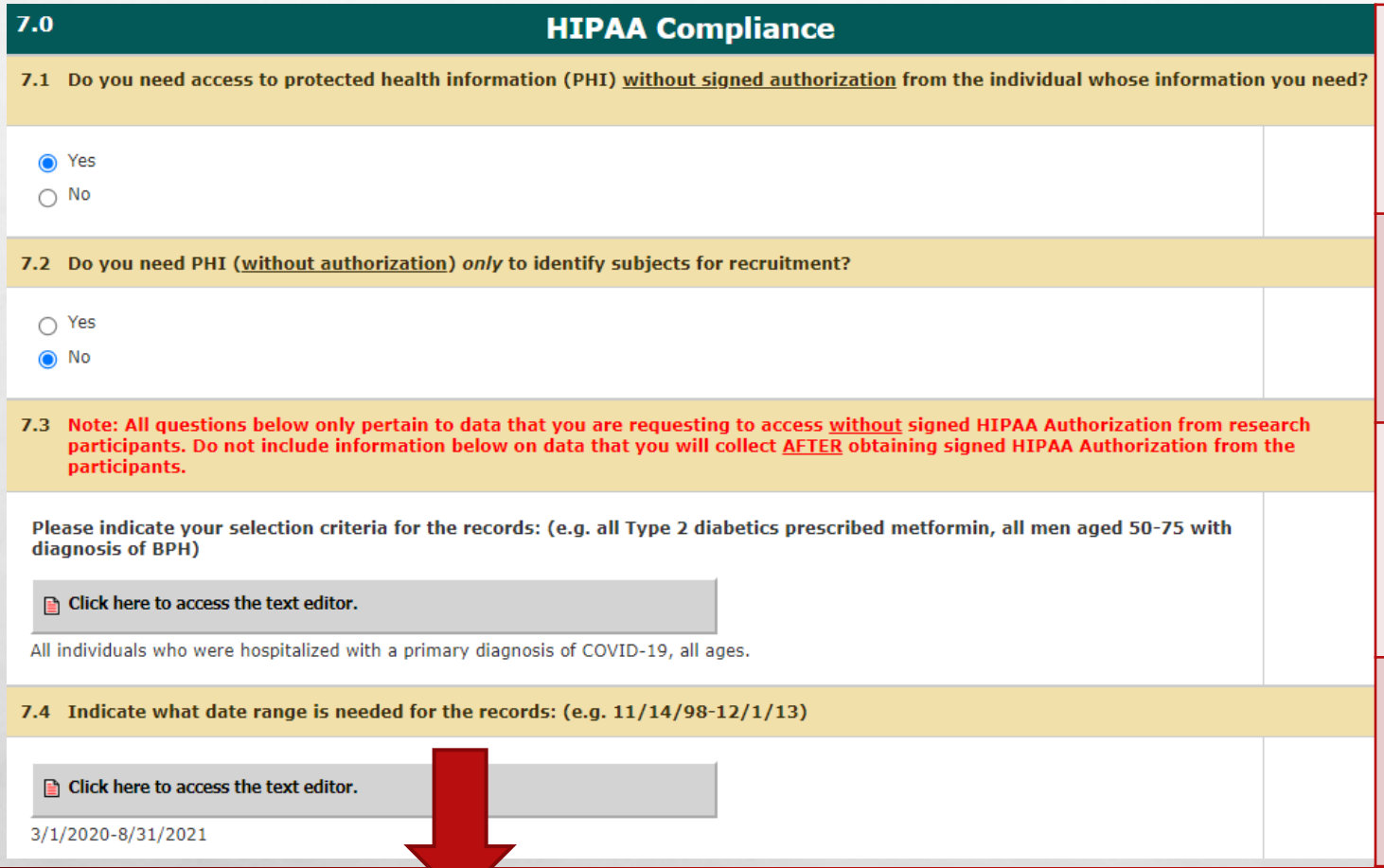
REQUESTING A WAIVER OF HIPAA AUTH

Protected Health Information (PHI) = any of the 18 HIPAA identifiers + private health information (including demographics such as age, race, ethnicity, gender)



- When this applies:
  - If you are accessing the EMR to pull data for research purposes, this requires a waiver of HIPAA Authorization, because you are automatically accessing identifiers in patient records.
  - If your dataset will contain indirect identifiers (under NHSR/Exempt 4), you must fill out HIPAA Compliance section so that the IRB determine you have a Limited Data Set.
- **HIPAA Compliance section fulfills this request for a waiver of HIPAA Authorization from the IRB.**

NHSR WITH HIPAA LIMITED DATASET



7.0 HIPAA Compliance

7.1 Do you need access to protected health information (PHI) without signed authorization from the individual whose information you need?

- (●) Yes
- ( ) No

7.2 Do you need PHI (without authorization) *only* to identify subjects for recruitment?

- ( ) Yes
- (●) No

7.3 Note: All questions below only pertain to data that you are requesting to access without signed HIPAA Authorization from research participants. Do not include information below on data that you will collect AFTER obtaining signed HIPAA Authorization from the participants.

Please indicate your selection criteria for the records: (e.g. all Type 2 diabetics prescribed metformin, all men aged 50-75 with diagnosis of BPH)

Click here to access the text editor.

All individuals who were hospitalized with a primary diagnosis of COVID-19, all ages.

7.4 Indicate what date range is needed for the records: (e.g. 11/14/98-12/1/13)

Click here to access the text editor.

3/1/2020-8/31/2021

Q1: By definition, inclusion of dates of admission/discharge/death in this dataset renders the data PHI.

Q2: this is always "no" for chart review /secondary analyses, because the whole point of the PHI is to use it in your analysis.

Q3: These criteria must be clear enough for the CDW to accurately interpret. It must also harmonize with what you said in your study summary.

