

Human Research Quality Review & Education Program

Frequently Asked Questions

What is the purpose of the Quality Review & Education Program?

The purpose of the program is to review how research is conducted, and to detect, correct and prevent potential and existing problems, through routine Quality Reviews and For-Cause audits. There are several objectives of the program. They include:

- ensuring research is conducted ethically, safely, legally and in compliance with the protocol and institutional IRB policies and procedures;
- raising awareness of requirements and promote researchers' accountability;
- ensuring that the conduct of research does not compromise the integrity of the results; and
- evaluating institutional needs and creating training and education.

What is the difference between a Quality Review and a For-Cause audit?

Quality Reviews are routine, initiated by the review team, and are equally distributed among types of research, taking into account criteria that include:

- Studies which are federally funded
- Investigator initiated studies
- Studies enrolling vulnerable populations
- Studies with high participant enrollment
- Studies with large numbers of reported deviations and adverse events
- Phase I or Phase II clinical trials
- Studies utilizing the WCM Data and Safety Monitoring Board (DSMB)
- Studies involving international research

Written reports detailing the findings of a Quality Review are only shared with the PI, research team and Quality Review team, unless a finding indicates possible serious or continuing noncompliance, or a possible unanticipated problem involving risks to subjects or others, in which case the report is also shared with the IRB.

For-Cause audits are those that are requested by the IRB, Department Chair, the Institutional Official, Research Integrity Officer, or Executive Leadership, and may be conducted in response to any of the following:

- Indication of an increased risk to participants
- Participant/family member complaint
- Follow-up from an external inspection, such as FDA, OHRP, or NYSDO
- Studies in progress that are outside the investigator's field of specialty
- Lack or unreported adverse events and/or DSMB reports
- Absence of reporting to the IRB, including failure to obtain continuing review approval
- Employee concern or complaint about the research

- Clinical trials involving an IND or IDE when a safety warning has been issued by the FDA, or when there has been a change in labeling that indicates an increase in risk
- Issue or allegation of non-compliance
- Suspected research misconduct

Written reports detailing the findings of a For-Cause audit are always shared with the IRB.

Apart from how they are initiated, and to whom the written reports with findings are disseminated, For-Cause audits and Quality Reviews are the same.

How many protocols will undergo a Quality Review?

Approximately 36 protocols will be selected for a routine Quality Review in the first year of the program with the goal to increase the total number of protocols in subsequent years.

How are studies selected for a Quality Review?

All active research studies approved by the WCM IRB are eligible to be reviewed. Protocols from all tiers of risk (minimal risk and greater-than-minimal risk) will be reviewed, however, higher risk studies will be the focus of more reviews than those considered to be lower risk.

Protocols will be randomly selected for Quality Review from within each tier of risk, but in a controlled manner so that repeated reviews of the same group within short periods of time are avoided, unless previous reviews have revealed problems.

I have an upcoming inspection from the FDA. Can I request assistance from the Quality Review team?

Yes. You may request assistance with preparation for an external audit by the FDA or other regulatory body by emailing researchaudit@med.cornell.edu.

How far in advance will I be notified if one of my studies is scheduled to undergo a Quality Review or For-Cause audit?

For-Cause audits may be unscheduled and/or occur without prior notice, whereas for a routine Quality Review our team will work with the Principal Investigator to arrange scheduling.

How long will the evaluation take?

Depending on the scope of the evaluation, the visit may take anywhere from a few hours to several days.

How can I prepare?

Once a date has been finalized, the principal investigator and study team will receive a plan that outlines the scope of the audit or Quality Review. Based on this information, one should take steps to make all needed documentation accessible to the Quality Review team, including anything residing on a departmental share drive, by granting any electronic permissions necessary. Private space should also be secured by the principal investigator or designee for the Quality Review team to be able to examine all records on the agreed upon dates. At least one study team member who can answer Quality Review team questions should be made available for the duration of the review. Investigators should also complete an Investigator Quality Review Preparation Checklist, available in the downloads section of the Human Research Quality Review & Education Program website.

What do I do if I need to reschedule?

The principal investigator should send a written request to researchaudit@med.cornell.edu, including a reason and proposed alternate dates.

What happens during a For-Cause audit or Quality Review?

A given audit or Quality Review involves interviews and comprehensive regulatory and participant documentation review.

