AUB Policy for Quality Improvement Program (QIP): Monitoring and Auditing Human Subjects Research

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American University of Beirut
Quality Improvement Program (QIP): Monitoring and Auditing Human Subjects Research
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Revised versions:

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I. OVERVIEW

The Human Research Protection Program (HRPP) is the administrative body at the American University of Beirut (AUB) that oversees the safety and welfare of participants involved in human subjects research in accordance with all applicable country law, institutional policies, and federal law when applicable. At the institutional level, the HRPP includes: the Office of the Provost (Institutional Official) representing AUB as an academic institution, the AUB Office of the Human Research Protection Program, the AUB Institutional Review Boards, the AUB Quality Improvement Program/Research Compliance Unit, the AUB Research Education Unit, Principal Investigators and research teams, the study sponsors, and the research participants themselves.

The AUB Quality Improvement Program/Research Compliance Unit (QIP/RCU) was established to promote and maintain ethical research conduct. The QIP/RCU, in collaboration with Institutional Review Boards, has the responsibility of assessing all components of the HRPP and providing quality assurance and quality improvement activities to the AUB research community engaged in the conduct of human subjects research. The HRPP Director and Provost oversee the auditing and monitoring of continuous quality improvement and quality assurance activities.

II. PURPOSE

This document describes the scope of activities performed by the AUB QIP/RCU, and outlines the types of audits/reviews that may be conducted at the level of the Principal Investigator, Institutional Review Board, and University. Additionally, answers to frequently asked questions (FAQs) about QIP/RCU activities are included.

III. DEFINITIONS

**Administrative hold:** is a voluntary action taken by the Principal Investigator (PI) or sponsor, to temporarily or permanently halt some or all research activities of an approved protocol (e.g., suspend recruitment, analysis, research procedures), in response to a request from the convened Institutional Review Board (IRB), IRB Chair/Vice Chair or the Institutional Official or his designee, while the IRB conducts its inquiry/investigation of an allegation of noncompliance. Administrative hold is not considered a suspension or termination. During

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1 As of August, 2010, the HRPP is in the process of fully establishing the QIP/RCU areas. In the interim, inquiries and investigations into allegations of noncompliance or other internal audit activities are staffed by individuals designated by the Director, HRPP and the Chair/Vice Chair of IRB, and may include professional staff of the IRB office, IRB members, and external consultants to the HRPP.

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Administrative hold, the research remains subject to continuing review and requirements for reporting noncompliance and unanticipated problems.

**Adverse Event:** Any undesirable and unintended (although not necessarily unexpected) effect occurring as a result of interventions, interactions, or collection of identifiable private information in research. In biomedical research, any untoward physical or psychological occurrence in research, including abnormal laboratory finding, symptom, or disease temporally associated with the use (although not necessarily related to) a medical treatment or procedure. Adverse events involving drugs are also referred to as adverse drug experiences. [Note: HHS regulations at 45 CFR 46 do not define or use the term adverse event; FDA uses the term adverse effect (21 CFR 312.64), adverse experience in 312.32, and the more generic term unanticipated problems (312.66).]

**Institutional Official (IO):** The Institutional Official/Provost is the person ultimately responsible for the development and implementation of the Human Research Protection Program (HRPP) and the coordination of all its components. The IO will report any serious or continuing noncompliance, suspension and/or termination of previously-approved research to appropriate AUB officials, the U.S. Office of Human Research Protection (OHRP), U.S. Department of Human Health Services (DHHS), the Federal Drug Administration (FDA), and/or other federal sponsors or other sponsors, when AUB is required to make this disclosure or elects to self-report.

**Institutional Review Board (IRB):** The administrative body at an institution responsible for ensuring that the rights, safety, and welfare of human research subjects are fully considered and protected in accordance with international, state, and University policies and procedures.