Q4: These are the dates for the data bounds. If the data is retrospective, the latest date quoted should be the date of IRB submission.

Anytime you ***access*** ANY of the 18 HIPAA identifiers, this section must be filled out. If you obtain data from the CDW, this section is the CDW's "permission" from the IRB of which variables they can provide.

NHSR WITH HIPAA LIMITED DATASET

7.5 Please list all data variables that are needed from the medical record or attach the file containing the data variables below. NOTE: If you are using the CDW to provide some or all of the data, the variables you list here will be utilized as your official data request by the CDW:

Click here to access the text editor.

age
date of admission
date of discharge or death
ICD problem list
Date of COVID diagnosis
admitted to ICU? y/n
intubated? y/n
days intubated

Are variables consistent with procedures and necessary to answer study question?

7.6 Will you be using the Clinical Data Warehouse (CI

- (●) CDW
- ( ) Study staff will access records
- ( ) Both

7.7 Does your research require access to any of the HIPAA identifiers?

- (●) Yes
- ( ) No

[x] All elements of dates (except year) for dates that are directly related to an individual, including birth date, admission date, discharge date, death date, and all ages over 89 and all elements of dates (including year) indicative of such age, except that such ages and elements may be aggregated into a single category of age 90 or older

Which dates will you access/record?

dates of admission
Dates of discharge
Dates of death
Date of COVID Diagnosis
Age > 89

NHSR WITH HIPAA LIMITED DATASET

7.8 Please describe why the research cannot be conducted without access to protected health information:

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Dates of death are necessary to pair with COVID diagnosis in order to answer our study question of mortality related to COVID. Individual advanced age is necessary as we hypothesize that the elderly will have significantly higher mortality and should be analyzed in detail. Dates of admission and dates of discharge will help us understand levels of care and LOS as it relates to age, which is a secondary aim of the study.

7.9 Why is it not practicable to carry out the research if authorization must be obtained from the participants?

Click here to access the text editor.

The population hospitalized with COVID during the initial phase of the pandemic experienced significant mortality. If we had to obtain authorization from individuals, we would not be able to include the deceased and our results would be very biased. In addition, the number of patients is far greater than we have resources to contact within a reasonable timeframe to conduct analysis.

7.10 What is your plan to protect any identifiable information from use and disclosure by unauthorized parties?

Click here to access the text editor.

The dataset will be kept on the BMC Network Drive in a password-protected folder and accessed only by members of the study team listed on this application. In addition, we are specifically not receiving direct identifiers, in order to better protect the confidentiality of this population.

7.11 When and how will you destroy any identifiers linked to the data?

(Please note: identifiers should be destroyed at the earliest opportunity as consistent with the design of the research study)

Click here to access the text editor.

The dataset will be destroyed 7 years after the close of the study, per BMC policy.

Q8: The question is WHY. Do NOT state: "research cannot be done without PHI."

Q9: This is your main justification of WHY something is not practicable. Practicable: "Able to be done or put into practice successfully." It does NOT mean "convenience" for the study team.

Q10: Know your safe storage locations for BMC and BU. Use the Orange Help icon if unsure! Do NOT say: "HIPAA-Compliant computer."

Q4: We need a timeframe or milestone (such as after publication). Note the question focuses on IDENTIFIERS, but it is usually easier to destroy the dataset.

WILL NOT RECORD DIRECT IDENTIFIERS / WILL NOT KEEP MASTER CODE

EXEMPT 4

EXEMPT 4

4(ii): You have access to identifiable information, but do NOT record them; any funder; any population

- **Exempt 4**: Secondary research for which consent is not required: Secondary research use of identifiable private information or identifiable biospecimens, if at least one of the following criteria is met:
  - i. reserved
  - 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). (Note: this exemption is only available if the identifiable health information remains within a covered entity, and requires IRB review to grant a waiver of authorization under Section 8.5.2.2);

EXAMPLE EXEMPT 4 STUDY

4.0 Review Path Determination

4.1 Review Path Determination

- ○ This project meets the definition of Not Human Subject Research (NHSR). Examples are non-research Quality Improvement/Quality Assurance projects; studies that involve obtaining anonymous data/tissues or coded data; or BMC/BU Medical Campus is not 'engaged' in human subjects research.
- ○ BMC/BU Medical Campus (the Relying Institution) cedes IRB review to another institution (the Reviewing Institution) under an Authorization Agreement.
- ○ The only research activities in this study involve chart reviews.
- ◉ This study fits into one or more of the federal Exempt categories or the study does not have external funding and fits into one or more of the Equivalent Protections Exempt categories.
- ○ None of the above. This study requires Expedited

(4) Anonymous use of data/specimens: Research involving the collection or study of 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, the investigator does not contact the subjects, and the investigator will not re-identify subjects. (if selected, check all that apply below):

- ☑ - At no point will a master code (link between a subject's identifiable data such as medical record number or name and the data set) be created even momentarily.
- ☑ - The Subject ID will never be located along side of any identifiable data such as a name or medical record number.
- ☑ - All data for each subject will be collected in one sitting and the medical record number will not be retained once the data is collected.

Unlike the Old Common Rule, ALL of these boxes must apply in order to qualify under Exempt 4 in the Revised Common Rule

EXAMPLE EXEMPT 4 STUDY

6.2 Study Procedures

Provide a description of all the study procedures. Be sure to describe study methods, how you will select and access data (if applicable), and interventions or interactions with subjects (if applicable).

Click here to access the text editor.

Our primary research question is to understand which variables are mostly closely associated with morbidity and mortality due to COVID-19. Study team will query Epic for patients from 3/1/2020-8/31/2021 who had a primary diagnosis of COVID-19. We will not use the CDW for this study because we need two variables from images they cannot access.

