BOSTON MEDICAL CENTER
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Last Updated: 5-14-20

COVID-19-Releated Research Workflow and Review Processes

This document is intended to provide guidance to researchers at Boston Medical Center seeking to conduct COVID-19-related research. Please note that depending on the project, additional steps and/or approvals may be needed; however, this guidance is intended to provide a general overview of the various steps researchers need to take order to get a research project approved and necessary agreements in place. Not all projects will require all steps. Questions can be directed to the contacts listed below.

Process:

1. **NDAs. If given a non-disclosure / confidentiality agreement ("NDA/CDA") by outside research collaborator, send to the Clinical Trials Office ("CTO"):**
    a. Fill out the CDA/NDA request form here: https://www.bmc.org/cda/nda-intake-form, which will route to CTO **(**please select COVID-related, where indicated)
    b. Alternatively, contact: Sandy.Lok@bmc.org

2. **Protocol Development. Review protocol (if developed by collaborator) or develop protocol / proposal for research project**
    a. Consult the following resources in protocol development or finalization:
        i. Department Research Chairs
        ii. CRRO / CTSI: http://www.bumc.bu.edu/crro/
    b. *Note*: if your project contemplates targeting BMC employees as research participants, please:
        i. Consult **Addendum 1** below
        ii. Be sure to check the appropriate boxes on the IRB application
        iii. Be aware that Leadership approval may be needed

3. **Department Approval. For Departments or Sections requiring chief or chair approval for research proposals (as needed)**

4. **IRB / IBC Review. Submit Institutional Review Board application and Institutional Biosafety Committee application (as needed)**

5. **Committee Reviews. Submit proposal to applicable COVID-19 research review committees:**
    a. For INTERVENTIONAL AND NON-INTERVENTIONAL INPATIENT projects (e.g., clinical trials, diagnostic devices, testing) on human subjects, submit to **the BUMC COVID Human Subjects Research Review Committee** as follows:
        i. Interventional research (e.g. drugs, biologics, treatments)
            1. Complete applicable cover sheet (**Exhibit A.1)** and protocol synopsis (**Exhibit B)**
            2. Email Johanna Chesley (johanna.chesley@bmc.org) and Ben Linas (Benjamin.linas@bmc.org)

        ii. Non-interventional, prospective sample collection review (e.g., blood, breast milk collection, semen collection)
            1. Complete cover sheet (**Exhibit A.2**) and protocol synopsis (**Exhibit B**)

2. Email Johanna Chesley (johanna.chesley@bmc.org) and Ben Linas (Benjamin.linas@bmc.org)
3. Sample processing and storage requests may also be sent to Biospecimen Committee to address pathology related needs.

b. For AMBULATORY SETTING projects (including interventional and non-interventional outpatient studies), submit the project for review as follows:
   i. Interventional:
      1. Complete cover sheet (**Exhibit A.1)** and protocol synopsis (**Exhibit B**)
      2. Email Minhao Yin (Minhao.Yin@bmc.org)

   ii. Non-Interventional:
      1. Complete cover sheet synopsis (**Exhibit A.2**) and protocol synopsis (**Exhibit B**)
      2. Email Minhao Yin (Minhao.Yin@bmc.org)

c. For projects requiring access to BANKED BIOSPECIMENS (*not prospective requests, see sections 5.a. and b. above for prospective specimen collection reviews*), submit to **the Biospecimen Committee** as follows:
   i. E-mail: Tyler.Flack@bmc.org and Gina.Daniels@bmc.org
   ii. Complete intake form
      1. Indicate on the intake form whether autopsy samples will be used. Such requests will be directed to Chris Andry, as needed.
   iii. Complimentary data from the CDW will be addressed as part of the biorepository review. Once approved by Biospecimen Committee, the investigator will be directed to the CDW to fulfill data needs.

d. For DATA-ONLY REQUESTS for COVID-related projects, submit as follows:
   i. Clinical Data Warehouse (CDW) Requests:
      1. E-mail: COVIDResearchAdmin@bmc.org
      2. Complete CDW COVID request form

   ii. Other Database/Resource Data Requests: For questions or data requests for COVID-related projects that do not involve the CDW (e.g., chart review), but would still access BMC or other source data, please contact Michelle.Irick@bmc.org.