**Noncompliance:** Any failure to follow: (a) provisions of an IRB-approved research study, (b) institutional policies, state laws or federal laws (for federally-sponsored research) governing human subjects research, or (c) the requirements and determinations of the reviewing IRB. Noncompliance can be categorized as non-serious (minor), serious, or continuing noncompliance. Noncompliance may pertain to the Principal Investigator (PI), the PI’s research team, or any member of the Human Research Protections Program (HRPP), including the IRB and the IRB administrative staff.

**Principal Investigator (PI):** An individual approved to direct a research project or program. He/she is responsible and accountable for the proper ethical conduct of the project or program, including the conduct of his/her research team members.

**Serious Adverse Events (SAEs):** An adverse event that is fatal or life threatening, permanently disabling, requires or prolongs hospitalization, or results in significant disability, congenital anomaly, or birth defect.

**Suspension:** A directive by the Institutional Review Board (IRB) to stop temporarily all or part of a previously-approved research protocol pending future actions by the IRB, Principal
Investigator or his/her study personnel and, where appropriate, pending formulation and implementation of substantial corrective action.

IV. SCOPE OF QIP/RCU

The AUB/HRPP oversees all human subjects research activities conducted at AUB or in conjunction with collaborating institutions. As part of this oversight, the QIP/RCU is tasked with the evaluation and improvement of human research protections through education, training, and monitoring. The QIP/RCU works with investigators, research staff, the Institutional Review Boards (IRBs), and consultants as applicable, to ensure research is compliant with regulations, guidance, institutional policies, the IRB-approved protocol, IRB decisions, and IRB policies and procedures and best practices for human research protection. The QIP/RCU conducts periodic spot audits, as well as for-cause assessments as directed by the IRBs, the HRPP Director or the Institutional Official (IO). The QIP/RCU may also conduct periodic compliance audits to assess IRB compliance with federal regulations (e.g., U.S. Office of Human Research Protections and U.S. Federal Drug Administration), HRPP policies, and other applicable AUB policies and procedures.

The QIP/RCU focuses primarily on the review of activities, policies, procedures and records. Information is obtained through interviews (which may include subjects/participants), observations, recruitment materials, IRB files/correspondence, and data/records reviews, and may involve any of the following groups:

- Investigators and research staff conducting research which involves human subjects/participants, including exempt and expedited research protocols;
- Institutional Review Board (IRB) Committees;
- HRPP staff supporting IRB activities;
- Individuals involved in HRPP education and outreach.

V. TYPES OF AUDITS/REVIEWS CONDUCTED BY QIP/RCU

The QIP/RCU conducts periodic spot audits/reviews, as well as for-cause (directed) audits.

a. Spot Audit/Review: A routine (not-for cause) audit/review, also referred to as a spot review, is an assessment or examination of a research-related practice or procedure with the possibility (or intention) of instituting change, if necessary. Periodic quality improvement (QI) reviews of study activities and study documentation are performed on site to provide investigators and research staff an opportunity to make improvements or adjustments to research practices/procedures leading to the improved quality of their research program. On-site visits are conducted and studies are randomly selected for spot reviews, or a specific portion or type of research activity (e.g. assent procedure for children) may be targeted for review involving a number of approved protocols and/or
investigators. Routine/spot reviews are pro-active and educationally-oriented. Principal Investigators are invited to request an on-site spot review of their research.

A targeted (not for cause) QIP review may involve an examination of a pool of protocols/investigative teams to assess current practices, and identify best practices, using a sample of approved studies and investigators.

b. For-Cause (Directed) Audit/Assessment: A for-cause (directed) audit is an audit of research or investigators to obtain (or verify) information necessary to ensure compliance with regulations and institutional requirements. A for-cause audit is generally based on a concern, complaint, or allegation of noncompliance that was brought to the attention of the Director/HRPP, an IRB Committee, or IRB Officer/Administrator. This type of audit is initiated at the request of an IRB, the Director/HRPP or the Institutional Official (IO).

