Common Quality Assurance Review Findings: Lessons for Improving Your Own Research

CLINICAL RESEARCH SEMINAR

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Seminar Objectives

- Discuss the role of deviations as a learning opportunity for research operations improvement.
- Describe common types of deviations identified in OHRA routine quality assurance (QA) reviews.
- Provide researchers with tips for identifying and addressing/preventing these issues in their own research, even without undergoing a QA review.
- Share additional resources for internal quality assurance checks and self-assessments.

Poll

What is your role in research here at BMC/BUMC?

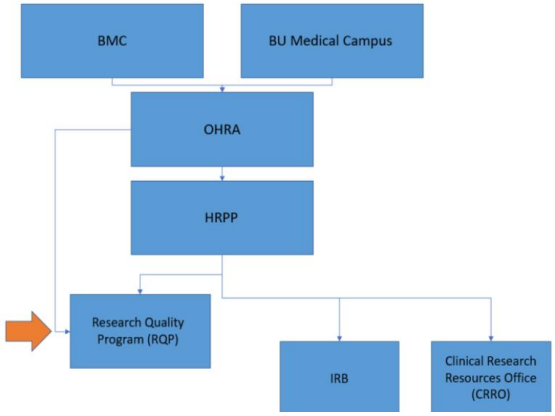
- Investigator or study staff (project manager, study coordinator, etc.)
- IRB/institutional research compliance
- Educational resources or other research support
- Other

About the OHRA Research Quality Program (RQP) & QA Reviews

BMC/BU Medical Campus – OHRA RQP

The Research Quality Program performs **targeted/for-cause audits** and **routine QA reviews** for human research studies being conducted by any investigator at Boston Medical Center/Boston University Medical Campus, including…

- Ceded studies
- International research



https://www.bumc.bu.edu/ohra/audits-for-research-oversight/

QA Review Objectives

Help study teams perform IRB-approved research in compliance with the applicable regulations, policies, and guidance in order to protect the safety of participants and the reliability/validity of study data.

Intended to be educational and consultative in nature.

- Identify and help correct potential problems in study conduct or documentation, including problems arising from IRB noncompliance
- Provide study teams with research best practice recommendations

QA Review Standards: Regulations and Policies

Applicable federal regulations. Examples:

- 45 CFR 46 (The Common Rule)
- CFR Title 21 (FDA)- e.g. 21 CFR 50, 312 (IND), 812 (IDE)

International Council for Harmonization (ICH) Good Clinical Practice (GCP)

Institutional policies & procedures

- BMC/BUMC Human Research Protection Program (HRPP) P&P
- P&P of the reviewing IRB/institution, if IRB review is ceded

IRB-approved study plan, as detailed in the protocol and INSPIR application

IRB
Institutional Review Board

QA Review Areas of Focus

Informed Consent Forms & Consent Procedures

Participant Screening & Eligibility

Protocol Adherence/Study Activities

Study Documentation (Source and Regulatory)

Adverse Events Monitoring & Safety Review

Confidentiality

Study Staff (Qualifications & Training)

BMC/BUMC HRPP Deviation Definitions

Major deviations are deviations that may:

(1) harm the participant's rights, safety or well-being,
(2) significantly damage the overall reliability of the study data, or
(3) represent noncompliance with IRB requirements that may be serious or continuing.

[BUMC/BMC HRPP Section 6.6.5.2]

Minor deviations are any unapproved changes in the research study design and/or procedures that do not have a major impact on the participant's rights, safety or well-being, or on the reliability of the overall study data.

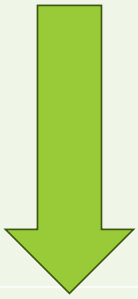
[BUMC/BMC HRPP Section 6.6.5.3]

Deviations are NORMAL!

Chat

What challenges or issues do you think are common in research conduct and regulatory compliance, in general or here at BMC/BUMC?

Common QA Review Findings

QA Finding Type	Major & Minor Deviations (2017-2023)
Most Common	Informed Consent
	Protocol Adherence
	Screening/Eligibility
	Confidentiality
	Adverse Event Assessment & Documentation
Least Common	Study Staff

Informed Consent

Unapproved or outdated version of the ICF used to obtain consent

An ICF version used to consent subject(s) was never IRB approved, OR an incorrect IRB-approved version was used (e.g., outdated version, incorrect study arm, etc.).

Preventive Actions

- Retrieve ICF from INSPIR (or IRB of record's portal), stamped and dated
- When new version is approved-
  - Discard old printed ICFs and/or replace version on e-consent platform
  - Share information about new ICF version approval with study team
- Know who the participant is ahead of time, identify correct ICF to use

Informed Consent

LIP not involved in the consent discussion

A Licensed Independent Practitioner was not involved in the informed consent discussion (as required for some studies by BMC/BUMC HRPP Policy 8.1.3.7), OR there is not adequate documentation to support than an LIP was involved.