6. **Legal Agreements. If transferring data, materials, or anything else with third parties / research collaborators, and/or to request any necessary agreements:**

a. For data and/or material transfer agreements, or proposed research collaborations that may entail the exchange of material and/or data:
   i. Complete agreement request form available here: https://www.bmc.org/sites/default/files/Research/documents/DUA.MTA_Request_Questionnaire.docx[1]
   ii. Attach any associated committee review intake forms (CDW, Biospecimen, etc.)
   iii. Email form with any data/material transfer agreement provided by external collaborator (if applicable) to DUA.MTARequest@bmc.org[2]

[1] E-mail DUA.MTARequest@bmc.org if you have any issues accessing the form.
[2] This will be routed to research attorneys, so no need to copy research attorneys on e-mails requesting DUA / MTA review.

7. **<u>Other Contracts / Subawards</u>. If sponsored/funded or other type of research agreement (e.g. subaward, CTA), send to CTO or Grants and Contracts as normal:**

   a. CTO: clinical trials and other research requiring IRB review
      i. CTO@bmc.org OR upload to Velos
   b. Grants and Contracts: basic science, non-interventional research, etc.
      i. Grants.admin@bmc.org

<u>For questions on any of the above referenced processes, key contacts include</u>:

- Clinical Trials Office ("CTO"): CTO@bmc.org
  - Johanna Chesley (Johanna.Chesley@bmc.org)
- Material transfer / data transfer agreement box:
  - DUA.MTARequest@bmc.org
- Research Attorneys:
  - Jamie Flaherty (Jamie.flaherty@bmc.org); Will McIntire (Will.McIntire@bmc.org)
- Questions on biorepositories
  - Tyler Flack (Tyler.Flack@bmc.org); Gina Daniels (Gina.Daniels@bmc.org)
- Questions on data transfers / accessing the CDW
  - Michelle Irick (Michelle.Irick@bmc.org); Tyler Flack (Tyler.Flack@bmc.org)
- Authorized Signatories
  - Grace Cashman (Grace.Cashman@bmc.org); Stephanie Wasserman (Stephanie.Wasserman@bmc.org)

[*Exhibits / Appendices Below*]

EXHIBIT A.1

COVER SHEET (PHARMACOLOGIC)

BUMC COVID Human Subjects Research Review
(Interventional Pharmacologic)

Protocol Title	
PI name	
PI title	
PI primary affiliation	
PI email	
PI cell #	
Sponsor	
Co-investigators	
# of BMC Participants	
Projected Start Date	
Compound Type	
Committee Approved Compounds	

Compound	Drug	Patient Type
Antiviral	Favipiravir	Inpatient
Antiviral	Selinexor	Inpatient
Antiviral	Hydroxychloroquine (Prophylaxis)	Ambulatory
Antiviral	Hydroxychloroquine (Out PT TX)	Ambulatory
Antiviral	Remdesivir (5773)	Inpatient
Antiviral	Remdesivir (5774)	Inpatient
IL-1 Inhibitor	Canakinumab	Inpatient
IL-6 Inhibitors	Tocilizumab (TCZ)	Inpatient
JAK Inhibitor	Ruxolitinib	Inpatient
Antibody	HT-CCP	Inpatient
C5 Inhibitor	Eculizumab- EAP	Inpatient
C5 Inhibitor	Ravulizumab- RCT	Inpatient
Topoisomerase 2 Inhibitor	Etoposide	Inpatient
IL-1b and IL-18 Inhibitor	MAS825	Inpatient

Proposed Compound Justification	
Inpatient/Ambulatory	☐ Inpatient ☐ Ambulatory
Ancillary Services	☐ Pathology/Lab Medicine ☐ Nursing ☐ Radiology ☐ GCRU ☐ Investigational Pharmacy

EXHIBIT A.2

COVER SHEET (NON-PHARMACOLOGIC)

BUMC COVID Human Subjects Research Review
(Interventional Non-pharmacologic)

Protocol Title	
PI Name	
PI Title	
PI Primary Affiliation	
PI Email	
PI Cell	
Sponsor	
Co-Investigators	
# of BMC Participants	
Projected Start Date	
Inpatient/Ambulatory	☐ Inpatient ☐ Ambulatory
Ancillary Services	☐ Pathology/Lab Medicine ☐ Nursing ☐ Radiology ☐ GCRU ☐ Investigational Pharmacy

EXHIBIT B

PROTOCOL SYNPOSIS

BUMC COVID-19 HUMAN SUBJECTS STUDY PROTOCOL SYNOPSIS

STUDY OVERVIEW

TITLE:

PROTOCOL NUMBER:

INVESTIGATIONAL PRODUCT:

PHASE:

TARGET INDICATION:

OBJECTIVES:

RATIONALE:

POPULATION

INCLUSION CRITERIA:

EXCLUSION CRITERIA:

STUDY DESIGN

STUDY DESIGN AND DURATION:

EFFICACY ENDPOINTS:

SAFETY ENDPOINTS:

BRIEF STATISTICAL PLAN:

SAMPLE SIZE DETERMINATION:

FEASIBILITY AND LOGISTICAL CONSIDERATIONS

AT WHAT POINT IN THE HOSPITAL COURSE DO YOU IMAGINE OBTAINING INFORMED CONSENT?