We will make a list of the MRNs who meet these criteria. We expect this to be approximately 500 patients. We will keep the MRNs in Column A of a password-protected Excel sheet, stored on the BMC Network Drive and accessible only to the study team listed on this application.

We will then enter the charts in Epic to record health variables listed below for each patient. None of the variables recorded are direct identifiers (no address, phone, name, email, MRN, or other unique identifier). We will have dates and advanced ages in our dataset. After populating the variables for a particular participant, we will delete the MRN in column A, such that no direct identifiers will appear for any patient next to the health data. Because we will delete the MRN, we will have to complete the data entry for a particular patient in one sitting, and will not be able to return to that patient's chart once data entry is complete and the MRN deleted.

Study team queries Epic for all patients with primary dx of COVID-19 in the timeframe. MRN list taken. Study team goes into Epic and abstracts all variables for first MRN in a single sitting, then promptly deletes the MRN from the list.

EXAMPLE EXEMPT 4 STUDY

Inclusion Criteria must be consistent with study procedures!

10.1 Inclusion Criteria

Include age ranges and sex. If study involves different criteria for different cohorts, please list separately.

Add a New Inclusion Criteria to the Study

Delete	Edit	Order Number	Criteria
		1	Diagnosis of COVID-19, any age, any gender
		2	Were on ventilators in the ICU

versus "primary diagnosis of COVID-19"

Not mentioned in study procedures!

Study team queries Epic for all patients with primary dx of COVID-19 in the timeframe. MRN list taken. Study team goes into Epic and abstracts all variables for first MRN in a single sitting, then promptly deletes the MRN from the list.

EXAMPLE EXEMPT 4 STUDY

This is necessary for an Exempt 4 determination.

12.2 Confidentiality of the Data

In the section below indicate how the study will ensure subject confidentiality and privacy on all study data/results, documents, CRFs, and other documents/files:

- ☐ Study data/results, documents, CRFs, and other documents/files will be identified with a unique study ID #. The study ID # will be linked to a master-code list that contains all study ID #s and direct subject identifiers (i.e. name, address, DOB, MRN, etc). The master-code list will be maintained separately from study files and access limited to the researchers.
- ☑ All study data, documents, CRFs, and other documents/files will be recorded as anonymous. There is NO master-code. There will be no reasonable way to link study data and documents to individual subjects, even temporarily AND subject identities cannot be reasonable ascertained via deductive disclosure.
- ☐ There is an alternate plan for how subject will be identified in study data, documents, CRFs, and other documents/files. Please specify in text box below.

You have checked off that all data are recorded anonymously, meaning that there is no way to link any of the study data to the individual participants. Please provide a brief study-specific description of how the data will be recorded anonymously.

Click here to access the text editor.

The MRN of each participant will be deleted immediately after their study data is populated. No study ID will link the data back to a master code of identifiers. The variables collected in the study dataset would not allow anyone to readily ascertain the identity of the individual. To further protect patient confidentiality we will store the MRN list / dataset securely on the BMC Network Drive in a password-protected Excel sheet. We will also convert the dates we record into "LOS" and "days since diagnosis" in order to minimize the presence of HIPAA indirect identifiers.

This description supports all requirements for the Exempt 4 determination, and also notes that indirect identifiers of dates will be accessed. Therefore, we expect to see the HIPAA Compliance section filled out because PHI is accessed without authorization!

HIPAA COMPLIANCE AND EXEMPT 4 – COMMON MISTAKES

RECALL: PHI = any HIPAA identifier + private health information under a covered entity

- Study teams answer "no" to "Do you need access to PHI without signed authorization from the individual?" because:
  - Don't know the definition of PHI or the 18 HIPAA identifiers
  - Don't know that *indirect identifiers* in their dataset + other variables constitutes PHI
  - Don't pay attention to the distinction between *accessing* of and *recording* of identifiers
  - Are NOT normally subject to HIPAA BUT need the CDW to pull their data with an LDS
  - Misread the question and think – "no one needs to sign anything, I'm good".
- Study teams don't justify the identifiers requested. Q8 – Q11 require **explicit** statements to justify necessity of waiver and data to satisfy the "minimum necessary" requirements. We do not assume data is necessary without justifications.
- Study teams don't know the approved data storage location and how that relates to confidentiality.
- Study teams don't know that direct identifiers should be destroyed at "earliest convenience" or how to define that.

RECORDING OF IDENTIFIERS AND / OR USE OF A MASTER CODE

EXEMPT 9 AND EXPEDITED 5

MASTER CODE IS USED

Definition of master code: a document containing direct identifiers and a study ID. The study ID then links to a study dataset with health information.

MASTER CODE

MRN	DOB	Study ID
300222	1/1/1995	C001
205223	5/31/1984	C002
651254	11/20/1990	C003
332641	8/6/1989	C004

STUDY DATASET

Study ID	Age	Sex	Date Admitted	RHR
C001	26	F	6/7/2021	98
C002	37	M	6/19/2021	83
C003	30	F	7/5/2021	110
C004	32	M	7/24/2021	115

Keep this in a secure, password-protected folder / REDCap instrument

Keep this in a separate, secure folder / REDCap instrument

A "temporary" master code is still a master code! Almost all master codes are temporary, as we require destruction of them when no longer scientifically justified.

MASTER CODE – WHEN DO YOU NEED ONE?

- When you think you will need to return to the charts for additional variables
- When the dataset is complex and patients may have multiple MRNs
- When you are pulling data yourself (not CDW or in addition to CDW)
- Longitudinal collection
- When you need to link two datasets together

CHART REVIEW PATHWAY

Exempt category 9: involving the study of [IDENTIFIABLE] materials (data, documents, records, or specimens) that have been or will be collected solely for nonresearch purposes.