Preventive Actions

- Before enrolling, determine whether LIP is required for your study type and understand what is required of them in discussion (purpose, risks, benefits, and alternatives)
- Identify qualified LIPs on your study team and delegate responsibility
- Develop plan for documenting LIP involvement in consent discussion- may vary based on format of discussion or study's documentation preferences

Informed Consent

Incorrect process used for consenting non-English speakers/LEP participants

Includes but not limited to enrolling non-English speakers when not approved by BMC/BUMC IRB, not involving the appropriate individuals in the consent process (e.g. interpreter or impartial witness), not using correct language documents, etc.

Preventive Actions

- Be aware of your IRB-approved plan for enrolling non-English speakers- approved to enroll? Translated ICFs or short form?
- Read BMC/BUMC HRPP policies and other applicable policies/regulations for information on personnel and documents that must be involved
- Ensure all study personnel involved in consent are trained on correct processes

Protocol Adherence/ Study Activities

Study activities not done per IRB-approved study plan

Required study activities were not performed at all, or the study activities were performed in a way that is different from what is described in the protocol/INSPIR application.

Preventive Actions

- Use study visit checklists to ensure all activities are performed
- Be familiar with how study activities are described in the IRB-approved study plan (protocol, study application, etc.) and follow as written
- When appropriate, write descriptions of study activities to allow flexibility, such as explanation for when/why an activity would not apply. Amend as needed
- Use IRB protocol exceptions for one-time actions with justification

Protocol Adherence/ Study Activities

Study visit/activity done out of protocol-specified window

Study visit took place outside of the appropriate time window in the IRB-approved study plan. Can be either too late or too early.

Preventive Actions

- Be familiar with IRB-approved timeframes for study visits/activities
- When appropriate, choose timeframes for activites that allow for flexibility. Amend timeframes as needed.
- Schedule study visits in advance to avoid availability issues
- Use IRB protocol exceptions for one-time actions

Screening/ Eligibility

Ineligible subject(s) enrolled in study, OR source documentation is insufficient to support eligibility

A participant who did not meet all eligibility criteria, or have sufficient documentation to support eligibility, was enrolled in the study. Can include participants with evidence of ineligibility (from available study data or medical records), or those who do not have documented information necessary for eligibility determination available.

Preventive Actions

- Be familiar with eligibility criteria list, follow as written
- When appropriate, write criteria to allow flexibility/clinical judgment. Amend as needed
- Use IRB protocol exceptions for one-time actions with justification
- Use an eligibility checklist to ensure all criterion are intentionally assessed; indicate source documentation

Screening/ Eligibility

Eligibility not assessed by qualified study personnel

Subject eligibility was determined by an unqualified study team member. This commonly occurs when some eligibility criteria call for clinician/investigator judgment, but they were not involved in eligibility assessment (or their involvement is not documented).

Preventive Actions

- Be aware of eligibility criteria that require investigator judgment
- Identify members of the study team that are qualified for assessment and develop a plan to involve them in eligibility determination
- Develop a plan to document appropriate personnel involvement in assessment

Confidentiality

Identifiable information stored without IRB approval, OR PHI accessed without IRB approval

HIPAA identifiers were retained/stored in the study record without appropriate IRB approval. OR PHI was accessed (e.g. for EPIC pre-screening) without HIPAA authorization from the patient or a waiver of HIPAA authorization from the IRB, or outside of the IRB-approved date range.

Preventive Actions

- Be familiar with your IRB-approved plan to handle PHI in your own study application or protocol; what you are and are not approved to do with PHI/identifiers
- Ensure all study staff are trained on HIPAA and how to handle PHI in this study
- When filling out the HIPAA Compliance section of the INSPIR application section, choose a date range for record review that will cover the necessary time period + buffer time (or list end date as 'end of data collection')

Adverse Event Monitoring/ Safety Review

Safety Monitoring Plan not adhered to

The Safety Monitoring Plan detailed in the IRB-approved study plan was not followed. Safety monitoring/review did not occur at all, OR safety monitoring did not occur at the correct time point(s). Includes adverse events monitoring/assessment, independent medical monitoring, etc.