VI. AUDITING OF PRINCIPAL INVESTIGATORS/RESEARCH TEAMS

a. Spot Audit/Review: The QIP/RCU may schedule spot reviews with designated investigators/research staff to determine whether and to what extent the Principal Investigator (PI) and research staff are complying with applicable regulations, IRB policies and procedures, in accordance with the IRB-approved research protocol and/or to assess the efficacy of IRB policies and practices.

Research studies are selected and prioritized for review in accordance with perceived risk or complexity of the research protocol. The following is a list of factors that may be considered in the selection process:

- Investigator-initiated studies;
- Significant risk device studies;
- Phase I and/or first in human use studies;
- Protocols in which the AUB Investigator is the IND or IDE holder;
- Studies involving vulnerable populations;
- Studies involving various waivers;
- Studies involving tissue banking or genetic testing;
- Studies involving stem cell research;
- Studies reporting multiple Serious Adverse Events (SAEs) or unanticipated problems;
- High risk studies reporting few or no adverse events;
- Protocols or PIs with frequent lapses in IRB approval;
- Studies involving deception or unusual debriefing procedures;
- Protocols receiving initial approval more than five years ago;
- Protocols where the PI has changed more than twice.
Although spot reviews normally involve the review of only a specific aspect of a study, the scope of the original spot review may be expanded and may become a for-cause (directed) audit if more serious deficiencies are found.

The QIP/RCU staff will ask that specific study-related records are available for review. All documents will be reviewed on site. PIs have the responsibility to assure provision of appropriate records, data, or documents that are requested, in writing, by the Director of the QIP/RCU. Examples of spot reviews include, but are not limited to reviews of:

- Executed informed consent documents;
- Eligibility criteria (inclusion/exclusion criteria);
- Informed consent process, including in-person observations;
- Approval documentation required before research commences;
- Sponsor correspondence;
- Screening/enrollment lists used to identify potential participants;
- Drug/device accountability records;
- Storage/retention of subject confidential information.

Following the completion of the spot review, the findings will be discussed with the PI. Specifically, a designated QIP/RCU staff member will address minor concerns directly with the PI and/or research staff. In cases of potential noncompliance, the QIP/RCU designee will assist the PI in reporting noncompliance to the appropriate IRB. Written reports of investigator-prompted spot reviews are not generated by QIP/RCU, and only aggregate data are kept by the QIP/RCU (i.e., audit results are retained but not directly linked to specific investigators or their studies), unless the spot review identifies noncompliance concerns.

When concerns of noncompliance (minor, serious or continuing) arise during the spot review, the QIP/RCU staff will notify the PI and Director/HRPP (as appropriate) of these concerns so that appropriate follow-up actions can be taken. Specifically:

- If the spot review finds the occurrence of non-compliance with the IRB-approved protocol, the PI is responsible for promptly reporting the occurrence to the IRB, in accordance with AUB’s policy on “HRPP/IRB Allegation of Noncompliance Policy”

- If spot review findings identify a need for revision/modification of the research protocol or informed consent process, the PI is responsible for submitting an amendment to the IRB in accordance with IRB “Amendment/Modification to Approved Protocol Policy”

When spot reviews arise from routine (not-for-cause) targeted internal reviews, rather than an investigator-initiated review request, the QIP/RCU staff will provide a written report of aggregated spot review findings that identify deficiencies, if any, in HRPP/IRB
policies or procedures, along with a suggested action plan or recommendations (if any), to the IRB Chair/Vice Chair and/or Director/HRPP, as appropriate.

