Development of Institutional Research Standard Operating Procedures for Studies using BMC facilities, Targeting BMC patients, or Using BMC patient data

Nov. 2, 2022

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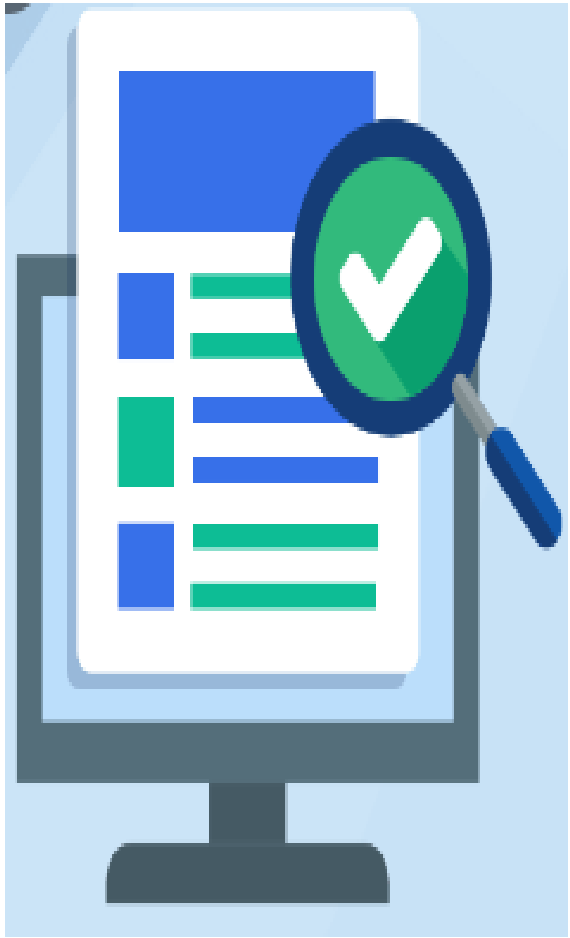
Objectives for Today's Seminar

- Define Standard Operating Procedures (SOPs)
  - Explain the importance of SOPs in clinical and human research
- BMC Institutional SOPs: How did we get here
- List steps for creation of SOPs at BMC
- Describe BMC SOPs: scope, availability, training, expectations

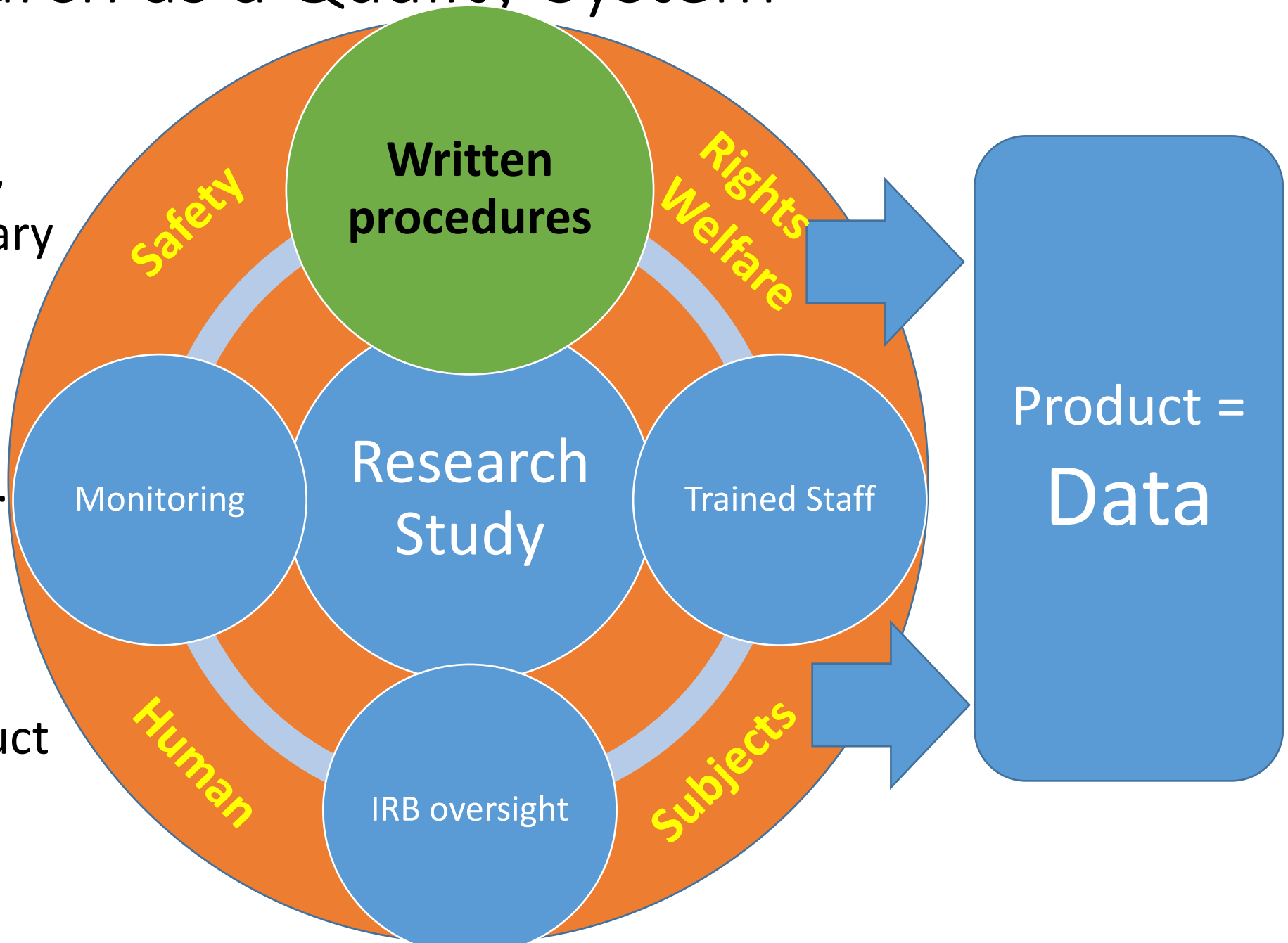
What are SOPs and Why are they important in clinical research?