4.0 Review Path Determination

4.1 Review Path Determination

- ○ This project meets the definition of Not Human Subject Research (NHSR). Examples are non-research Quality Improvement/Quality Assurance projects; studies that involve obtaining anonymous data/tissues or coded data; or BMC/BU Medical Campus is not 'engaged' in human subjects research.
- ○ BMC/BU Medical Campus (the Relying Institution) cedes IRB review to another institution (the Reviewing Institution) under an Authorization Agreement.
- ◉ The only research activities in this study involve chart reviews.
- ○ This study fits into one or more of the federal Exempt categories or the study does not have external funding and fits into one or more of the Equivalent Protections Exempt categories.
- ○ None of the above. This study requires Expedited review or the review of the Full Board.

Note: Chart Reviews can cover Exempt 9 or Expedited 5. Secondary analyses should use the Exempt or Expedited pathways.

CHART REVIEW MEETING CRITERIA FOR EXEMPT 9

Exempt 9 under equivalent protections: Research involving the study of materials (data, documents, records, or specimens) that have been or will be collected solely for nonresearch purposes (such as medical treatment or diagnosis).

Exempt 9: You record direct identifiers; MUST be internal funding, cannot access Part 2 data or target prisoners

Note: Exempt 9 is NOT an exempt category under OHRP regulation. Rather, it is exempt only through our institutional policies. Thus, you will not see this category at every institution. We have provided it as a convenience to researchers without external funding to have a shorter application.

EXEMPT 9 – CHART REVIEW PATHWAY

7.0 Chart Review

7.1 Does this study have external funding?

○ Yes ◉ No

7.2 Are prisoners a focus of the study question for this chart review?

○ Yes ◉ No

7.3 Will the Boston Medical Center and BU Medical Campus IRB be asked to act as the IRB of record (through a reliance agreement) for any other sites in this study?

○ Yes ◉ No

7.4 Does the study involve obtaining medical record data that would identify a participant as a patient at any of the BMC federally-assisted substance use disorder clinics (Project RESPECT, Office-Based Addiction Clinic, CATALYST Clinic, or others (see (?) Help Icon for full list)?

○ Yes
◉ No

To qualify for Exempt 9, the answer to these 4 questions must all be "no." If any of them is "yes", INSPIR will populate the Expedited application automatically.

Example: As with previous Exempt 4 example, you are studying patients with a primary dx of COVID-19. However, now you need to access record specific nuances from image findings. You have too many variables to finish a patient in a single sitting. Therefore, you need a master code.

EXAMPLE EXEMPT 9 CHART REVIEW

6.7 Study Procedures

a. Provide a description of the chart review. Be sure to describe the source of the records, how you will determine what records will be reviewed, the date range for the records to be reviewed, and the anticipated number of records.

Click here to access the text editor.

Our primary research question is to understand which factors are most closely associated with morbidity and mortality due to COVID-19. Study team will ask the CDW to query Epic for patients from 3/1/2020-8/31/2021 who had a primary diagnosis of COVID-19. We will ask the CDW to pull as many of the variables listed in our HIPAA section as possible, but we expect there will be information from image reports that will require manual review and/or quality checks. Therefore, we will request that they provide us with the master code. Anticipated number of records is 5,000.

Besides MRN and DOB in the master code, our separate study dataset will contain dates and advanced individual ages, but no geographic information.

b. Indicate how confidentiality will be assured:

The master code and study dataset will be housed in BMC Box.com, in separate, password-protected folders. Access will be limited to researchers listed on this IRB application.

c. If the data are identifiable and/or if a master-code exists, when and how will the data be de-identified or the master-code be destroyed?

We will destroy the master code upon publication of our results, or no later than 3 years after the close of the study. We will convert the dates in our study dataset to non-identifiable variables (date of admission/date of discharge--> "LOS" and other dates --> "days since diagnosis with COVID-19") prior to analysis of the dataset to further protect confidentiality. Our final dataset will be destroyed 7 years after the close of the study.

7.5: "Does the study involve retaining the data in a repository for future extra research use(s) that are unrelated to the aims of this specific study?" This is now allowed under Exempt 9; answering yes will populate the "Retention of Data or Samples" section toward the end of the application.

HIPAA SECTION MUST SUPPORT PROCEDURES

Q3	All individuals who were hospitalized with a primary diagnosis of COVID-19.
Q4	3/1/2020-8/31/2021
Q5	**Master code:** MRN/DOB **Study dataset:** Age; date of admission; date of death; ICD problem list; Date of COVID diagnosis; All PCR tests and dates; admitted to ICU? y/n; intubated? y/n; # days intubated; chest xrays/MRI/CT images and reports
Q6	BOTH
Q7	YES – Names, MRN, All elements of dates (Date of admission, date of birth death, COVID dx, PCR dates, age>89), Any other unique ID number (PACS ID)
Q8	Direct identifiers are necessary to select the exact individuals who meet our study criteria. PHI are critical to identify, verify, and collect images and data in a retrospective review. Other identifiers such as dates and advanced age are necessary to analyze correlations between them and outcome of mortality.
Q9	Many individuals in our dataset are expired. It may be difficult to contact them given the socio-economic circumstances surrounding the COVID-19 pandemic and BMC's populations. If we could not obtain everyone's authorization, our sample would be too biased to be meaningful. In addition, our large sample size would require enormous resources and time to which would delay obtaining valuable information during the COVID pandemic.
Q10	The master code will be kept on the BMC Network Drive in a password-protected folder and accessed only by members of the study team listed on this application. The study data set will also be kept on the BMC Network Drive, in a separate password-protected folder from the master code.
Q11	The master code will be destroyed as soon as data analysis is complete, or after 2 years, whichever is sooner. The dates in the study dataset will all be converted into "Days since admission" as soon as the data is populated, in order to de-identify the dataset. (Date of admission will become "day 0".) The study dataset will be destroyed 7 years after the close of the study, per BMC policy.
Q12	I declare that the requested information constitutes the minimum necessary data to accomplish the goals of the research.

