



Avoiding & Responding to the Most Common IRB Application Stipulations

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Disclaimer

- Applying the regulations/policies/ethics is an art, not a science.
- Opinions will vary. Inconsistencies will inevitably happen.
- These slides represent our current thinking on the regulations and the BUMC/BMC HRPP policies and procedures.
- However, this presentation is about the common stipulations we see in a “typical” study. They may or may not apply to your study.

Your mileage may vary.

Primary Source of Stipulations:

#1 Inconsistent information

- Procedures need to be consistent: protocol, application, ICF

#2 Missing information

- E.g textboxes incomplete or documents not attached



Key Personnel: Department Chair/Section Chief

- The Department Chair/Section Chief role is filled by the person that supervises the Principal Investigator. If the PI is a department chair, then this study role would be filled by their superior.

3.5 Please ONLY list the PI's Department Chair/Section Chief below. The system will automatically route for signoff to any additional "Special Routing" approvals, so please do not list those here.

Ogrodnik, Matthew, IRB Director

Department Chair/Section Chief 

 Add User

****Add the name of the individual authorized to approve and sign off on this study from your Department (e.g. the Department Chair or Dean). This should be someone other than the Principal Investigator. For more information, click on the (?) Help icon.**

Review Path Determination

The Review Path Determination refers to the level of regulatory review required for a specific project.

- In most cases, investigators are asked to change the review path only if they have selected a path that does not provide sufficient information to make a regulatory determination (e.g., if submitted as Exempt, but Non-Exempt/Expedited review is required).

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.

Training for Study Personnel

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.

Adding Study Personnel

Internal Study Personnel

- Personnel who are primarily affiliated with BUMC or BMC
- Added through Internal Personnel Change Request

External Study Personnel

- Personnel who are from external institutions;
- If external personnel are engaged in human subjects research, then they must be added through an authorization agreement via an amendment. Please contact IRB Coordinator, Roz Schomer at roz@bu.edu for specific study questions.

Funding Source

Choosing the correct funding option:

- “Student/Resident Research with no External Funding” requires a Supervising Principal Investigator

6.1 Funding Source

What is the source of your research funding? If you have multiple sources of funding (including sub-awards), check all that apply.

- Student/Resident Research with no External Funding (choose if the PI is a student/resident and the study is student/resident research)
 - Department/Internally Funded (choose if the PI is not a student/resident and the study has no specific funding)
 - Government
 - Industry
 - Foundation/Other
 - Training Grant (e.g. T32, K-award)
-

Funding Details

Filling out the funding details:

- All details are frequently not filled out,
- A particularly important field: “Is Institution the Primary Grant Holder”

Sponsor Name:	Boston University
Sponsor Type:	Private - Non-profit
Sponsor Role:	
Project Period:	From:04/01/2019 to:04/10/2019
Is Institution the Primary Grant Holder:	Yes
Contract Type:	Contract
BU SAP Grant Number or BMC AU Number:	123456789
Award Number:	123456789
Grant Title:	CRRO Presentation
Award Recipient: (If Award Recipient is not the same as identified on the study.)	BU/BUMC IRB

Study Summary

- **Summary written in lay language.**
- **Updating the summary:**
 - The study summary should be updated to reflect any major changes to study design, such as the addition of a research procedure.

7.0 Study Summary	
7.1 Provide a brief summary of the project in terms understandable to a non scientist (in 500 words or less). Do NOT copy from a grant application.	
 Click here to access the text editor.	
This presentation for a Clinical Research Seminar details the most common IRB application stipulations including how they may be avoided and how they can be addressed should they occur.	
6-Months Later:	
We would like to add a pre- / post- evaluation of audience members. This will include an optional box to indicate willingness to be interviewed about the presentation and the evaluation. Those willing to participate in the interview will be asked to provide their contact information.	

Navigation Menu

The Navigation Menu contains branching logic that creates the required sections based on your responses.

