"I have SOPs and know how to use 'em!"

Ryan Schroeder, Director, Clinical Research Network, BMC
Mary-Tara Roth, Director, Clinical Research Resources Office, BU Medical Campus
Duncan Schulte, Research Regulatory Project Manager, Clinical Research Network, BMC

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SOP STEERING COMMITTEE

Steering Committee

Executive Leadership:
Ravin Davidoff, David Center
Co-Chairs
CRN: Ryan Schroeder; CRRO: Mary-Tara Roth
Research Operations:
Executive Director, Tina Dasilva
CTO: Johanna Chesley
Research Compliance/Education: Kaye Mottola
BMC Research Compliance:
Craig Bennett, Jami Wood
CTSI/GCRU:
George O'Connor, Helia Morris, Ridiane Denis
OHRA:
Matt Ogrodnik
IRB:
Jamie Merrill

SOP Approvers

Chair: Tina Dasilva, Research Operations

OHRA: Matt Ogrodnik

BMC Research Compliance: Craig Bennett

SOP Review Departmental Volunteers

- Invitations went out to research department chiefs to seek volunteers from subject matter experts within BMC and BU.
- **New SOPs Going Forward**: After the initial library of SOPs are established, department representatives can initiate requests for additional SOP development to add to the central library

SOP Working Group

Duncan Schulte
Clinical Research Network
Regulatory Project Manager

Rana Leed, MPH
Human Research Education Manager

Mary-Tara Roth, RN, MSN, MPH
CRRO Director

Ryan Schroeder
Clinical Research Network, Director

Seminar Objectives

- Describe the importance of SOPs to clinical and human research
- Review BMC SOPs
  - Why were they developed?
  - What are they?
  - Who needs to use them?
  - Is there required training?
- How to use SOPs in development of study-specific workflows?

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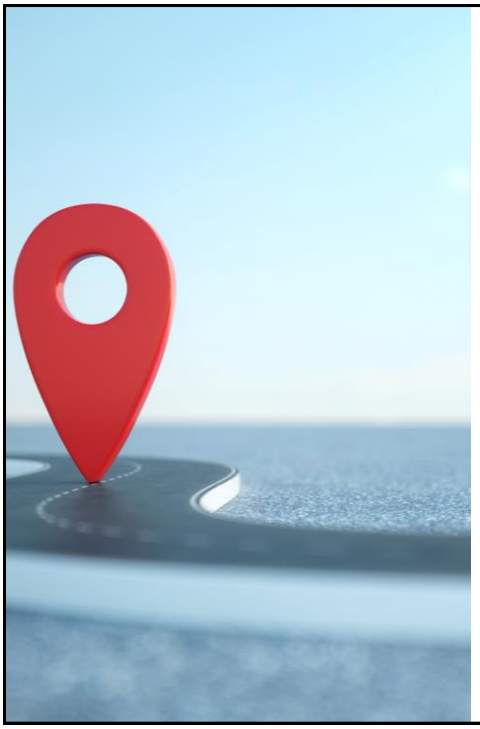

BMC has new SOPs and here's why.

AUDIT FINDINGS RELATED TO SOPS & TRAINING GAPS:

- BMC was missing foundational clinical research SOPs
- BMC did not have an SOP development, review and approval process to ensure compliance with requirements of study protocols, internal policy and ICH GCP standards
- Findings related to training inconsistencies and management of training documentation

HIGH LEVEL GOALS

- Ensure the trust and safety of our patients who volunteer to participate in research
- Ensure the quality of research conducted at BMC to the highest standards
- Provide our physicians and staff with the tools and training to perform their roles with standards of excellence
- Create a set of unified standards for the conduct of clinical research at BMC that spans across BU and BMC affiliation
- Create a long-standing sustainable structure that supports development and maintenance of SOPs that will guide research conducted at BMC

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Upcoming Key SOP Dates/Milestones

- **January 1, 2024:** all **new** studies targeting BMC patients, utilizing BMC facilities and/or services, or using BMC patient data will require completion of training prior to IRB approval
- **January 1, 2024**: **new** BMC staff working on studies within scope are required to complete training within 90-days of employment start date
- **December 31, 2024**: All clinical research investigators and staff are encouraged to complete training (*regardless as to whether studies started prior to 1/1/24*)

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Importance of SOPs

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What are SOPs?

