

SOP: QA 902 Version No.: 04 Effective Date: 12/10/2010	QUALITY IMPROVEMENT & QUALITY ASSURANCE ACTIVITIES	Supersedes Document: Dated: 11/06/2008
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Steering Committee approved 1/31/11

1. POLICY

One of the missions of the Aurora Health Care Research Subject Protection Program (RSPP) is to protect the integrity of clinical research by providing oversight of approved protocols of human subject research under its review. The Aurora Health Care Research Quality Assurance Specialist, operating within the RSPP, will conduct quality assurance assessments (review or “audit”) to ensure that the best possible research practices are used in human subject research at Aurora Health Care. Assessments will be conducted on IRB approved protocols to ensure compliance with the protocol, Aurora IRB SOPs, accreditation standards, ICH Good Clinical Practice (GCP) Guidelines, as well as all applicable federal regulations and other state and local laws.

Specific Policies

Terms used in this policy, but not defined herein shall have the meanings set forth in the Glossary.

1.1. Protocol selection

Protocol selection may include, but is not limited to:

- Random (routine)
- For cause (actual or believed protocol, policy, accreditation, law or regulation violation; continued violations as determined by quarterly review of Violation Log)
- At the direction of the IRB
- Research subject, family, or research personnel complaint
- Investigator-sponsored research where no alternative oversight exists
- Follow-up of corrective actions resulting from routine or for-cause audits
- Self-directed quality assurance activities (Investigator request prior to sponsor or FDA auditing, assessment of new clinical research coordinator training)

1.2. Document review

The following documents will be reviewed by the Research Quality Assurance Specialist during the audit process:

- All IRB submissions and correspondence

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- Regulatory essential documents
- Sponsor documents and correspondence
- Study protocol
- Signed informed consents
- Case report forms
- Subject study source documents
- Research subject files
- Subject medical records
- Study logs of drug/device accountability, distribution, and storage forms
- Unanticipated adverse device event reports
- Unanticipated problem reports and UPIRSOs
- Serious adverse event reports reported to the sponsor
- Protocol deviations, violations, and exceptions
- FDA audit results
- Physician progress notes
- Monitoring reports
- Staff training records
- PI and research staff CV and licenses

Other documents, as necessary, may be reviewed specific to the type and situation of the audit being conducted.

1.3. Audit Process

1.3.1. Site notification

The Research Quality Assurance Specialist will contact the principal investigator, study coordinator, and manager (when applicable) by telephone, e-mail, or letter to notify

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the site of the anticipated audit. An explanation of the scope, rationale of the audit, what material/documents will be required for review, and the duration of the audit process will be provided. The letter will be sent at least 2 weeks in advance of the anticipated audit. If the research staff is unavailable during the proposed date and time, the Research Quality Assurance Specialist will work with the research staff to arrange an alternative date that is mutually agreeable.

In the case of IRB-directed or for cause audits, no prior notification is necessary.

1.3.2. Site preparation

The quality assurance review is a formal audit. It is expected that the research staff be prepared for the audit upon arrival of the Research Quality Assurance Specialist at the study site. A pre-audit meeting may be conducted to discuss the audit process and address any concerns or questions from the principal investigator or research staff. Failure to comply with any aspect of the Quality Assurance audit process will be handled under the Noncompliance Policy (CO 601). Expectations for preparation of the audit include but are not limited to:

- A study-specific regulatory binder that is organized and contains all essential documents described in E6 of the ICH GCP guidelines
- Signed and dated consent forms for all enrolled subjects and screen failures when applicable
- Completed case report forms
- Subject medical records and other source documents to support study data
- Drug and device accountability records

1.3.3. On-site audit

(i) The auditing process will include a review of regulatory documentation for the study as well as a comparison of source documentation (see section 1.2) against the requirements of the study protocol, to ensure compliance with the protocol, all appropriate federal and state regulations, IRB SOPs, and ICH GCP guidelines. The time required to conduct the audit will depend on the complexity of the study as well as the number of research subject files reviewed. .

(ii) Audit checklists will be used to document proper performance of the audit.