Written reports summarizing the aggregated data and statistical information from QIP spot/targeted reviews, including any recommendations for HRPP/IRB policy or procedural changes arising from the conclusions and best practices identified through the spot review should be completed within 30 days after the completion of data collection/interviews.

b. **For-Cause (Directed) Audit/Assessment:** The QIP/RCU may be tasked with a for-cause (directed) audit by an IRB, the Director/HRPP or the Institutional Officer (IO). These audits are required as part of the inquiry/investigation process when an allegation or concern is raised about (1) human subjects’ safety and well-being, (2) investigator, including the PI and/or any member of the investigative team, non-compliance (concerning IRB requirements, institutional policies and procedures, OHRP/FDA regulations, and/or other guidelines), or (3) integrity of the study data. The QIP/RCU’s role in the for-cause audit is established by the **HRPP/IRB Allegation of Noncompliance Policy** [https://cms.aub.edu.lb/irb/Documents/noncompl.pdf](https://cms.aub.edu.lb/irb/Documents/noncompl.pdf)

For-cause Audits are conducted by the QIP/RCU, in coordination and conjunction with an IRB Subcommittee described in the **HRPP/IRB Allegation of Noncompliance Policy** [https://cms.aub.edu.lb/irb/Documents/noncompl.pdf](https://cms.aub.edu.lb/irb/Documents/noncompl.pdf) on site or remotely, without prior notice to the principal investigator (PI). In some circumstances, the IRB may request the PI (or in the absence of the PI, a named co-investigator or emergency contact designated by PI) to place an “administrative hold” on the study to protect the safety and well-being of subjects, or the IRB may place the study on “suspension” until the audit is complete and determinations of noncompliance and appropriate corrective actions are made by the IRB Full Committee. Depending on the level of real or potential risk/harm to subjects, an “administrative hold” decision by the PI should take place within 24 hours of notification by IRB Chair. If the IRB is unable to contact the PI and there is no emergency point of contact, the IRB may proceed with a “suspension” decision. A PI who elects to put the questioned protocol on administrative hold should be able to continue research on other already approved protocols unless there is strong reason to believe that the same alleged infraction is occurring on other approved protocols. In the course of the investigation, the investigating IRB Subcommittee can always expand the scope of its investigation to other approved protocols which the IRB would then also request the PI to place on administrative hold. *(For more detailed information about actions which may be taken by the IRB for new applications from PIs or other members of investigative team who may be involved in the research study in question, please refer to AUB’s policy on “HRPP/IRB Allegation of Noncompliance Policy”)* [https://cms.aub.edu.lb/irb/Documents/noncompl.pdf](https://cms.aub.edu.lb/irb/Documents/noncompl.pdf)
The scope of the “for-cause” audit will be initially limited to investigation of the matter (the allegation), but the scope may be expanded based on the initial results of the audit.

Issues that can trigger For-Cause (Directed) Audits/Assessments include, but are not limited to:

- Directive issued by an IRB, Director/HRPP, or IO;
- Unexpected research participant death;
- Research subject, family or research staff complaint/concern;
- Numerous and/or significant serious adverse events (SAEs) and/or protocol violations;
- Reports of noncompliance by investigators, research personnel, subjects or others;
- Results of audits or monitoring by other entities (internal or external to AUB);
- Results of For-Cause Audit regarding allegation of noncompliance involving same PI or member of investigative team causing IRB to expand scope of audit to examine whether noncompliance has occurred in other previously approved studies involving this PI or other members of investigative team;
- Concerns expressed by Department Chair, Dean, or other institutional committees.

Following completion of the audit, the findings will be discussed with the PI (or designee). In conjunction with the IRB Subcommittee charged with examining allegations of noncompliance, the QIP/RCU will prepare a written report that consists of a summary of the allegation(s), as well as interview summaries and copies of pertinent supporting information, documents or correspondence. The report may include the Subcommittee’s recommendations for aligning the research protocol, if necessary, with institutional policies and regulatory requirements and/or corrective actions, if any. The written report will be shared with the IRB Chair/Vice Chair.