Standard Operative Procedures

- "Written instructions for doing a specific task in a certain way." *NIH NCI*
  - Describe step-by-step process
  - Ensure process follows same steps no matter who is doing the activity

SOPs are an essential component of any Quality System!

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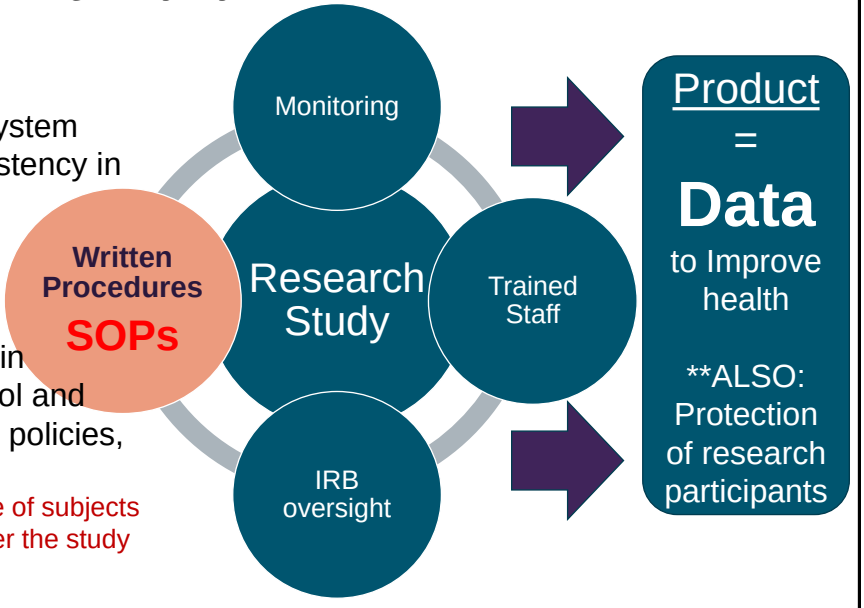
Clinical Research as a Quality System

SOPs:

- Key element of a Quality System
- Designed to promote consistency in processes

GOALS:

- Ensure consistency
- Ensure study is conducted in accordance with the protocol and applicable standards (regs, policies, etc.)
  - Protect rights, safety, welfare of subjects
  - Ensure quality data to answer the study question



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"Quality is free…. What costs money are the 'unquality' things – all the actions that involve not doing jobs right the first time."

Philip B. Crosby, *Quality is Free*

SOPs are a quality control measure: Help to get it right, the first time….

Benefits of SOPs in a human research quality system

- Provide a framework for excellence in research
  - Key to protecting subjects
  - Key to ensuring reliable, high quality data
- Helps to ensure the study meets necessary standards for conducting the research
  - Reduce errors → reduce risk
- Promotes consistency/reproducibility in conducting the study *within* sites, *between* individuals, *between* sites
- Gives study teams more control in overall quality
  - Proactive vs. reactive
  - Increase staff efficiency
    - Improves quality; ultimately saves time
- Promotes staff confidence
- Aids in training and onboarding of staff
- Build quality from the start; helps the study team be "audit-ready"
  - Lessens findings from audit and monitoring visits
  - Lessens work associated with addressing findings

Sponsors look favorably on institutional SOPs; provide assurance of high-quality research conduct at the institution

Why institutional SOPs?

- Part of our institutions' (BMC and BU) efforts to ensure the highest quality research
- It is becoming more and more an expectation of industry sponsors and government funders that institutions have SOPs to guide clinical/human research
  - Indicator of quality research
- Institutions can also have confidence that study teams are using/sharing institutionally-endorsed SOPs that align with the regulations, institutional policies, best practices – these practices help meet institutions' goals for research.