Clinical Research as a Quality System

Documents the policies, procedures, and controls necessary for an organization to create and deliver high-quality products or services.

GOALs:
Ensure consistency;
Ensure quality product



Standard Operating Procedure (SOP)

"Written instructions for doing a specific task in a certain way."

From NIH NCI

Definitions for SOPs in Clinical Research

- ICH GCP promotes the development and maintenance of SOPs and defines them as: **"Detailed instructions to achieve uniformity of performance of a specific function."** ICH GCP 1.55

- FDA regs pertaining to cGMPs: **"…… written procedures that accurately describe and detail essential job tasks."** DC Peterson, 9/2/06 BioPharm International

- **"…written instructions that identify the activities and responsibilities needed to achieve a standard, controlled procedure that ensures compliance to GCP and applicable regulatory requirements ..."**
  S. Prokscha in Writing and Managing SOPs for GCP

Regulatory Requirements for SOPs

- **FDA guidance on Investigator Responsibilities (Oct. 2009)** has as multiple references to procedures for "adequate supervision for the conduct" of a trial:

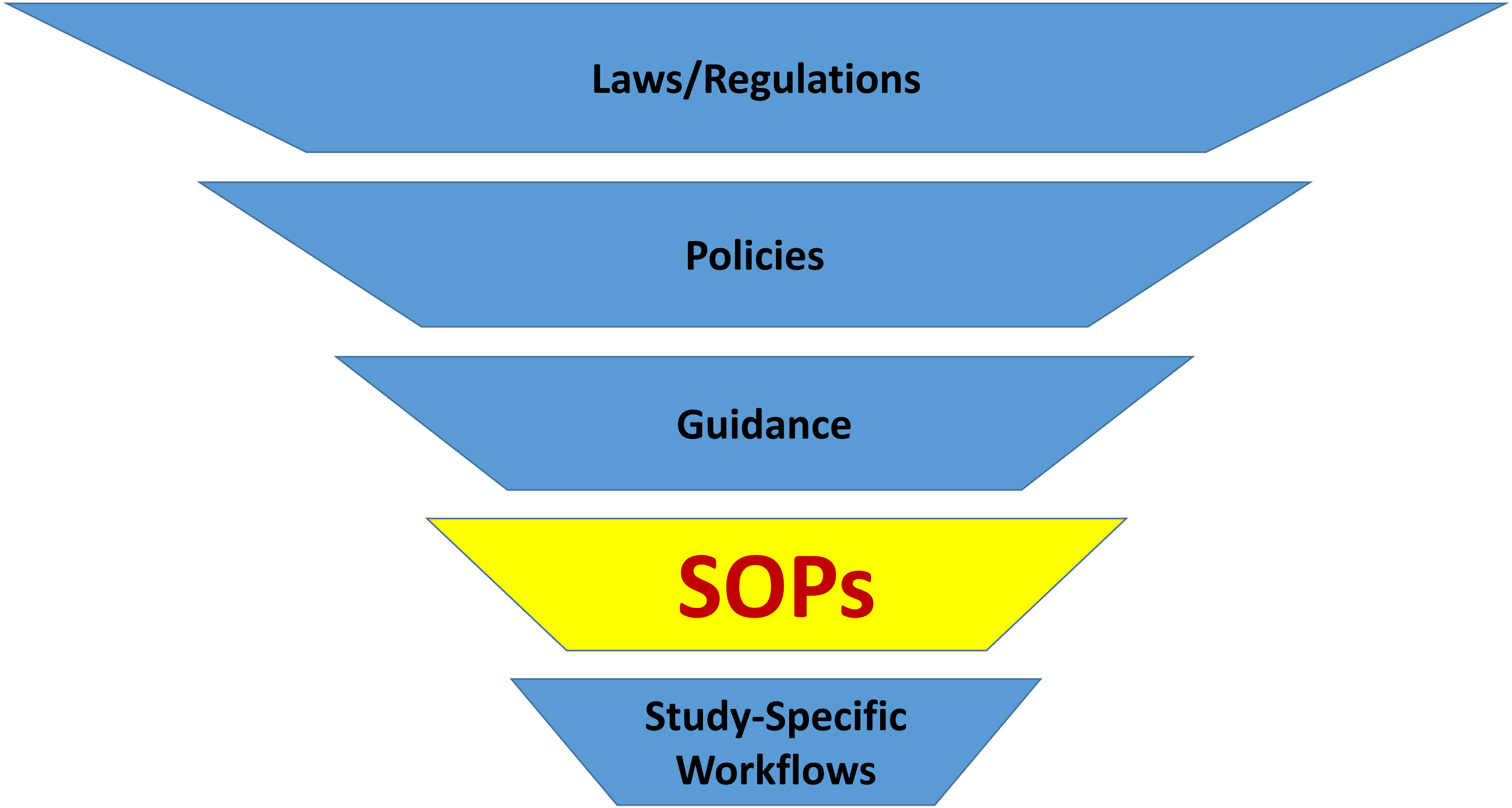