If the audit findings identify a need for revision of the research protocol or informed consent processes, the PI is responsible for submitting an Amendment/Modification to the current Approved Protocol in accordance with IRB policy. However, if the results of the audit identify potential noncompliance (minor, serious or continuing), the IRB Chair/Vice Chair schedules a discussion of the Report at the next IRB Full Committee meeting. All IRB members receive the written report for the For-Cause Audit, including any corrective action plan or recommendations for discussion and further determination of action by the IRB, in accordance with the HRPP/IRB Allegation of Noncompliance Policy. [https://cms.aub.edu.lb/irb/Documents/noncompl.pdf](https://cms.aub.edu.lb/irb/Documents/noncompl.pdf)

VII. AUDITING OF IRB/HRPP ACTIVITIES

The QIP/RCU may conduct periodic spot reviews/audits to determine whether and to what extent the IRBs and the IRB staff are complying with applicable ethical principles, federal

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regulations, HRPP policies and practices, as well as international standards on human research protection. The evaluation may include the review of meeting minutes, detailed examination of protocol files, and/or attendance at IRB meeting(s).

The QIP/RCU will provide a written report of the IRB spot review/audit findings, including a suggested action plan and recommendations, if any, to the Director/HRPP.

At the request of the Director/HRPP or the IO, QIP/RCU may review the HRPP documents, policies and practices on a routine basis to assure that written policies and procedures are aligned with current IRB and HRPP practices. Internal audit of the HRPP is a means of evaluating compliance with applicable ethical principles, U.S. Federal and Lebanese national laws, and AUB policies and procedures as well as other international standards for human research protection. An internal audit will also include a review of HRPP’s participant and community outreach and education programs. The audits will also provide a benchmark for improvements in the HRPP.

VIII. CONTINUOUS QUALITY IMPROVEMENT

Based on the results of routine Spot Audit/Reviews and For-Cause (Directed) Audit/Assessments, as well as feedback received from the communities served by the IRB, the QIP/RCU will work in partnership with the IRBs and other components of the AUB HRPP to identify root causes of problems, and develop, implement or recommend action plans to correct issues and provide education and outreach to promote effectiveness of improvements.

Significant changes to the HRPP that are implemented as a result of quality assessment and quality improvement activities are monitored to ensure effectiveness and consistency. This leads to continuous improvement of the HRPP and the protection of human subject research participants.

IX. FREQUENTLY ASKED QUESTIONS (FAQs):

What is the relationship between the QIP/RCU and the IRBs?

The IRBs and the QIP/RCU are both components of the AUB HRPP. The QIP/RCU is charged with evaluating and enhancing human research protections through monitoring and coordinating education and training with the Research Education Unit of the HRPP. The IRBs are charged with reviewing and overseeing human research to ensure protection of research participants. The feedback from the quality improvement reviews is a way for IRBs to inform and improve their activities and those of the investigators and their research team members.
What can an investigator or research staff member do to prepare for a routine (not -for-cause) QIP/RCU review or spot audit?

Organizing study-related records (even without a QIP/RCU review) can be beneficial in helping to track study progress and meet required deadlines (such as continuing review). Some helpful tips:

- Review your system for maintaining current and completed records. As necessary, train all who generate, access, and store records on how to use the system.
- Back up electronic records that you can’t afford to lost if failures occurred.
- Assess the security of stored records to prevent unintended loss or access.
- Ensure that documents are organized and can be made available for review.
- Use the self-assessment tools on the QIP/RCU web site to review your files for the appropriate contents.
- Contact the QIP/RCU staff for assistance in improving study performance.
X. RESOURCES:

University of Illinois at Chicago, Policy – Office of Vice Chancellor for Research Quality Improvement Program – Monitoring and Auditing

Ohio State University Quality Improvement (QI) Program FAQs

University of Chicago Medical Center – Quality Assurance Auditing Policy for Clinical Research

Pennsylvania State University Vice President for Research, Office for Research Protection, Quality Management initiatives, Post-approval Review Activities

Yale University: Policy on Research Compliance and Oversight

Stanford University, Internal Audit Activities – Continuous Quality Improvement