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Development/Maintenance of BMC SOPs

- Working Group and Steering Committee
- Identify and create critical SOPs (15 total)
- Assembled network of research experts across BMC and BU to review and provide feedback
- Incorporate feedback and finalize drafts for Steering Committee approval
- Decisions on scope of SOPs and training requirements
  - Scope: SOPs will specifically guide clinical research studies that target BMC patients, use BMC patient data, or utilize BMC facilities and/or services.
    - Training on and use of SOPs is required for research "in scope"
    - The SOPs are a great resource for those "outside of scope"!
- Phased deployment of SOPs: use of and training
  - Jan 1, 2024, training required for new studies and new staff (within scope)
  - Dec 31, 2024, training encouraged for all studies within scope
- Maintenance of SOPs
  - Annual review/updating as necessary
  - On-going feedback from SOP users
    SOP Feedback Intake Form
  - Development of new SOPs as needed per steps above

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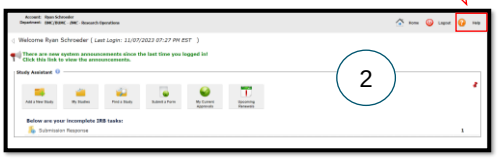
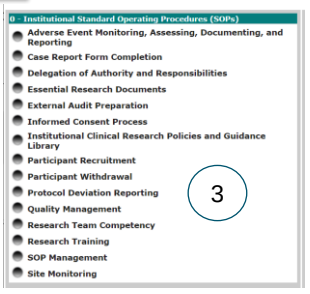
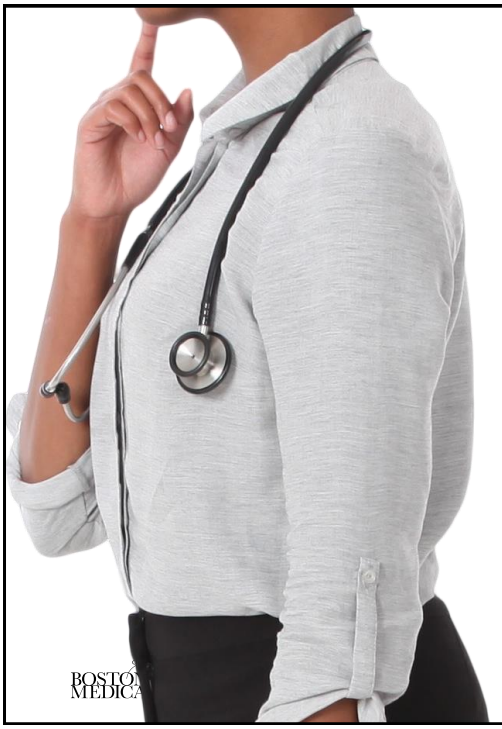
What SOPs were developed, and where can I find them?





Approved BMC/BU SOPs

- Institutional Research Policies and Guidance Documents SOP
- Research Training
- Quality Management
- Research Team Competency
- Essential Research Documents
- Participant Recruitment
- Protocol Deviation Reporting
- Adverse Event Monitoring, Assessing, and Reporting
- Case Report Form Completion
- Site Monitoring Visits
- Participant Withdrawal
- External Audit Preparation
- Delegation of Authority and Responsibilities
- Informed Consent Process
- SOP Management



Who Do These SOPs Apply To?

These SOPs guide all clinical research studies that target **BMC patients**, use **BMC patient data**, or utilize **BMC facilities and/or services**.

- BMC patients: any individual with a clinical encounter generating a BMC specific medical record
- BMC patient data: patient data derived from BMC medical records and/or systems
- BMC facilities: clinical or non-clinical space owned or operated by BMC
- BMC services: a unit or group operated or managed primarily by BMC staff (e.g. IPS, CRN, CDW, CTO, Laboratory Services, etc.)

1 Two Tiers of Training – Not a One Size Fits All Approach 2

Fundamental SOP Training- All SOPs listed must be reviewed and acknowledged by all individuals whose research activities are not exempt categories 4, 9, 10 or Expedited Non-Exempt Category 5. **In general, these are studies that are interacting with research subjects.**

- Institutional Clinical Research Policies and Guidance Library
- Research Training
- Quality Management
- Research Team Competency
- Essential Research Documents
- Participant Recruitment
- Adverse Event Monitoring, Assessing, and Reporting
- Case Report Form Completion
- Site Monitoring Visits
- Participant Withdrawal
- External Audit Preparation
- Delegation of Authority and Responsibilities
- Informed Consent Process
- SOP Management