The PI is always interviewed twice – once to start the audit/Quality Review and a second time to discuss findings – and members of the study team and/or participants are interviewed as needed. The PI's first interview occurs at the beginning of the audit/Quality Review, whereas the PI exit interview occurs within 3 days of completion of the evaluation.

The Quality Review team will evaluate regulatory documentation, including IRB documentation, study team credentials and participant documentation, such as informed consent(s), assent(s), and medical record, in detail. During this time, a member of the study team able to answer questions should be made available.

When applicable, the Quality Review team will also tour the research facility to verify control, storage, and accountability of investigational new test articles and/or to confirm availability of related research equipment.

The Quality Review team may also view the study team conducting the informed consent process.

What topics will be covered during the initial principal investigator interview?

The principal investigator will meet with one or more members of the Quality Review team for a 30-minute PI interview about topics such as:

- Assessment of general understanding of research activities
- How and what responsibilities are delegated
- When, where, and how data are collected
- How privacy and confidentiality are maintained
- Who, how, and where of the informed consent process
- Adverse events assessment
- Recruitment practices

What topics will be covered during an interview with a member of the study team?

The interview is a discussion guided by the individual's role on the protocol and may include:

- Grasp of regulatory obligations
- Training prior to assuming protocol responsibilities
- Informed consent process
- Reporting to the IRB and other regulatory bodies
- Data storage and procedures for maintaining research participant privacy
- Study team communication regarding ongoing protocol management
- Questions about the research facility

What and how much documentation will be evaluated during the For-Cause audit or Quality Review?

The Quality Review team will evaluate regulatory documentation, including IRB documentation, study team credentials and participant documentation in detail. This may require arranging for Quality Review team access to any systems used

internally such as a folder on a department share drive, a REDCap project, or other system used by the study team. The plan received by the PI and study team prior to the evaluation will indicate how many participant charts will be reviewed.

What specific documentation will be evaluated?

For all audits, **regulatory documentation**, including but not limited to:

- Protocol
- Investigator's Brochure (if applicable)
- Logs (Screening/Enrollment/Delegation/Deviation/Monitoring Visits/Training)
- Records of retained tissue or fluid samples
- Laboratory certifications and lab normal ranges (when applicable)
- Correspondence
- Investigational product labeling, accountability, receipt, storage, dispensing, and destruction logs (if applicable)
- FDA correspondence and annual reports
- All IRB approved documents and correspondences, including:
 - IRB initial applications, renewals, amendments with associated Modifications Required letters, Deferral letters, and Approval letters from the IRB
 - Recruitment material (e.g., flyers, advertisements, newsletters, letters, e-mail) with documented IRB and sponsor approvals
 - Safety Report submissions and associated acknowledgments
 - DSMB Report submissions and associated acknowledgments
 - Filed IRB correspondences, including approval letters
 - All stamped approved revised versions of the Informed Consent document, assents, and short form for non-English speaking subjects
 - All stamped approved HIPAA Authorization Forms
 - Documentation demonstrating timely reporting of adverse events and protocol deviations according to the Immediate Reporting Policy, including Further Information Required and Acknowledgment letters from the IRB
 - Exception Requests and associated IRB approvals

A review of **study team credentials and training** such as:

- Required Human Subjects Training
- Protocol-specific training
- Conflicts of interest
- Updated CV and Licenses
- Appropriate certification, when required

A review of **participant source documentation**, consisting of the following:

- Evaluation of signature, date, and time (where applicable) on informed consent(s), assent(s), and HIPAA Authorization documents, including copy in the medical chart
- Confirmation of participants' eligibility
- Study visit assessment
- Assessment of participant adherence to protocol: drug accountability, deviations, etc.
- Adverse events (AEs and SAEs) assessments and reporting
- Concomitant medication documentation

- Medical History documentation
- In the case of Investigator-Initiated Trials, the research record and informed consent form will be reviewed for the first participant to have been enrolled and received study treatment
- In the case of Investigator Requested audits, the auditor will select a sample of at least 20% of participants, but no less than 5. The participant's research record, informed consent, and other related documents will be reviewed. The Principal Investigator or study team may request additional records to be reviewed.
- In the case of External Audit and Inspection Preparation, the auditor will select a sample of at least 20% of participants, but no less than 5. The participant's research record, informed consent, and other related documents will be reviewed.