  The investigator should develop a plan for supervision and oversight of the clinical trial at the site… A plan might include the following elements…

  - A procedure for the timely correction and documentation of problems identified by study personnel, outside monitors or auditors…..
  - A procedure for documenting or reviewing the performance of delegated tasks...
  - 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 the risks
  - A procedure for ensuring that source data are accurate, contemporaneous, and original
  - Procedures for ensuring study staff comply with the protocol and adverse event assessment and reporting…..

Makin’ a cup o’ “Morning Joe”

What process must be followed to get the same result every time?

KE Woodin, CRC’s Guide to Coordinating Clinical Research, 2009


Laws/Regulations
Policies
Guidance
SOPs
Study-Specific Workflows

SOPs in a Clinical Research Quality System

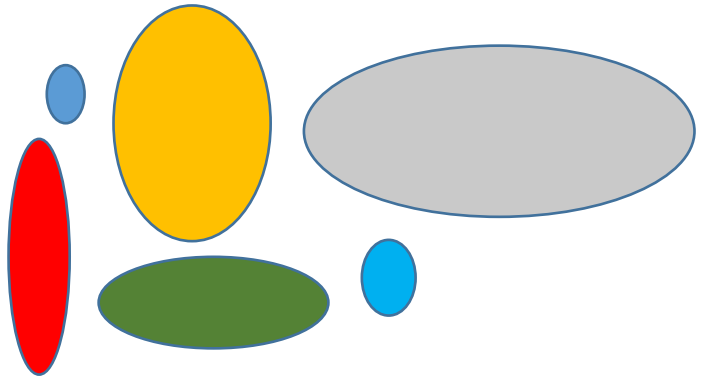
- Key objectives in conducting clinical trials:
  - Generation of quality data
  - Keep research subjects safe by minimizing risks

- Attained by:
  - Conformity of processes, AND
  - Processes based in regulations, guidance, GCP, policies, best practices