- Examples: separate protocol (more on this later), investigational drug or device, genetics, retaining data and/or samples for extra use



8.1 Separate Protocol

Is this a new submission with a separate protocol? This protocol must be from the sponsor or cooperative group or be based on the [protocol template](#) found on the IRB website, and must include the purpose, inclusion/exclusion criteria, design/procedure, and data safety and monitoring plan. A separate protocol is REQUIRED for all initial submissions of medical or surgical clinical trials. A GRANT APPLICATION IS NOT A PROTOCOL.

- Yes
- No
- Not applicable, this is not a new submission

Subjects

- Carefully read the prompts for the “Special Populations” section - there is a difference between “recruited” and “targeted”!

10.5 Special Populations (for more information, click on the (?) Help icon)

Please indicate if ANY (even one) of the following populations will be recruited (Note: Enrollment from any of these categories requires prior IRB approval):

- Minors who are wards of the State**
- Cognitively impaired subjects (will require use of an LAR, and assessment of ability to consent)**
- Employees, students, or trainees under the direct supervision of the PI**
- Minors**
- Minors independently making their own healthcare decisions**
- Non-English speaking subjects**
- Pregnant Women**
- Prisoners**
- Women of child-bearing potential

Please indicate if any of the following populations will be targeted by your research:

- BMC Residents or Fellows
- BU Dental Students
- BU Medical Students and/or Graduate Medical Sciences Students
- BU School of Public Health Students
- Homeless**
- Individuals with psychiatric disorders**
- Terminally ill patients**

Subjects

- Common stipulation: In Subject Section, please select “Pregnant Women” and “Women of childbearing potential.” While these groups are not going to be explicitly targeted, there is nothing in the eligibility criteria that excludes them. Please revise and in next section, please revise to note that no additional precautions are required for these vulnerable populations since their enrollment will be incidental and there are no additional group-specific risks.
- Conversely, there can be instances in which the inclusion of pregnant women wouldn’t be appropriate (i.e. investigational drug study in which the drug has been shown to cause birth defects).
- Additional protections are required when members of a vulnerable population will be enrolled:
 - How will you protect rights and welfare?
 - Obtain informed consent?
 - Prevent undue influence/coercion?
 - Risk minimization?
 - Protect confidentiality?

Design/Procedure

- Answer ALL of the questions (The 6 questions we ask do not represent an exhaustive list of all information the IRB may need to review your study)!
- Never copy what is written in your grant into the Design and Procedure section.
- Answer ALL of the questions within the section. As you're writing this section, you want to ensure that you are providing SUFFICIENT detail for your study. Sufficient detail does not mean that your response to this section needs to be 15 page word document.



Risks, Benefits & Justifications for Approval

- List the risks, how you will mitigate the risks, what the benefits are, and what the risk/benefit ratio is
- All studies have risks, even chart reviews have a risk of loss of confidentiality
- Distinguish between direct and no direct benefit; if later, must discuss social/science benefit
- If your study procedures inquire about self-harm thoughts or population is a risk for self-harm, a suicidality or other contingency plan in place to manage risks needs to be in place
- Give a study-specific justification for why the risk/benefit ratio is acceptable or favorable

13.3

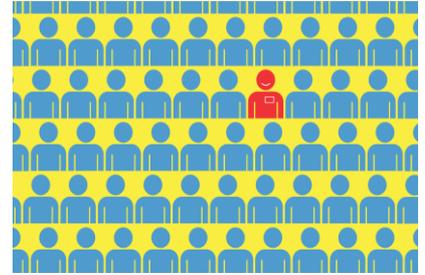
Risk to Benefit Ratio

Describe how risks to subjects are reasonable in relation to anticipated benefits:



[Click here to access the text editor.](#)

Recruitment?



1. Lacking sufficient detail to assess scheme.

“We’re going to recruit from our own patients in the XXX clinic”.