My study was just evaluated. How long will it take before I receive a report?

A written report is issued by the Quality Review detailing the findings, including corrective actions, within 3 weeks of the exit interview.

Who else sees the written report?

In the case of routine Quality Reviews, only the PI, research team, and Quality Review team see the report, unless findings indicate possible serious or continuing noncompliance, or a possible unanticipated problem involving risks to subjects or others, in which case the report is shared with the IRB. Otherwise, the report stays with the PI, research team, and Quality Review team.

In the case of a For-Cause audit, at a minimum, the IRB, Assistant Dean of Human Research Compliance, Associate Dean of Clinical Research, department chair, and division chief will also view the report. Other relevant and key stakeholders may view it as necessary.

How much time do I have to respond to the written report?

The principal investigator has 21 days to implement corrective actions and respond in writing. If an extension is needed to complete any corrective actions, the request, including how many additional days are needed, must be sent to researchaudit@med.cornell.edu. The extension is not to exceed an additional 21 days.

What if my protocol is out of compliance with state or local regulations, WCM policies, and/or the IRB-approved protocol?

If this occurs, the principal investigator is required to implement a corrective action plan commensurate with the degree of noncompliance. In some cases, the written report you receive will guide you as to what corrective actions might best fit your circumstances in the opinion of the Human Research Quality Review & Education Program. If this happens, the principal investigator can choose to follow these prescribed corrective actions or implement his or her own. In either case, corrective actions must be detailed in the principal investigator's response to the written report so that, in the case of a For-Cause audit, they can be presented to the IRB by the audit team at a convened meeting.

What is the role of the IRB in the For-Cause audit or Quality Review process?

The IRB is not involved in the Quality Review process, unless findings indicate possible serious or continuing noncompliance, or a possible unanticipated problem involving risks to subjects or others, in which case the report is shared with the IRB. In the case of a For-Cause audit, findings are always shared with the IRB.

Once the IRB is briefed on the findings and corrective actions implemented by the principal investigator, it may determine that a given finding constitutes serious or continuing noncompliance, or an unanticipated problem involving risks to subjects or others, in which case the finding will need to be reported to the Health and Human Services Office of

Human Research Protections (OHRP) and/or the United States Food and Drug Administration (FDA), the sponsor, and funding agency in accordance with IRB responsibilities as dictated by federal regulations 45CFR46.103(b)(5)(ii) and 21CFR56.108(b)(2), respectively.

Whether or not the IRB determines serious or continuing noncompliance, or an unanticipated problem involving risks to subjects or others, has occurred, it will issue a determination letter, which is distributed to the principal investigator, Assistant Dean of Human Research Compliance, Associate Dean of Clinical Research, Department Chair, and Division Chief.

As part of the determination letter, the IRB may issue corrective actions in addition to ones prescribed in the written report or selected as appropriate by the principal investigator, such as:

- Restricting research of the PI or study team or limit the amount of activity on certain projects.
- Suspending or terminating one or more research projects conducted by the PI
- Requiring educational sessions for the PI and study team.
- Suspending enrollment of new participants on one or more research projects conducted by the PI.
- Requiring additional reporting to the IRB or conducting early Continuing Review
- Requiring re-reviewing of research by the IRB, DSMB, or CSEC (Clinical Study Evaluation Committee).

The IRB also determines, when a principal investigator appeals an audit finding, whether the finding was accurate or not accurate.

How do I appeal a For-Cause audit finding?

If you disagree with the accuracy of a For-Cause audit finding, notify researchaudit@med.cornell.edu of the request to appeal with a signed memo 2 weeks prior to the IRB meeting at which the findings are to be discussed. The audit findings and appeal will both be presented at an IRB meeting by the audit team.

What if, after I appeal a For-Cause audit finding, the IRB determines the audit finding should stand?

If this occurs, the PI has 7 days from the date of notification to provide and implement a corrective and preventative action plan.

What if, after I appeal a For-Cause audit finding, the IRB determines the audit finding was not accurate?

If this occurs, the PI is not required to complete corrective actions, and, if appropriate, an amended written report will be issued.

Who should I contact if I have questions?

Contact the Quality Review team at researchaudit@med.cornell.edu.