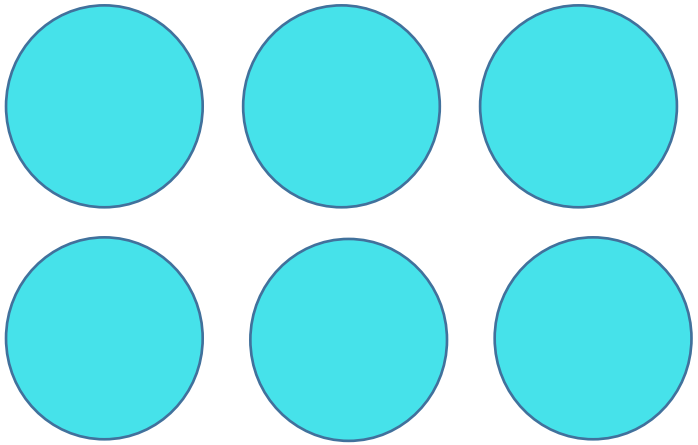
  - (Having one without the other isn’t sufficient)

No Process/Inconsistency in following process

Results

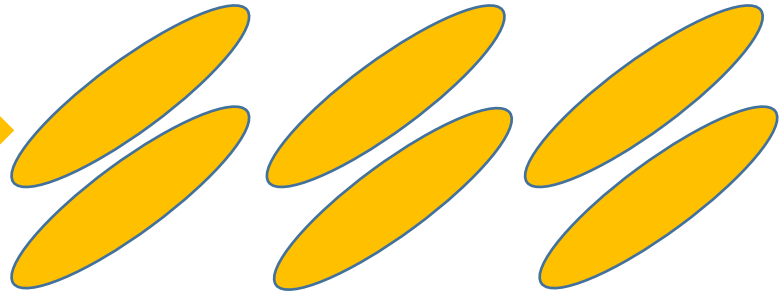


Process 1 Results



Process 2 Results

Not based in regulation, policies, etc.



Anatomy of an SOP

- Title/header/footer/pg#s/version#/signatures/version history
- Intro/Purpose/Objective: why is policy needed
- Scope
- Responsibility
- Procedures
- Definitions
- Resources: links to tools
- References: applicable regs, policies, and guidelines

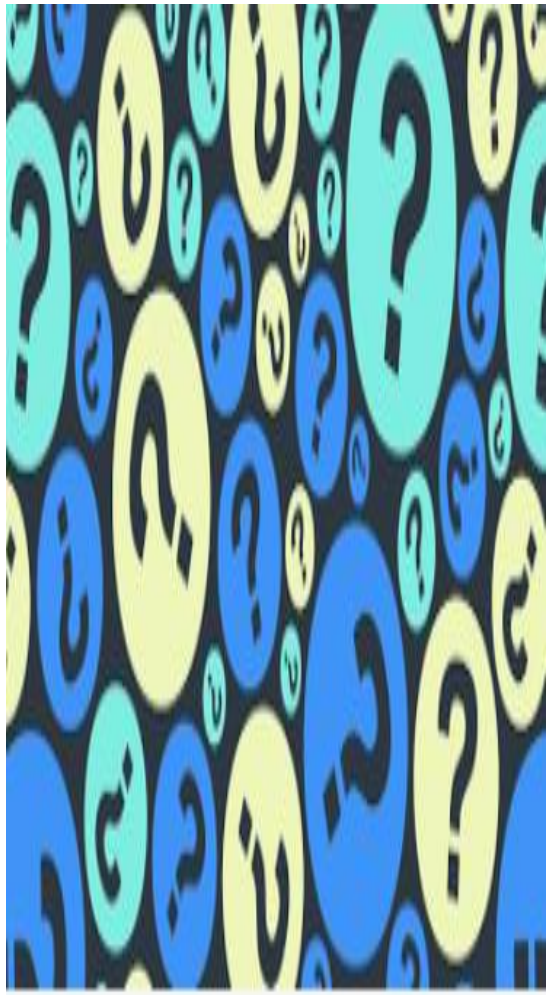
Why SOPs?/Benefits of SOPs

- Promotes consistency/reproducibility in conducting the study
  - Within sites, between individuals, between sites
- Increased quality/reliability of data
- Increased research participant safety
- Enhanced performance of staff
- Enhanced confidence of staff
- Aids in training of staff and onboarding
- Improve efficiency of staff
- Demonstrates compliance with applicable regulations, guidance, policies, etc.
- Reduce errors/reduce non-compliance

Zoom polling questions

- Do you currently utilize Standard Operating Procedures (SOPs) in conducting your research?
  - Yes for some or all of our research studies
  - No we don’t currently utilize SOPs in our research studies

- For those of you who DO utilize research SOPs, how would you best describe them?
  - Our research team developed SOPs based on our protocol
  - We follow departmental research SOPs
  - We follow SOPs provided by the lead site or Sponsor
  - Some combination of the above
  - Other (Detail in Zoom Chat)



BMC INITIATIVE TO DEVELOP SOPs
How did we get here?