Preventive Actions

- When writing DSMP in protocol, consider feasibility of safety monitoring/review. Amend to improve feasibility, if necessary.
- Develop a workflow to ensure safety monitoring occurs, by appropriate personnel
  - Use study visit checklists to ensure AE monitoring occurs at all required timepoints
  - Identify personnel responsible for safety monitoring/review and delegate
  - Schedule meetings with independent medical monitors far in advance and at regular intervals

Adverse Event Monitoring/ Safety Review

Documentation for AE monitoring/assessment missing or incomplete

Documentation to support AE monitoring or assessment at required timepoints (per IRB-approved study plan) is missing or incomplete in the study record. Oftentimes, AE monitoring is only documented if an AE is detected; in the absence of AEs, there is no evidence that monitoring occurred.

Preventive Actions

- Develop a plan to document AE monitoring at all required timepoints
- Develop a plan to document assessment of detected AEs (e.g. AE form)
- Identify study personnel responsible for documentation of AE monitoring and assessment (sometimes multiple members of the team)

Study Staff Qualifications/ Training

Study personnel not approved by IRB

Member of the study team was not added/approved as study personnel on INSPIR before conducting research activities.

Study staff have missing or expired HSP/GCP training

Study personnel did not complete institutionally-required HSP and/or GCP training prior to conducting research activities, or training was expired while personnel continued to conduct activities.

Preventive Actions

- Add ISPC submissions to new staff onboarding checklist/workflow
- Delegate one member of the team to submit ISPC when staffing changes occur
- Delegate one member of the team to manage personnel trainings and certifications, including HSP and GCP, to ensure all are completed and up-to-date

Chat- Scenario #1

Scenario: The protocol for study H-12345 states that a blood draw for CBC labs will be done at the screening visit and results will be used to assess eligibility (CS out-of-range values are exclusionary). The RA notices that participant 005 has CBC lab results available in his EPIC EMR from one week ago, ordered by their PCP. To avoid making the participant undergo another blood draw so soon, she decides to use the available results in EPIC and skip the blood draw at the participant's screening visit.

1) Would this be considered a deviation? Why or why not?

Yes. Protocol does not currently allow for screening visit blood draw to be skipped, even if recent lab results are available.

2) What could the study team have done differently to prevent this issue?

- Protocol exception to allow this participant's recent lab results to be used for eligibility assessment

- Write the protocol description of activities and eligibility criteria to allow available recent labs (e.g., within two weeks before screening) to be used in place of screening visit labs

- Ensure all team members are aware that study activities must be done as-written in the IRB-approved study plan; no unapproved modifications allowed

Chat- Scenario #2

Scenario: The protocol for study H-12345 states that AEs will be solicited in a phone call to the participant 24 hours +/- 6 hours after study drug infusions. The Principal Investigator has been delegated to make this call. However, the PI is on vacation the day after participant 005's first infusion and it not able to call the participant until 48 hours after the infusion.

1) Would this be considered a deviation? Why or why not?

Yes. Study visits/activities must take place with the protocol-specified timeframe (here, 24 hours +/- 6 hours after infusion).

2) What could the study team have done different to prevent this issue?

- Write the protocol DSMP to allow more flexibility in when AE monitoring occurs after infusions (if appropriate)

- Delegation the AE phone call to more members of the study team to avoid issues when someone is OOO- others can collect information about any events, and PI can assess them later (for severity, relatedness, etc.)

Chat- Scenario #3

Scenario: The protocol for study H-12345 states that the second study drug infusion should occur within 21 +/- 2 days after the first infusion. Participant 005 is scheduled to receive their second infusion of the study drug 22 days after their first infusion. However, they call the study team a few days before the appointment and explain that they need to reschedule to next week because they tested positive for COVID-19. Their new appointment is 26 days after their first infusion.

1) Would this be considered a deviation? Why or why not?

Yes. Even though this was out of the study team's control, visits/activities must take place with the protocol-specified timeframe.

2) What could the study team have done different to prevent this issue?

- Protocol exception to allow this participant's next infusion to be scheduled outside of the protocol-specified timeframe (if appropriate)

- Before enrollment, could have written the protocol Schedule of Activities to allow more flexibility (e.g. larger buffer time for schedule)
  - If the study team notices they need to schedule visits out-of-window often, consider amending protocol

Resources

But… How can I identify these issues in my own research?