POLL EXAMPLE STUDY:

A study team submits a chart review to examine rates of depression in women 18-30 years old and contraceptive method. Date range of records for review is 01/01/2017 – 12/31/2018. The study has NIH funding. The CDW will provide a list of medical record numbers of eligible participants. The study team members will collect all data in one sitting for each participant. They will delete the medical record number after data collection is complete for each participant. At no point will a master-code be created even temporarily.

What is the likely determination?

- NHSR
- Exempt 4
- Exempt 9
- Expedited 5

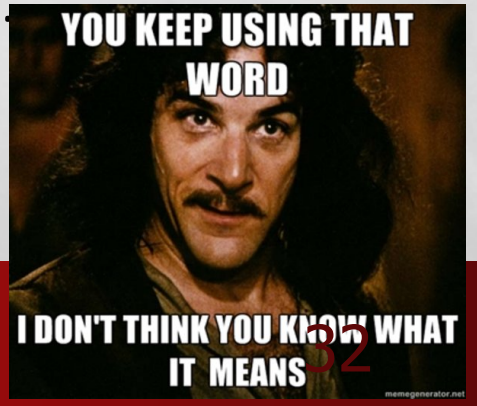
WORDS MATTER:
"ANONYMOUS" VS. "CODED" VS. "DE-IDENTIFIED"

45 CFR 46 OHRP regs based on the Belmont report is one standard of identifiability

45 CFR 164: HIPAA is another (stricter) standard of identifiability

- **Coded:** data labeled with a study ID which is linked to a master code
- **De-identified:** research team had identifiers but they are entirely and utterly destroyed now (all 18, if HIPAA applies). This includes the master code.
- **Anonymous:** research team never collected or stored direct identifiers with data.

Most often, people say "De-identified' when they mean "Coded".



EXTERNAL FUNDING, SENSITIVE DATA, REPOSITORIES, OR OTHER CONSIDERATIONS (I.E., FHS)

EXPEDITED 5

NON-EXEMPT VS EXEMPT REVIEW

- Non-Exempt subject to federal regulations where exempt research is not
- Must meet approval criteria outlined under 45 CFR 46.111 (the 111 criteria)

- **Two categories of review under non-exempt:**
  - *Expedited*:
    - Minimal risk, fit within pre-defined expedited categories of research, does not require review by the convened board.

  - *Full/Convened Board:*
    - Research does not fit within pre-defined expedited categories of research, potentially greater than minimal risk, requires review by the full board for approval

EXPEDITED REVIEW

Expedited Category 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).

When do chart reviews and secondary analyses require expedited review?

- *Identifiable data is collected AND:*
  - External funding
  - Identify a participant as a patient at any of the BMC federally-assisted substance use disorder clinics (data collected is identifiable)
  - If prisoners are a focus of the research (data collected is identifiable)

- BMC/BUMC will serve as IRB of record for other sites (generally, we do not enter into authorization agreements for exempt research)
- Chart review's main purpose is to create a repository
- Using data from the Framingham Heart Study

EXPEDITED REVIEW

How does IRB review of expedited research differ from exempt research?

- Research must meet 45 CFR 46.111 approval criteria

- Under ‘Section 4 Review Pathway Determination’ **choose** either:
    - Chart Review OR
    - Expedited/Full Application
- Fill out the full IRB application that populates
    - Navigation Menu *(expedited/full application only)*
    - Subjects
    - Design/Procedure
    - Risks/Benefits
    - Data & Safety Monitoring
    - Consent

Content of the Confidentiality & HIPAA Compliance sections is largely the same between exempt and non-exempt research.

WAIVER OF INFORMED CONSENT

Researchers do not generally obtain consent from participants in chart reviews and secondary analyses as seen in previous review paths. In non-Exempt research (Expedited or FB), researchers must request a waiver of informed consent supported with adequate justifications.

Criteria for Waiver of Informed Consent:

1. the study is not greater than minimal risk; AND

2. that waiving the requirements for informed consent will not adversely affect the rights and welfare of study subjects; AND

3. that the research cannot be practicably carried out without the waiver of informed consent or alteration of the consent process; AND

4. If the research involves using identifiable private information or identifiable biospecimens, the research cannot practicably be carried out without using such information or biospecimens in an identifiable format (for research that is submitted for initial approval on or after July 1, 2017); AND

5. that (if applicable) there is a plan to disseminate pertinent information to study subjects or legally authorized representatives after the study is completed.

WAIVER OF INFORMED CONSENT

1. The study is not greater than minimal risk – WHY?

- *Procedures are benign:* The research is a secondary analysis OR chart review only, there is no interaction with participants.
- *Confidentiality Protections:* The mechanisms to protection confidentiality are adequate to protect the data from unauthorized disclosure outside the research context.

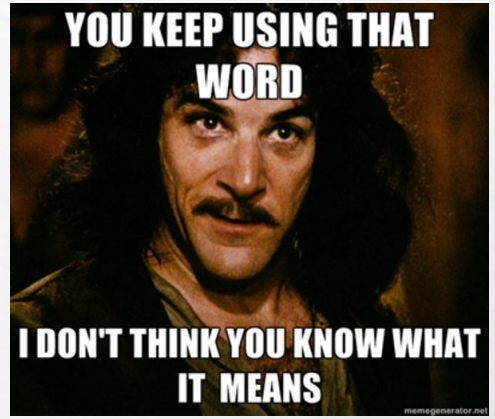
2. That waiving the requirements for informed consent will not adversely affect the rights and welfare of study subjects – WHY?

- *Confidentiality Protections:* The mechanisms to protection confidentiality are adequate to protect the data from unauthorized disclosure outside the research context.
- *Prior Consent Obtained (if applicable):* Participants' consent for future research was obtained during the consent process for the Framingham Heart Study.