WHAT RESOURCES WILL YOU HAVE TO IMPLEMENT THE PROTOCOL?

ADDENDUM 1

GUIDANCE – ENROLLING BMC STAFF AS RESEARCH PARTICIPANTS

Guidance: Considerations for Research Involving BMC Employees as Participants

This guidance highlights key legal, ethical, and practical considerations to consider for BMC research projects enrolling BMC employees as participants. This is not intended to be an exhaustive list; depending on the research plan / protocol, or changes in law, there may be other issues or points to consider. To mitigate such risks, researchers should review and adopt the strategies described in the far right-hand column, as may be applicable.

Researchers intending or expecting to enroll BMC employees should discuss with the IRB / check off the corresponding boxes on the IRB's INSPIR application. Certain projects proposing to enroll BMC employees may be routed to BMC leadership for review and sign-off. If you have any questions about this guidance, please feel free to contact Jamie Flaherty (Senior Research Counsel): jamie.flaherty@bmc.org, another member of the Legal team, or your IRB analyst.

Potential Concern	Concern Type	Description	Example	Strategy to Mitigate Risks
Americans with Disabilities Act ("ADA")	Legal	The ADA prohibits an employer from (1) requiring that an employee undergo a medical examination, or (2) making inquiries of an individual regarding whether he or she is an individual with a disability unless the examination or inquiry is job-related and consistent with business necessity. Research protocols, depending on what they entail, could include activities that could be considered a "disability-related inquiry." The EEOC has provided some examples of such inquiries, which include asking	Research protocol involves broad health questionnaire or screening that could potentially prompt the employee to disclose a disability.	1. Research protocols involving BMC employees should ideally contain no disability-related questions 2. Ensure study / research records are completely separate and distinct from employee / HR / personnel records 3. If possible, have consenting and research activities take place offsite so that participation in the study is kept separate from employment duties 4. Draft the consent form[1] to include language stating that participation in the program or refusal to do so will not affect the individual's employment status or opportunities for advancement a. Sample language: "If you are an employee of Boston Medical Center, your decision will not affect your

[1] The IRB can assist with providing guidance on appropriate language for consent forms.

Potential Concern	Concern Type	Description	Example	Strategy to Mitigate Risks
		broad questions that are likely to elicit information about a disability.		employment. Participation in this study is completely voluntary and separate from your employment, and will have no bearing on your employment status or affect opportunities for career advancement." 5. Consent form should also state records will be kept distinct from personnel records 6. Prevent supervisor awareness of employee involvement in research (i.e., supervisors should not seek to recruit their supervisees, should not ask about participation in any studies, be involved with the consent process, etc.)
Genetic Information Nondiscrimination Act ("GINA")	Legal	To the extent a research study entails genetic testing, GINA (1) prohibits use of genetic information in employment decision-making; (2) restricts employers and others subject to GINA from requesting, requiring, or purchasing genetic information; and (3) requires that genetic information be maintained as a confidential medical record, and places limits on disclosure of genetic information. 29 CFR 1635.1(a). Under GINA, "requesting" is interpreted broadly, and includes requesting information about an individual's current health status in a way that is likely to result in the employer obtaining genetic information. See 29 CFR 1635.8(a).	Protocol involves genetic testing or solicits genetic information via study questionnaire.	1. Avoid having employees involved in genetic testing studies 2. Same steps to alleviate ADA concerns (see above) a. Language in consent form could specifically provide: "If you are an employee of Boston Medical Center, your decision will not affect your employment. Participation in this study is completely voluntary and separate from your employment, and will have no bearing on your employment status or affect opportunities for career advancement. By signing this consent form, you understand and agree that any information or samples you provide are provided voluntarily and for purposes of the Study, and that Boston Medical Center is neither requesting nor requiring any genetic information from