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 management of essential documentation
- Findings related to training inconsistencies and management of training documentation

CRN SCOPE & VISION

Community Engagement

Facilitate bi-directional dialogue between the community and our researchers to improve trust and co-create future research

Optimized Budgeting

Utilize costing and negotiation expertise in CRN to increase study funding and remove financial barriers to diverse participation

Rapid Activation

Focused, senior level resources to rapidly activate our most important studies

Research Staffing

Provide highly experienced staffing for under-resourced PIs and studies of strategic importance

Build Infrastructure

CRN will share and implement best practices broadly to improve research infrastructure at BMC

Art: Ugo Rondinone (“Clockwork for Oracles”), Institute of Contemporary Art – Boston, 4/11/08 – 3/1/10

STANDARD OPERATING PROCEDURES PROJECT

Roadmap:

- Establish BMC and BU SOP Steering Committee
- Identify and Create Critical SOPs (15 in total)
- Assemble a network of research experts across BMC and BU to review and provide feedback
- Incorporate feedback and finalize drafts for Steering Committee approval
- Create an access and educational strategy to deploy SOPs

BMC and BU Partnership

Powered by:

- Clinical Research Network
- Office of Human Research Affairs
- Clinical Research Resources Office
- Funding support from Research Ops and CTSI

SOP 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

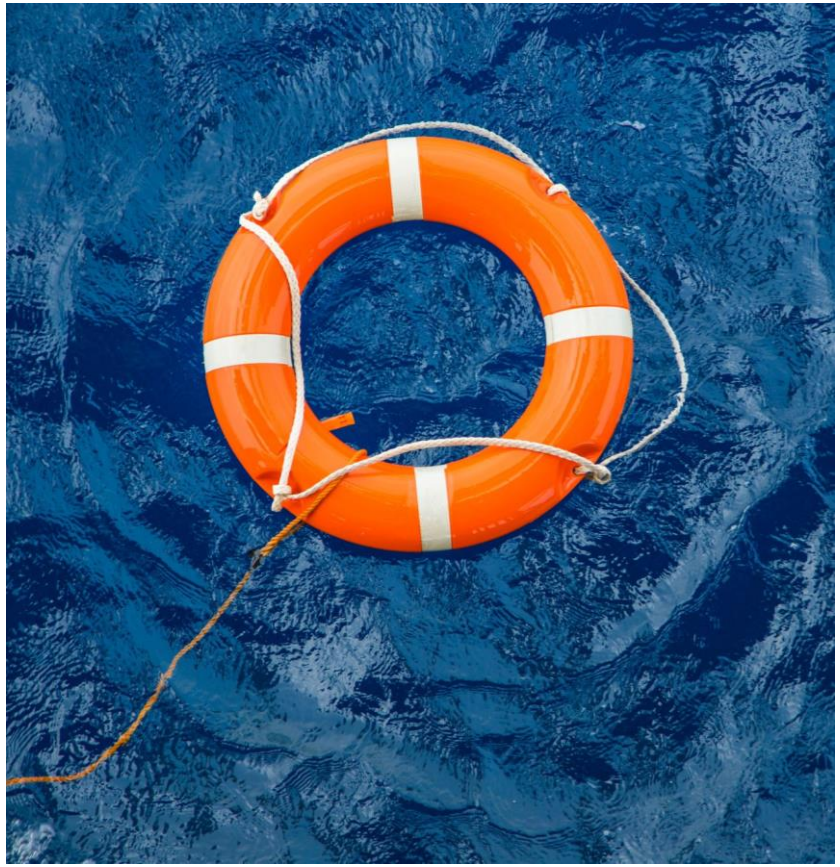
Rana Leed, MPH
Human Research Education Manager

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

Ryan Schroeder
Clinical Research Network, Director

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 regardless of BU or BMC affiliation
- Create a long-standing sustainable structure that supports development and maintenance of SOPs that will guide research conducted at BMC
- Successfully carry out our audit resolution plan