3. That the research cannot be practicably carried out without the waiver of informed consent – WHY?

- *Data is retrospective (already in existence at the time of IRB submission):*
  - Participants may have moved away, passed away, or changed contact information. These participants are not expected to be at BMC in the near future. The sample size is so large that the research team does not have the resources available to attempt to contact every patient. Systematic differences in who provides consent for the research would introduce bias that could undermine the validity of research design.
- *Data is prospective (data to be analyzed does not exist yet):*
  - More difficult to justify the waiver of consent
  - Full board review might be required for secondary data analyses if the data to be collected will be collected for research purposes only (e.g., FHS)

RETROSPECTIVE VS. PROSPECTIVE



Definitions:

- Retrospective data **already exists** at the time of IRB submission.
- Prospective data **does not yet exist** at the time of IRB submission.

IRB Review:

- Whether your data is retrospective or prospective; AND for what purpose(s) the data was originally collected.
- The aspect of retrospective v. prospective data alone does not immediately impact the regulatory determination (exempt, expedited, full board). The purpose of original data collection does, however.
    - EX: An investigator wants to compare FHS data from exams conducted in 2010 and exams that will be conducted in the upcoming exam cycle. Full board review is required because the **data does not yet exist** AND the **purpose of original data collection is for research purposes.**
- The aspect of retrospective v. prospective data does impact justifications for impracticability for the waiver of consent and waiver of HIPAA Authorization. **The bar for waiving consent, and particularly for waiving HIPAA authorization, is much higher if the data will be collected in the future.** This is especially true for prospective chart reviews as the patient can be contacted if they are coming in to generate clinical data for the medical chart.

REVIEW

COMPARE AND REVIEW OF REGULATORY CATEGORIES

	NHSR	Exempt 4	Exempt 9	Expedited 5
Access to / recording of indirect identifiers allowed	Yes - with HIPAA Compliance section (HCS)	Yes – with HCS	Yes – with HCS	Yes – with HCS
Access to direct identifiers allowed	No	Yes – with HCS	Yes – with HCS	Yes – with HCS
Recording of/obtaining direct identifiers allowed	No	No	Yes – with HCS	Yes – with HCS
Funding	Any	Any	Internal, only	Any
Master code	No	No	Yes	Yes
Site	Any #	Any #	Single-site; multi-site if no BMC identifiable info shared	Any #
HIPAA Compliance (BMC data OR data where required by entity providing data to BU researcher)	Only needed if indirect identifiers (Limited Dataset) involved	Only needed if study team will access identifiers (or if LDS obtained in secondary analyses)	Must request waiver of HIPAA Authorization	Must request waiver of HIPAA Authorization
Can access sensitive data (Part 2, prisoners)	Yes b/c not individually identifiable	Yes b/c individual identifiers not recorded	No	Yes b/c all waivers and extra documentation obtained.
Waiver of Consent	n/a	n/a	n/a – consent is not required	Required

OHRP "IDENTIFIABLE PRIVATE INFO" VS. HIPAA IDENTIFIERS

Identifiability vs. [HIPAA] *Identifiers*

Having a HIPAA identifier doesn't (necessarily) make the data identifiable

- Identifiable Private information
  - Direct identifier + health/personal info

Mastercode file:
- Jane Smith
- Research ID Code: 1234

In research record:
- Subject 1234
- Diagnosis: Rheumatoid arthritis
- Medications list

- Protected Health Information
  - HIPAA identifier + health info
  - (18 HIPAA identifiers, incl. name, MR#, dates, zip code, etc.)

CDW provides:
- Diagnosis: Rheumatoid arthritis
- Medications list
- Date of prescription of xxxxx medication
- Current outcomes

Scenario on left is Human Subjects Research under OHRP; Scenario on right is NHSR under OHRP, with an LDS under HIPAA

QUIZ – 2 QUESTIONS

Q1 A BMC study team will access patient data from BMC's L&D unit and input it into a shared REDCap project with Brigham and Women's Hospital. Patient data will all be coded, with each side retaining its own master code and not sharing the master code with the other institution. Both sides are internally funding their work. The dataset will contain dates of delivery and dates of discharge. They will have a DUA in place. What is the likely determination?