Conduct a Self-Assessment Review:

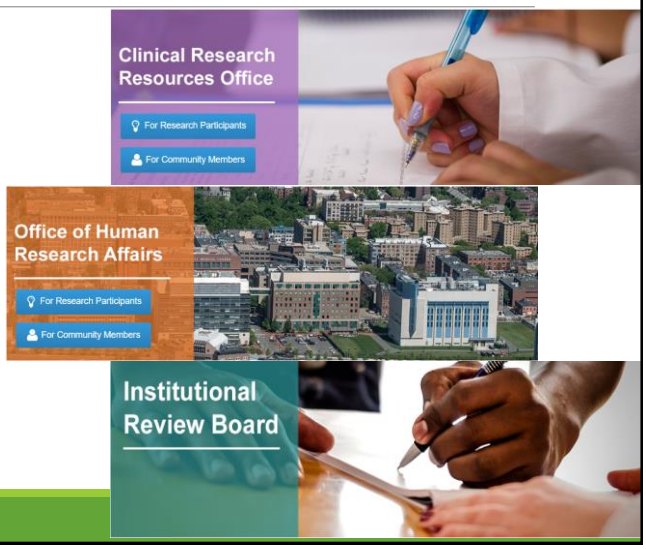
- Self-assessment is a research team's planned review of their own study documents and processes to verify adherence to the IRB-approved study plan and compliance to policies and regulations
- Benefits include:
  - Supports participant safety and rights protection
  - Strengthens data integrity and reliability
  - Recommended as best practice
- See the March 2023 Clinical Research Seminar for further guidance on conducting self-assessments

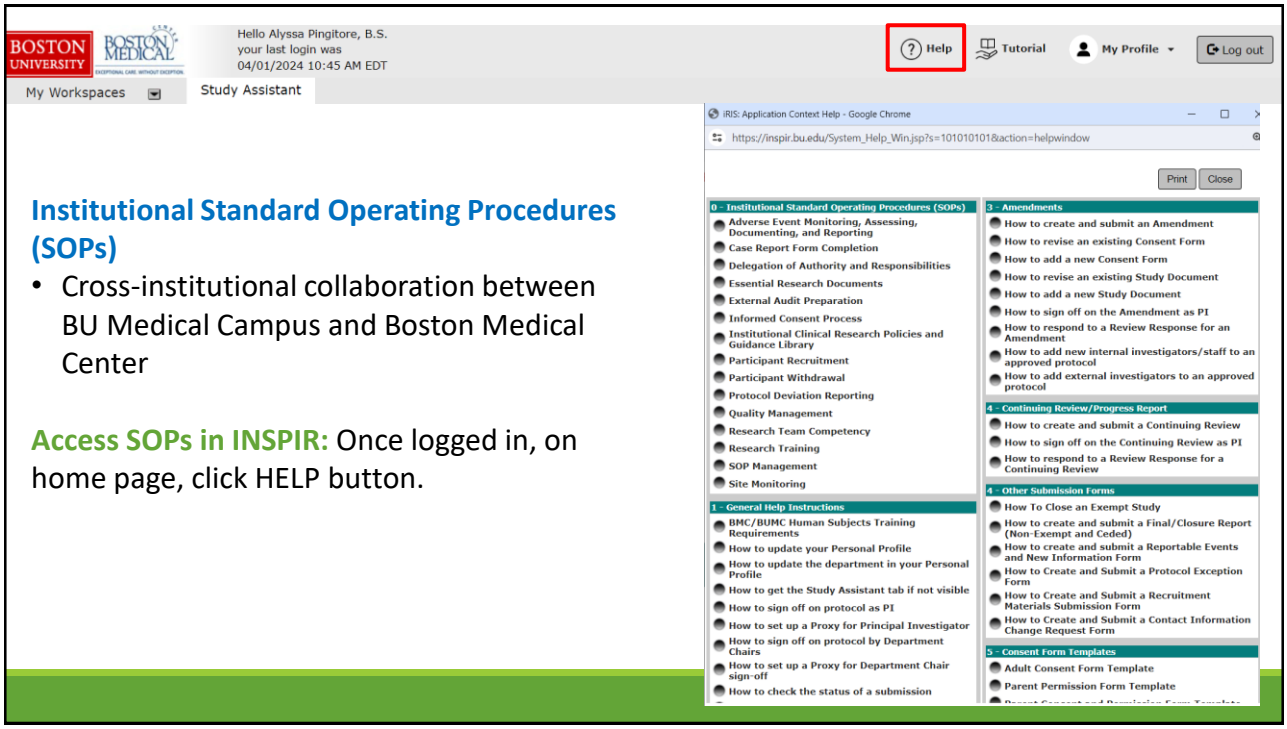
Check out these resources!

Office of Human Research Affairs
- Quality Assurance Reviews
- Contact us

Institutional Review Board
- IRB Templates
- INSPIR II Instructions for Investigators

Clinical Research Resources Office
- Study Documentation Tools
- Self-Assessments
- Education/Training Portfolio





Institutional Standard Operating Procedures (SOPs)

- Cross-institutional collaboration between BU Medical Campus and Boston Medical Center

Access SOPs in INSPIR: Once logged in, on home page, click HELP button.