Abbreviated SOP Training- Subset of SOPs that must be reviewed and acknowledged for all whose research activities the IRB has determined to be exempt categories 4, 9, 10, or expedited non-exempt category 5-only. **In general, these are studies that are limited to data and/or biospecimen analysis.**

- Institutional Clinical Research Policies and Guidance Library
- Research Training
- Quality Management
- Research Team Competency
- Essential Research Documents
- Protocol Deviation Reporting

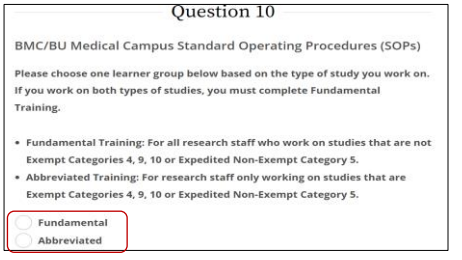
CITI Training – How to Access?

Step 1: Log on to CITI: www.citiprogram.org and sign in as you usually do to access CITI training.

Step 2: At the Welcome page, click on Boston University Medical Campus/Boston Medical Center "**View Courses**."

Step 3: Scroll down to "**Learner Tools**" at the bottom and select "**Add a Course**."

Step 4: Scroll down to **Question 10**; select appropriate training.



Step 5: Review each SOP and take each SOP quiz.

Step 6: If you successfully complete the training it will be uploaded into your INSPIR record of required trainings.

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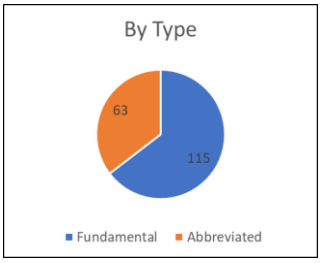
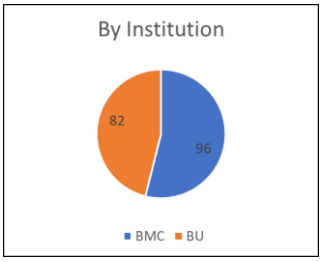
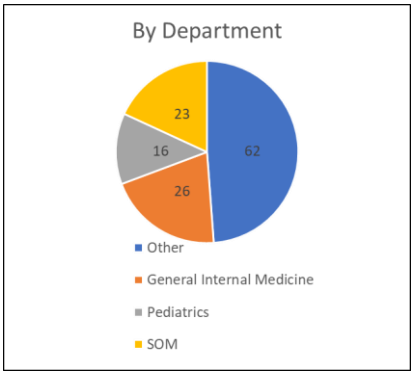
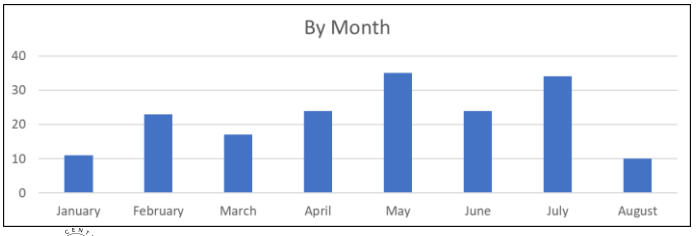
SOP Training Update









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Department List with at least 1 person completing Fundamental or Abbreviated Training

- Amyloidosis Center
- Anatomy and Neurobiology
- Anesthesiology
- Biomedical Genetics
- Biostatistics and Epidemiology Data Analytics Center (BEDAC)
- Boston Medical Center
- Cardiology
- Center for Behavioral Science Research
- Clinical and Translational Science Institute (CTSI)
- Clinical Research Resources Office
- College of Arts and Sciences (CAS)
- College of Engineering
- Colon And Rectal Surgery
- Community Health Sciences
- Computational Biomedicine
- Department of Medicine
- Dermatology
- Division of Graduate Medical Sciences
- Emergency Medicine
- Endocrinology, Diabetes, Nutrition, Weight Management
- Environmental Health
- Epidemiology
- Family Medicine
- Framingham Heart Study
- General Clinical Research Unit (GCRU)
- General Dentistry
- General Internal Medicine
- Genetic Counseling Program
- Geriatrics
- Health Law, Policy and Management - HLPM
- Hematology/Medical Oncology
- Henry M. Goldman School of Dental Medicine
- Infectious Diseases
- Medical Education
- Nephrology
- Neurology
- Nursing
- Obstetrics and Gynecology
- Office Based Addiction Treatment (OBAT)
- Office of Human Research Affairs
- Ophthalmology
- Orthodontics
- Otolaryngology Surgery
- Pediatric Infectious Diseases
- Pediatrics
- Periodontology and Oral Biology
- Pharmacy
- Physiology & Biophysics
- Psychiatry
- Psychology
- Pulmonary Disease and Critical Care
- Radiation Oncology
- Radiology
- Research Operations
- Rheumatology
- Sargent College of Health and Rehabilitation Sciences
- School of Medicine
- School of Public Health
- School of Theology
- Surgery
- Vascular Neurology
- Virology, Immunology, Microbiology