Potential Concern	**Concern Type**	**Description**	**Example**	**Strategy to Mitigate Risks**
				you by virtue of your participation in this Study."[2]
Clinical Laboratory Improvement Amendments ("CLIA")	Legal / Ethical	Laboratories testing employee samples must be CLIA certified in order to return results. If testing is done in a non-CLIA certified lab, results cannot be returned. This raises ethical questions and complexities, however, if such results may not be returned.	Research protocol involves taking blood. Blood test reveals employee is HIV positive.	1. Unlinking samples tested (though query whether that is ethical / would hinder employee interest in the study) 2. Having lab tests run in CLIA-certified lab 3. Making it clear in the consent form that results will not be returned unless conducted in CLIA-certified lab
Undue influence, coercion, pressure on employees to participate	Ethical (and regulatory)	Employees may feel pressured to participate in BMC research projects. FDA has acknowledged the potential for coercion or undue influence when employees participate in research: "For example, when an employing party seeks to enroll employees in a clinical investigation sponsored or conducted by the employing party, the protocol should contain safeguards to ensure that participation is voluntary and that there is no undue influence by supervisors, peers, or others." FDA Informed Consent Guidance. The HHS Office of Research Protection has similarly flagged such concerns: "Employee participation raises questions about the ability of employees to exercise free choice, for example, because of the possibility	Employee learns that other members of his/her team are participating and feels pressure to participate. Employees seeking testing at Working Well clinic for COVID presumably already are scared, don't feel well, etc., but may feel pressured to participate given importance.	1. Respecting employee autonomy if they truly do wish to participate in research 2. Separating research records from HR records 3. Specific employees should not be targeted 4. Outreach should be passive (i.e., not in person, but rather posted broadly with flyers, general e-mail circulated, etc.) 5. Supervisors should not recruit or be involved with the recruitment of their supervisees 6. Supervisors should not discuss participation in any studies with their supervisees 7. Emphasize voluntariness in recruitment materials, consent form, etc. 8. Employees should preferably not be compensated for participation. If they are, it should be commensurate with the time and effort associated with the study activities, and consistent with amounts received by non-employee participants (if any)

[2] The IRB can assist with providing guidance on appropriate language for consent forms.

Potential Concern	Concern Type	Description	Example	Strategy to Mitigate Risks
		that a decision to participate could affect performance evaluations or job advancement, even if it is only the employee's perception that this is the case. In the case of coercion, refusal to participate might result in a loss of benefits (e.g., salary increases, time off). In the case of undue influence, a decision to participate could result in a job promotion. Employees are likely to view their employers as authority figures to whom they must show deference, which could undermine the freedom of their choice." HHS Informed Consent FAQs.		
Data integrity / self-experimentation	Ethical, practical	Employee participation in a research study with which he or she is involved raises questions of self-experimentation, bias, data integrity, etc.	Research coordinator / PI / study team member decides to complete questionnaire, provide samples, test his/her own blood, etc. for his/her own study	1. Researchers should not participate in their own research study
Human Resources	Practical	Employees may request time off to participate, or may use working time to participate in a study. If ever terminated or disciplined, employee could argue it stems from his or her participation in study, or lack thereof, or as a result of information learned about employee during study.	Instead of clinical time, employee spends time completing research questionnaire, engaging in research activities, etc. If employee is later disciplined, employee could potentially argue that it is discrimination due to something the	1. Ensure separation of research records and HR records 2. Ensure employee-participants understand that participating in the study is separate and distinct from their BMC employee responsibilities

Potential Concern	Concern Type	Description	Example	Strategy to Mitigate Risks
			institution may have learned due to his / her participation in the study.	
Institutional reputational or other harm	Legal, practical	Want to facilitate and encourage important research to be conducted, but ensure steps are taken before BMC confidential information, proprietary policies or process, or employee identifiable information is published, shared, or released externally Study results could open BMC up to legal risk, cause concern among employees, etc.	Study describes steps BMC has taken to address X. Results may reveal some sensitive BMC information or some gaps / areas for potential improvement. Depending on what the results are and how sensitive, could expose BMC to legal and reputational risk.	1. Consider whether project is more quality improvement / quality assurance[3] 2. If truly sensitive, perhaps the project might need to be a privileged internal assessment. Consult Legal or Compliance if you have any questions. 3. Understand what may be appropriate to publish and release (generally aggregate results, study results) and what may not be (BMC proprietary or confidential information, identifiable or individual-level employee data). Consult Legal or Compliance if you have any questions.

[3] For article describing difference between quality improvement ("QI") projects and research, see: https://irb.research.chop.edu/quality-improvement-vs-research. QI projects generally are "designed to implement knowledge, assess a process or program as judged by established/accepted standards."