1. NHSR
2. Exempt 4
3. Exempt 9
4. Expedited 5

QUIZ

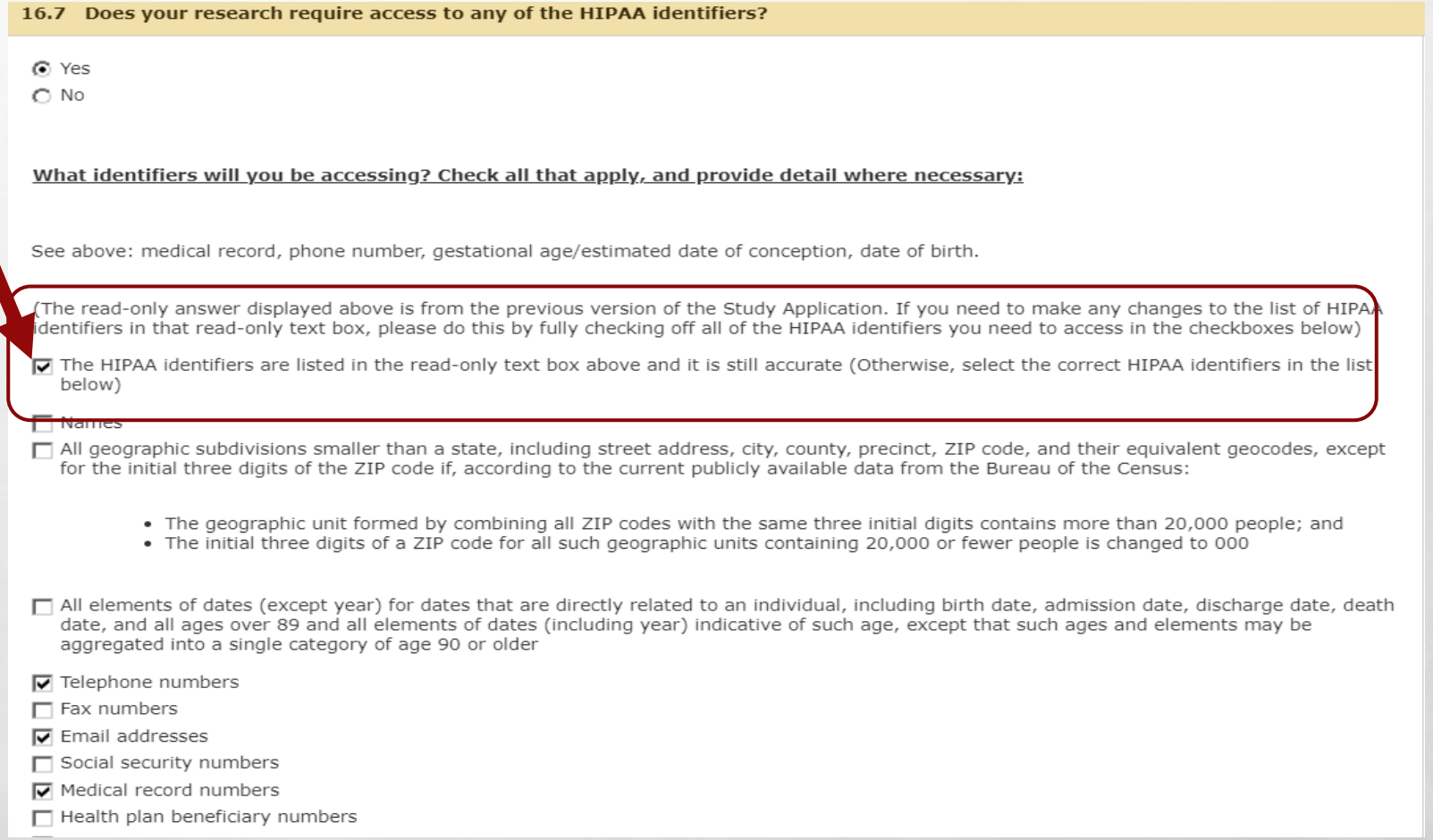
Q2 Later, this study team submits an amendment application. They now want to now access the L&D data specifically of women who are patients of Project RESPECT (a federally assisted SUD clinic subject to Part 2 protections) who gave birth. How would this change affect the regulatory determination?

1. The exempt determination would not be altered. The amendment description is sufficient and no changes are needed to the application.
2. They would now qualify for an exempt determination under category 4, the application must change review paths.
3. Review under Expedited category 5 is now required; the application must be updated along with the amendment to account for a new level of review.

READ THE APPLICATION! AND OTHER TIPS

If you've checked off this, you shouldn't need to check off anything else. If you need to make an update, don't check this box.

- Do not copy from previous applications! Read directions as requirements change regularly
- Know your IT terms - don't explain what the BMC Network DOES (firewall, encryption, etc.), just state you will use it.
- Keep the jargon out
- If you attach variables or other documents, they MUST support what you put in the application.
- Only attach what we ask for!



16.7 Does your research require access to any of the HIPAA identifiers?

- (•) Yes
- ( ) No

What identifiers will you be accessing? Check all that apply, and provide detail where necessary:

See above: medical record, phone number, gestational age/estimated date of conception, date of birth.

(The read-only answer displayed above is from the previous version of the Study Application. If you need to make any changes to the list of HIPAA identifiers in that read-only text box, please do this by fully checking off all of the HIPAA identifiers you need to access in the checkboxes below)

- [x] The HIPAA identifiers are listed in the read-only text box above and it is still accurate (Otherwise, select the correct HIPAA identifiers in the list below)
- [ ] Names
- [ ] All geographic subdivisions smaller than a state, including street address, city, county, precinct, ZIP code, and their equivalent geocodes, except for the initial three digits of the ZIP code if, according to the current publicly available data from the Bureau of the Census:
  - The geographic unit formed by combining all ZIP codes with the same three initial digits contains more than 20,000 people; and
  - The initial three digits of a ZIP code for all such geographic units containing 20,000 or fewer people is changed to 000
- [ ] All elements of dates (except year) for dates that are directly related to an individual, including birth date, admission date, discharge date, death date, and all ages over 89 and all elements of dates (including year) indicative of such age, except that such ages and elements may be aggregated into a single category of age 90 or older
- [x] Telephone numbers
- [ ] Fax numbers
- [x] Email addresses
- [ ] Social security numbers
- [x] Medical record numbers
- [ ] Health plan beneficiary numbers

QUESTIONS?

THANK YOU!

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Emily Crowley, MPH

- 617-358-6558; eacrow@bu.edu

Khaled Khattar (IT specialist)

- 617-358-5351; kkhattar@bu.edu

Main IRB number: 617-358-5372

Resources:

- https://www.bu.edu/crtimes/
- https://www.bumc.bu.edu/irb/inspir-ii/inspir-ii-instructions-for-investigators/
- http://www.bumc.bu.edu/ohra/hrpp-policies/hrpp-policies-procedures/