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Examples of how SOPs can promote and result in better quality

QA findings and SOPs

How can using SOPs improve quality of study conduct?

QA Review Finding
Informed Consent:
Incorrect/Unapproved version of Consent form used

Example:

Participant signed a Spanish version of the informed consent form that was missing the IRB approval date stamp. The Spanish version of the consent form had never been submitted to the IRB and was therefore unapproved.

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How would the SOPs have guided this study team?

Informed Consent Process and Documentation

- Only the current IRB-approved version of the consent form can be used. If a hard-copy consent form is used printing the consent directly from the IRB system on the day of the visit is best practice but can be printed out a few days in advanced if needed. Similarly, if e-consent is used, research teams must ensure the most up-to-date version of the IRB-approved consent form is used.
- The consent discussion should only be conducted by the Investigator or Research staff members who are 1) delegated this role by the PI (see Delegation of Authority and Responsibilities SOP), and 2) have the appropriate training and qualifications to perform this study task. Training and delegation should be documented in the regulatory files.
    - For research studies that involve a drug, device or surgical procedure, the process and consent discussion must involve a Licensed Independent Practitioner (LIP) unless the IRB has approved an alternative process that protects rights and welfare of participants. The LIP should discuss the purpose, risks, benefits and alternatives of the research. If conducting the full consent discussion, the LIP can sign and date the consent form as the staff member conducting the discussion. If the consent process involves another member of the research team who signs and dates the consent form, then there should be sufficient documentation (such as a progress note) to show that the LIP was involved. See HRPP Policies and Procedures 8.1.3.7.

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QA Review Finding
Informed Consent: No LIP Involved

Example:

For 6 study participants, there was no documentation that a LIP was involved in the consent process as required for studies involving an investigational drug.

According to the study team, study coordinators were conducting the informed consent process independently with no LIP.

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How would the SOPs have guided this study team?

Informed Consent Process and Documentation

- Only the current IRB-approved version of the consent form can be used. If a hard-copy consent form is used printing the consent directly from the IRB system on the day of the visit is best practice but can be printed out a few days in advanced if needed. Similarly, if e-consent is used, research teams must ensure the most up-to-date version of the IRB-approved consent form is used.
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QA Review Finding
AE Monitoring/Reporting: No Documentation of AE Assessment

Example:

Follow-up calls with study participants indicated multiple potential adverse events.

There was no documentation that a study doctor reviewed/assessed AEs, which may have impacted participant safety and/or the validity of study data

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How would the SOPs have guided this study team?

Documenting Adverse Events

- When an AE is identified, the PI or research staff must document the event(s) within study records. Some research teams might also decide to document the event within medical records if the event has implications for clinical care.
- Documentation may be completed on paper or electronically. Research teams should develop or have available these forms prior to beginning enrollment. Best practice includes an AE log to record high-level information and participant-specific documentation forms to record additional details. Research teams can make their own decisions where they document specific information: a log and/or participant-specific documentation forms.
- Regardless of the specific form or log, documentation should include the following:
  - Key dates associated with the events and event reporting
    - Date the event occurred
    - Date of first knowledge of the event by any member of the research team
    - Date of initial assessment
    - Date(s) of any follow-up assessments
    - Date(s) event is reported (IRB, Sponsor, etc. See Reporting section below.)
    - Date of resolution if and when known
  - Key history of the event including resolution details if and when known
  - Relevant medical history if appropriate for event
  - A plan for medical or clinical follow-up if appropriate for the event
  - Assessment of the event as described below (seriousness, severity, relatedness, expectedness) as appropriate/relevant for the study
  - Staff member documenting the event
  - Investigator(s) providing assessment and medical review. This individual should be qualified by training, experience, and license as applicable to the study, and delegated the role by PI if this individual is not the PI
  - Reporting requirements and outcomes when appropriate