EXPECTED OUTCOMES

Strengthen collaborative relationship between BMC and BU to operationalize change

Cultivate a culture of compliance

Maintain a centralized library of standard operating procedures that study teams can rely on

Re-design training resources

Ascend

Professional Growth

Improved Site Performance

Community Access to Cutting Edge Research

Development of BMC Institutional Clinical Research SOPs

Development of BMC Institutional Clinical Research SOPs

- Workgroup organized 15 SOPs into 3 batches
- Each SOP of the batch was assigned to one of the 4 Workgroup members
  - Write SOP based on template/style, based in applicable regulations, policies, guidance, best practice

    (backed up by accepted standards)
- When draft was ready, the 4 Workgroup members met to go through the SOP line-by-line
- New draft reviewed by Workgroup members for final input before being finalized for review by Departmental volunteer group

Development of BMC Institutional Clinical Research SOPs

- After all SOPs in a batch were in final draft form
  - Sent to the Departmental volunteers and SOP Steering Committee members via an anonymous REDCap survey.
- REDCap survey asked questions on:
  - Readability
  - Content gaps
  - Whether SOP in conflict with any current departmental procedures
  - Other comments

Development of BMC Institutional Clinical Research SOPs

- Once Departmental volunteer feedback from the reviewed batch was received, it was compiled into a report, by SOP.
- SOP Workgroup reviewed and addressed each comment provided by the Departmental volunteers, integrating feedback as applicable.

Excerpt from SOP Review Comments from Departmental Volunteer Reviewers and Workgroup Responses

Delegation of Authority and Responsibilities SOP *(final data pulled 8/15, survey closed 8/12. Additional review added 8/22.)*	
• Might want to put include: "Ending date." is very important to update with any study staff turnover. As a staff member terminates, it is important for them to date and initial the DOA themselves."	• Language added to emphasize the importance of being vigilant regarding documentation of end dates.
• May wish to rethink sequencing of Definitions and move to front of doc.	• No changes. Definitions across all SOPs were moved to the end of the document to highlight their utility as a reference for the content of the SOP and to not bog down a reader seeking the content of the SOP directly.

Development of BMC Institutional Clinical Research SOPs

- Steering Committee was updated on status of changes and comments from volunteers integrated into SOPs
- Final step: Steering Committee Approvers then met to formally approve final versions of the SOPs in the batch
- Concurrently, the Workgroup performed a benchmarking survey of AHCs to understand more about who has institutional SOPs on research conduct and specific training requirements for these SOPs.
  - 25 institutions responded to the survey; data reviewed/discussed by Steering Committee to help inform our processes on applicability and training.

Development of BMC Institutional Clinical Research SOPs

- All 15 SOPs from all three batches were approved by 10/1/2022
- Next steps:
  - Finalize training requirements
  - Finalize hosting
  - Develop ongoing institutional efforts to promote these SOPs to become part of the research culture at BMC and BU Medical Campus


SOP Library

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

Example: Participant Recruitment

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.)

Institutional Expectations

RESPONSIBILITY

The Principal Investigator and all research staff are responsible for understanding and following all institutional policies and guidance including all Boston Medical Campus and Boston University Medical Campus (BMC/BUMC) SOPs that are applicable to their study.

PROCEDURES

SOP Applicability

- Unless the specific SOP states otherwise, it should be assumed that an SOP either contains specific requirements or best practice guidance that is applicable to all studies regardless of risk, study design, sponsor, funding, etc.
- It is an investigator's responsibility to review the SOPs and understand their requirements.
- If there is a question on which SOPs apply to a specific study, investigators should contact the Clinical Research Network (CRN) for guidance.

SOP Training

- **New BMC employees/Investigators:** BMC Research Operations is working on a new onboarding program that will introduce the SOP library
- **New Studies:**
  - Method: Read → Knowledge Check (Quiz) → Acknowledge
  - Administered via IRB Application process within CITI
  - Two tiers of training requirements based on interventional nature of studies

How Can I Access the SOPs?

- SOPs will be stored internally (not public-facing)
- We will ensure they are easily accessible to both BU and BMC clinical research professionals
- Can they be shared with sponsors? Yes!

Two Tiers – Not a One Size Fits All Approach

1

Fundamental SOP Training- All SOPs listed must be reviewed and acknowledged by all individuals whose research activities are within scope.

- 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

2

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

THANK YOU

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