APPENDICES

HIPAA IDENTIFIERS

- **Health Information Identifiers** are any of the following of an individual or of relatives, employers, or household members of the individual:
  - Names; or
  - **All geographic subdivisions smaller than a state, including street address, city, county, precinct, ZIP code, and their equivalent geocodes, except for the initial three digits of the ZIP code if, according to the current publicly available data from the Bureau of the Census:**
    - The geographic unit formed by combining all ZIP codes with the same three initial digits contains more than 20,000 people; and
    - The initial three digits of a ZIP code for all such geographic units containing 20,000 or fewer people is changed to 000; or
  - **All elements of dates (except year) for dates that are directly related to an individual, including birth date, admission date, discharge date, death date, and all ages over 89 and all elements of dates (including year) indicative of such age, except that such ages and elements may be aggregated into a single category of age 90 or older; or**
  - Telephone numbers; or
  - Fax numbers; or
  - Email addresses; or
  - Social security numbers; or
  - Medical record numbers; or
  - Health plan beneficiary numbers; or
  - Account numbers; or
  - Certificate/license numbers; or
  - Vehicle identifiers and serial numbers, including license plate numbers; or
  - Device identifiers and serial numbers; or
  - Web Universal Resource Locators (URLs); or
  - Internet Protocol (IP) addresses; or
  - Biometric identifiers, including finger and voice prints; or
  - Full-face photographs and any comparable images; or
  - Any other unique identifying number, characteristic, or code, including any code that includes or is derived from any of the identifiers on this list.

These are "indirect identifiers" under a "Limited Dataset" or LDS

Be careful! "First three letters of mother's last name + last four of phone number" could be identifying!

DATA STORAGE

- **What is no longer approved at BMC:**
  - computer hard drive/ Flash drive/ "HIPAA-Compliant computer"/BMC-Controlled computer or "password-protected BMC Computer"
  - Qualtrics/ Google Forms
- **What IS approved at BMC for secure data storage**
  - BMC Network drive
  - BMC Box.com
  - REDCap – master code in separate instrument
  - Paper under double lock

BU Options – use the orange question mark within the "Confidentiality" section itself! Read the definitions of data levels ("public"; "internal"; "confidential"; "Restricted", and "HIPAA")

- BU: http://www.bu.edu/tech/support/storage-options/

If you are using BMC data but are a BU researcher, you should store on BU option for HIPAA-level approval and execute a DUA

EXPEDITED REVIEW: 46.111 CRITERIA

1. Risks minimized
2. Favorable Risk/Benefit Ratio
3. Equitable Selection
4. Consent process – may be waived, if applicable
5. Documentation of consent – may be waived, if applicable
6. Data safety monitoring, if appropriate
7. Adequate Confidentiality
    a. Additional safeguards for vulnerable populations, if appropriate

****When justifying anything, do NOT restate the criteria: ie, "We have minimized the risks and the risk/benefit ratio is favorable."** This is the IRB's job to determine that these criteria are met through your justifications. **For example:** "We are minimizing our risk to breach of confidentiality by securely storing our master code and study dataset on Box.com, in separate, password-protected folders. We will delete the master code after we are accepted for publication."

HUMAN SUBJECTS PROTECTION TRAINING

BMC and Boston University Medical Campus require that all researchers involved in human research must receive formal training. Depending on the type of research you conduct, there are several levels of required training.

- **Human subjects protection training** – required for all individuals involved in human subject research studies (exempt and non-exempt) who have contact with subjects or their identifiable data.
- **Good clinical practice (GCP) training** – required for all individuals involved in the conduct of clinical trials.
- The CITI human subjects protection course, either the biomedical or social-behavioral course, must be completed for initial training. Human subjects protection training must be renewed every three years.

In CITI: register under: **Boston University Medical Campus**

BMC/BUMC IRB RESOURCES

BUMC IRB WEBPAGE: HTTP://WWW.BUMC.BU.EDU/IRB/

- INSPIR II INSTRUCTIONS FOR INVESTIGATORS: HTTP://WWW.BUMC.BU.EDU/IRB/INSPIR-II/INSPIR-II-INSTRUCTIONS-FOR-INVESTIGATORS/
- TEMPLATES: HTTPS://WWW.BUMC.BU.EDU/IRB/INSPIR-II/IRB-TEMPLATES/
- IRB PERSONNEL DIRECTORY: HTTP://WWW.BUMC.BU.EDU/IRB/ABOUT-US/PERSONNEL/
- HRPP POLICIES & PROCEDURES DOCUMENT: HTTP://WWW.BUMC.BU.EDU/OHRA/HRPP-POLICIES/

- IRB APPOINTMENTS: EMAIL US AT MEDIRB@BU.EDU FOR AN APPOINTMENT WITH A STAFF MEMBER
- BMC/BU MEDICAL CAMPUS CLINICAL RESEARCH RESOURCES OFFICE (CRRO): HTTP://WWW.BUMC.BU.EDU/CRRO/
  - CONSULTATIONS: HTTP://WWW.BUMC.BU.EDU/CRRO/RESEARCH-AND-REGULATORY-CONSULTATIONS/

OTHER RESOURCES

- DATA USE AGREEMENTS BY INSTITUTION:
  - DUA.MTAREQUEST@BMC.ORG
  - HTTPS://WWW.BU.EDU/RESEARCHSUPPORT/FORMS-POLICIES/DATA-USE-AGREEMENT-FORM/
- QUALITY IMPROVEMENT HUB
  - HTTPS://WWW.BUMC.BU.EDU/IRB/SUBMISSION-REQUIREMENTS/WHEN-TO-SUBMIT/QUALITY-IMPROVEMENT/
  - HTTPS://WWWAPP.BUMC.BU.EDU/OCR/CLINICALRESEARCHNEWSLETTER/ARTICLE.ASPX?ARTICLE=800
- BU AND BMC DATA DESTRUCTION POLICY
  - HTTPS://WWW.BUMC.BU.EDU/OHRA/HRPP-POLICIES/HRPP-POLICIES-PROCEDURES/#6.6.6
  - HTTPS://WWW.BUMC.BU.EDU/OHRA/HRPP-POLICIES/HRPP-POLICIES-PROCEDURES/#6.6.7.1