- Who is going to approach? PI or RA?
- How are you going to approach? In-person? Over-the-phone?
- When and where is this approach? During scheduled clinical appointment?
Private exam room?
- Will you be using any scripts? Any flyers? Are those attached?
- Will you be doing a pre-screen in the chart before approaching?
- If different cohorts/groups, how will you tailor your approach?

Recruitment?

2. Recruitment involves pre-screening in the medical record yet the HIPAA section is not filled out

- HIPAA section should **ONLY** list variables needed to determine eligibility

3. Recruitment materials have compensation info in big & bolded text or use the phrase “new treatment” w/o noting it’s investigational.

- All recruitment material needs to confirm to 7.2.2.6.3 of our policies



Recruitment: Ugh moments (and how to fix them)

- **Cold calls**
 - Opt-out letter
- **Approaches in the waiting room**
 - Clinic staff hands a flyer when checking in
- **Approaches by the study team in the clinic**
 - Introduction by known clinician (Warm Handoff)
- **Recruiting the same day as a clinical procedure**
 - Sending recruitment material ahead of procedure with follow-up phone call
- **Snowball sampling where investigator is getting list of potentially eligible people's contact info**
 - Subjects hand flyers to potentially eligible people with investigators' info



Screening

12.5 Screening

Will any sensitive information or protected health information (PHI) collected during the screening without obtaining consent be retained that can be linked to the potential subjects OR does the study require any clinical screening procedures (blood draw, fasting, etc) performed solely for the purpose of determining eligibility in this research?

Yes No

Will any potential subjects be directly contacted to obtain screening information?

Yes

No

Not Applicable - all screening activities have been completed for this already-approved study



Screening



Top Issues with Screening:

- 1) Incorrect Answer
 - a) If you're consenting and then having a screening visit, answer "NO"
 - b) If you need to obtain **any** information directly from the subject before consent, answer "Yes"
- 2) If you're interacting with potential subjects, you need to use a screening agreement.
- 3) The screening section isn't filled out completely.

16.0

Screening Procedures

16.1 Describe the procedures that will be used for screening to determine subject eligibility. If screening procedures are described in a separate protocol, indicate the protocol section here.

You need to have sufficient detail in order to assess your screening procedures.

Who is doing WHAT to WHOM, HOW, WHERE, and WHEN.

Remember to attach your screening documents/questionnaires

16.2 Describe what eligibility data will be stored and how it will be stored, who will have access, and when these data will be destroyed. For screening failures, please detail how and what data will be retained, if any, along with when these data will be destroyed. Please describe whether identifiers are being retained from those who screen out. Please note if contact information is being retained for future research.

Read and Answer this section, clause by clause. Most common mistake: What are you doing to do with screen fail data?

16.3 Describe the screening consent process. Full consent for screening is required if either of the following is true:

- identifiable sensitive information or PHI will be retained (retained as opposed to destroyed after being used to determine eligibility), or
- the screening involves clinical procedures

A Brief Screening Agreement may be used for all other screening. For full consent form templates and the Brief Screening Agreement Template, click [here](#).

Just like the main consent section: Who is doing the screening consent process; Where will the screening consent process take place; how, etc.

Unless you're retaining the data, you almost always can use the BSA.

HIPAA for Recruitment/Pre-screening

When accessing PHI w/o authorization, the IRB must grant a HIPAA waiver. To do this, we need to assess:

1. Why you need PHI
2. Why it's impracticable to get HIPAA authorization
3. How you'll protect the PHI
4. When you'll destroy identifiers.

You should only be assessing the absolute minimum to make an eligibility determination. **This isn't a chart review.**

HIPAA - Recruitment/Pre-Screening

#1 - You're pre-screening via medical records or reviewing the daily clinic schedule but the HIPAA section is not completed

#2 - You've completed the HIPAA section but the data points, storage, procedures, justifications, etc refer to the main study. The HIPAA section **ONLY** refers to the data, storage of data you need **BEFORE** consent/authorization.