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Putting SOPs to work…a case study

Duncan Schulte, CRN Regulatory Project Manager

SOPs can bridge the gap between a study protocol and study-specific workflows

Study Protocol

Table 2. Schedule of study procedures

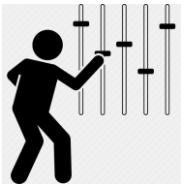
	Screening	Baseline
PROCEDURE	Day -14 to 0	Day -2 to 0
Informed consent	X	
Demographics	X	
Medical History	X	
Concomitant Medications	X	X

Study-Specific Workflows

Ex. Informed Consent Process- Workflow considerations

- Must meet regulatory requirements
- Use of IRB approved consent form
- Consideration of special populations
- Schedule of personnel obtaining consent
- Space and time for conducting consenting process
- Documenting consent process
- Availability of consent form ahead of consent discussion
- Flow from consent to Screening procedures
- Providing consent form copies after signing
- Remote or eConsent scenarios

SOPs help a study team to:

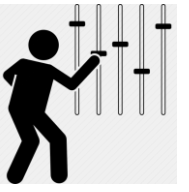


Calibrate to a standard
- Regulatory requirements
- Best practices
- Study team responsibilities

Communicate the standard
- Create expectations for PI/study team
- Improve training of staff and onboarding
- Deliver localized standards to a sponsor

Cultivate a culture of compliance
- Quality management
- Self assessment
- Consistency of effort

Calibrate to a Standard



- **Does the consenting plan for this study meet all the requirements?**
  - BMC SOP on Informed Consent (from INSPIR)
  - HRPP Policies
  - IRB Approved Plan
  - Study Protocol
  - Sponsor Expectations
- **You likely need to recalibrate when:**
  - Planning start-up of a new study
  - Changes to regulations or site operations affect workflows
  - Issues with compliance become a pattern of activity

Communicate the Standard

- **Create expectations for PI/study team**
  - Space and Time commitments
  - Document Storage Locations
  - Roles and Responsibilities
- **Improve training of staff and onboarding**
  - Localized details that provide best practice in context
  - E.g. CITI GCP vs. SOP
- **Deliver localized standards to a sponsor**
  - Respond quickly with accurate information
  - Stop encroachment of Sponsor oversight or lack thereof

Examples:
- Informed Consent
- Study Monitoring

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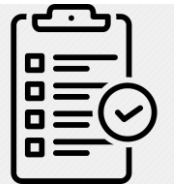
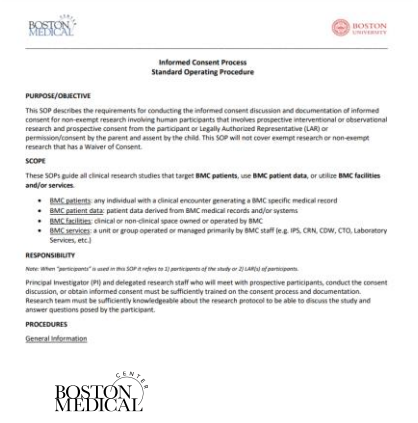
Cultivate a Culture of Compliance



Goal for Informed Consent Workflow Ex:
- A procedure for ensuring that the consent process is being conducted in accordance with [regulatory requirements] and that study subjects understand the nature of their participation and risks



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Informed Consent Process
Standard Operating Procedure

PURPOSE/OBJECTIVE

This SOP describes the requirements for conducting the informed consent discussion and documentation of informed consent for non-exempt research involving human participants that involves prospective interventional or observational research and prospective consent from the participant or Legally Authorized Representative (LAR) or permission/consent by the parent and assent by the child. This SOP will not cover exempt research or non-exempt research that has a Waiver of Consent.

SCOPE

These SOPs guide all clinical research studies that target **BMC patients**, use **BMC patient data**, or utilize **BMC facilities and/or services**.

- BMC patients: any individual with a clinical encounter generating a BMC specific medical record
- BMC patient data: patient data derived from BMC medical records and/or systems
- BMC facilities: clinical or non-clinical space owned or operated by BMC
- BMC services: a unit or group operated or managed primarily by BMC staff (e.g. IPS, CRN, CDW, CTO, Laboratory Services, etc.)

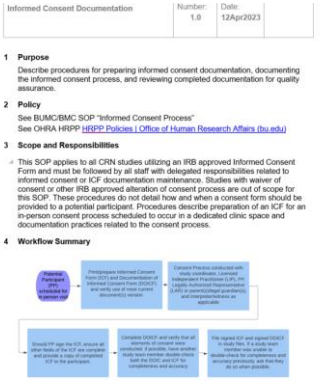
RESPONSIBILITY

Note: When "participants" is used in this SOP it refers to 1) participants of the study or 2) LAR(s) of participants.

Principal Investigator (PI) and delegated research staff who will meet with prospective participants, conduct the consent discussion, or obtain informed consent must be sufficiently trained on the consent process and documentation. Research team must be sufficiently knowledgeable about the research protocol to be able to discuss the study and answer questions posed by the participant.

PROCEDURES

General Information



Informed Consent Documentation | Number: 1.0 | Date: 12Apr2023

1 **Purpose**

Describe procedures for preparing informed consent documentation, documenting the informed consent process, and reviewing completed documentation for quality assurance.

2 **Policy**

See BUMC/BMC SOP "Informed Consent Process"
See OHRA HRPP HRPP Policies | Office of Human Research Affairs (bu.edu)

3 **Scope and Responsibilities**

This SOP applies to all CRN studies utilizing an IRB approved Informed Consent Form and must be followed by all staff with delegated responsibilities related to informed consent or ICF documentation maintenance. Studies with waiver of consent or other IRB approved alteration of consent process are out of scope for this SOP. These procedures do not detail how and when a consent form should be provided to a potential participant. Procedures describe preparation of an ICF for an in-person consent process scheduled to occur in a dedicated clinic space and documentation practices related to the consent process.

4 **Workflow Summary**

Protocol: XXXXX 301 | VX21-147-301 — BU/BMC Study IRB #: H-XXXXXX
PI: Dr. XXXXXXXX — Advarra IRB #: SSU00203391

Documentation of Informed Consent Form (DOICF)

Participant Name:		**Consent obtained by:**	
Version of Consent Used:		**Date of Consent:**	

Elements of Consent Process (Check all that apply)

Yes	N/A	
☐	☐	The study was adequately explained and the consent form was reviewed with the participant in a manner that minimized undue influence or coercion.
☐	☐	All of the participant's questions were answered and all the consent elements, such as purpose, procedures, and risks were reviewed.
☐	☐	The participant was given sufficient time to consider participation.
☐	☐	The participant agreed to participate in the study and personally signed and dated the consent form.
☐	☐	Verbal consent/assent was obtained (as approved by the IRB).
☐	☐	Obtained consent from Legally Authorized Representative (as approved by the IRB).
☐	☐	The current IRB approved consent form was used
☐	☐	The consent form was signed and dated by the researcher.
☐	☐	The consent process was witnessed by an impartial witness (if applicable).
☐	☐	The participant was given a copy of the signed informed consent form.
☐	☐	The consent process was completed prior to the start of research procedures

Limited English Proficient (LEP) Participant

Yes	N/A	
☐	☐	An IRB approved translated consent form was utilized
☐	☐	An Interpreter was utilized for the consent process (If yes, document interpreter ID# in 'Notes' below)
☐	☐	The witness (interpreter or other adult witness fluent in both languages and not associated with the study) signed the IRB approved consent form

Notes about the consent process (e.g. who was involved in consent process, what questions did the participant have, interpreter number, whether a teach-back process was used, etc.):

Looking Forward

- More info and links about SOPs and training requirements:
  - Institutional Standard Operating Procedures (SOPs) | Office of Human Research Affairs (bu.edu)
- The SOPs are living processes and as such will change over time.
  - Regulatory Updates
  - BMC/BU Resource Updates
  - Institutional Policy Updates
  - Evolution of Best Practices
- We will keep them updated and we see our research community as valued partners in this effort!

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Thank You!

THANK YOU

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