#3 - Missing details or poor justifications (see my cheatsheet)



HIPAA - For recruitment

If you need to look at MRs or the daily clinic schedule, please state “YES” to the HIPAA section

Q3. Any patient presenting with XXXXX (from patient eligibility criteria)

Q4. Estimated start and end date of range of records needed in mm/dd/yyyy format.

Q5. All the datapoints you need to assess eligibility and to be able to approach the patient (date of appointment). Don't forget the identifiers: MRN (to access chart), Name, and Dates

Q7. Identifiers: MRN, name, dates, contact info - as applicable

Q8. "Recruiting without already knowing that the potential subject is probably eligible would require an inordinate amount of time for study staff and ineligible subjects" or similar

Q9. "Approaching ineligible subjects would waste their time and be confusing; eligible and interested subjects will provide authorization during consent." or similar

Q10. "All identifiable information will be transmitted, stored, analyzed, or otherwise exist only on electronic systems that meet the standards for protection of PHI."

Q11. "Identifiers will be destroyed as soon as eligibility has been determined for a potential subjects" or similar. NOTE: Often times need to keep identifiers through recruitment period to prevent rescreen. If you're doing this, state it here with note that list of names/mrns destroyed.

Speaking of HIPAA: Chart Review

- Use this pathway when your only research activity is a chart review of internal clinical records.
- If unfunded, chart review pathway is shorter than exempt.
- If externally funded, the application will change.
- Common Issues:
 - Specify: 1. WHO is extracting data, 2. HOW it will be extracted and 3. FROM WHAT SOURCE
 - Details about the abstraction: 1. temp list, delete as abstract, or 2. use a coding scheme
 - CDW involved? If not, why not?
 - Use specific date ranges in mm/dd/yyyy format
 - Confidentiality: State that -- Mastercode stored separate. All identifiable information will be transmitted, stored, analyzed, or otherwise exist only on HIPAA-compliant electronic systems that meet the standards for protection of PHI established by Boston Medical Center. Working dataset stored on password protected, encrypted computer.
 - **Fill out the HIPAA section!**



Chart Review: HIPAA section

(For future reference)

Q1: This should be YES since you are accessing medical records without authorization.

Q2: Please select "No" since you will need PHI for more than simply recruiting.

Q3: This should be your eligibility criteria - what will you be searching in EPIC to get what you want?

Q4: This should be the date range used in sections above.

Q5: Please state, "MRN (not stored with study data but needed for abstraction)" and then a listing of every data point including what you listed in Q7.

Q6: Complete as appropriate

Q7: Please state MRN and any of the other 17 identifiers (dates are commonly forgotten)

Q8: Research cannot be conducted without access to PHI as this is a retrospective study. The PHI are critical to identify, verify, and collect study images/data.

Q9: It is not practicable to obtain authorization from participants as this is a retrospective study and subjects are not nor will be at Boston Medical Center in the foreseeable future. Given the date range, contact information may be out of date, people may have moved, or passed away. Given the sample size, it would be impractical to obtain authorization from each subject.

Q10: All identifiable information will be transmitted, stored, analyzed, or otherwise exist only on HIPAA-compliant electronic systems that meet the standards for protection of PHI established by Boston Medical Center

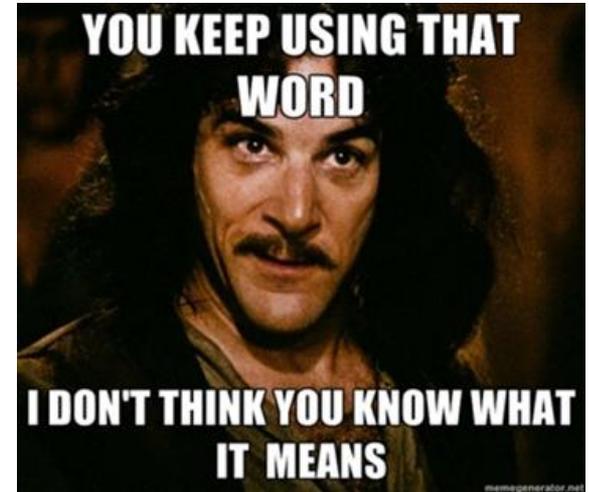
Q11: If there is a mastercode, please note when it will be deleted. Otherwise state that MRN will only be used to access record and never stored.

Confidentiality: Coded ≠ De-identified ≠ Anonymous

Coded: Identifiers have been removed (e.g., from data or specimens) and replaced with a code (words, numbers, etc) not derived from or related to the personal information. **BUT** identifiers are retained in a separate document that links with the code (mastercode, linking code, etc)

De-identified: All direct personal identifiers are permanently removed (e.g., from data or specimens), no code or key exists to link the information or materials to their original source(s), and the remaining information cannot reasonably be used by anyone to identify the source(s). *Note: HIPAA covered data is de-identified when it does not contain any of the 18 identifiers specified by the HIPAA Privacy (or has been determined to be de-identified by a statistician in accordance with the Privacy Rule).*

Anonymous: Identifiable (direct or indirect) information was not collected, or if collected, identifiers were not retained and cannot be retrieved.; Data/samples are *anonymous* if no one, not even the researcher, can connect the data to the individual who provided it.



Consent Form

- Use the IRB approved template on our website unless you have a Sponsor-provided consent (certain section require revisions)
- Use a consent statement for exempt studies such as survey studies

 [Exempt Information Sheet Template](#)

- Use the full consent form for all other studies where subjects will be consented

 [Adult Consent Form Template](#)

 [Parent Permission Form Template](#)

 [Parent Consent and Permission Form Template](#)

Consent Form

- Don't modify templated language
- Pay close attention to the instructions in the consent template
- Aim to have your consent form read at an 8th grade level or below
- Review the signature lines carefully and select what applies to your study
- The Certificate of Confidentiality language is required for all NIH funded studies
- Include the correct headers/logos and contact information



Data Safety Monitoring...plan? board?

Specific requirements depend on the risk level of the study.

- **Minimal Risk:** An appropriate plan consists of the PI reporting all Unanticipated Problems, Adverse Events, and deviations to the IRB according to IRB reporting requirements.
- **Greater than Minimal Risk:** A separate document detailing the Data Safety Monitoring Plan is required. If the study requires a separate protocol, the DSMP will often be included within this protocol.
 - A Data Safety Monitoring Board is not a requirement; however, many sponsored studies will have a DSMB or Data Monitoring Committee. In the case of a monitoring entity, the IRB will request the DSMB's or DMC's charter document.

Payment & Costs

Payment:

- Any payment for participation or reimbursement of travel costs is not considered a benefit

Costs:

- Refers to costs that the subject may be responsible for covering



Attaching a Separate Protocol

When?

- For studies that meet the definition of a clinical trial as describe in the BUMC/BMC HRPP policies and procedures; **and**
- Involve a medical intervention (drug, biological agent or device) or a surgical intervention/procedure intended to modify a health outcome

What's the deal?

- Attaching a separate protocol (answering yes to 8.1) collapses the application to avoid duplication of information;
- If your study does not require a separate protocol, but one is attached, this protocol must be updated throughout the life of the study.



Attaching Study Documents

Cannot approve word documents with tracked changes - please accept!

Word document is the preferred format because of comparison software, PDF's are second

In the event of a PDF document (such as a sponsor-provided protocol), please submit a redlined version of the document. If not possible, please outline the specific changes in a separate document.

Applies to all documents, but especially to consent forms:

- Please attach updated consent form documents as a revision to the currently approved consent form. This helps to keep track of consent documents and changes made over time.



Before submitting, remember to...

S - Simple

C - Consistent

R - Reread

E - Employ the templates

A - Address all the questions/instructions

M - Missing information



Was your question left
unanswered? Not to fret, just ask!

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