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(iii) The number of subject files audited will be at minimum 10 percent of the total local enrollment. Files reviewed will be randomly selected. In the case of a for cause audit, all subject files may be audited.

(iv) All, or a representative sample of subject signed consent forms and consent source documentation, will be reviewed.

(v) If at any time during the audit process any of the following issue is identified, the RSPP Manager will be notified immediately. The RSPP Manager will notify the Senior IRB Chair and the Institutional Official as needed.

- Any issue that potentially places subjects at risk,
- Any issue that indicates that subjects were exposed to unexpected serious harm,
- Any issue that indicates that subjects are in danger of imminent harm,
- A finding that IRB policies and procedures or any federal or state regulations were not met.

1.3.4. Preliminary Report and Meeting

After completion of the audit, a preliminary report will be written and a meeting will be requested with the principal investigator, study coordinator(s), and research manager (when applicable), to discuss the findings and review the preliminary report. This meeting should be scheduled as soon as possible after completion of the quality assurance audit with the expectation that all study team members attend, and the meeting be held in a timely fashion. The purpose of the preliminary report and meeting is to provide the opportunity to clarify questions, correct errors, and identify corrective action(s) if indicated and/or to make recommendations to improve the conduct of clinical research. The study team is required to follow up with the Research Quality Assurance Specialist within 1 week of completion of the preliminary report to address any outstanding issues or concerns that were not able to be resolved during the preliminary meeting. In some cases, the principal investigator may be asked to provide a written response to the preliminary report of the audit findings.

1.3.5 Final Report

Following completion of the preliminary meeting and resolution of all outstanding issues, the Research Quality Assurance Specialist will prepare a final report detailing the audit observations. The final report will identify 1) recommendations for any corrective actions and 2) required actions. Based on the audit findings, an audit performance score

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will be generated using the guidelines outlined in the Research Quality Assurance and Compliance (RQAC) Committee Manual. Depending on the performance of the audit, the principal investigator may be asked to follow up with a corrective action plan to the RQAC Committee as detailed in the RQAC Committee Manual.

(i) A copy of the Final Report will be sent electronically to the principal investigator. The report will request written acknowledgment of receipt. The principal investigator will be instructed to file the final report in a location separate from the study file/binder(s). A copy of the Final Report will also be sent to the Division of Clinical Research Manager (when applicable), the Research Coordinator, and Institutional Official.

(ii) A copy of the Final Report will be filed in the office of the Research Quality Assurance Specialist.

(iii) A copy of the Final Report will be also be submitted to the RQAC Committee for recommendations to made on an individual, departmental or system-wide basis.

(iv) An aggregate summary of audit findings will be presented to the IRB, IRB Steering Committee, and research community on an annual basis to make recommendations for programmatic quality improvement.

1.4 Corrective Actions

If allegations or findings of non-compliance, as defined in Aurora IRB Noncompliance policy (SOP CO 601), or apparent research misconduct, as defined in the Aurora IRB Research Misconduct policy (SOP CO 602), are identified during the audit, the process defined within each of these policies will be invoked. Allegations or findings of Noncompliance that are identified during an audit will also be reviewed by the RQAC Committee, along with any other findings identified during the review. The RQAC Committee may advise the IRB with regard to the development of an action plan to address Noncompliance. The possible actions the RQAC Committee may recommend to the IRB are included in the RQAC Committee Manual. However, all regulatory findings and determinations are the responsibility of the IRB.

Follow-up audits will be scheduled when deficiencies have been identified, and which correction is substantially important in providing adequate protection of the rights and welfare of participants.

1.5 Observation of Consent Process and/or the Conduct of Research

As warranted, the IRB may direct the Research Quality Assurance Specialist to observe the consent process and/or conduct of the research. Observation reports will be

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reviewed by the RSPP Manager, and if necessary, the IRB Chair and/or Institutional Official. As necessary, the IRB will be informed of observation results.

1.6 Quality Assurance/Quality Improvement of the IRB

1.6.1 Quality Assurance Reviews of IRB Processes and Procedures

The Research Quality Assurance Specialist will conduct periodic reviews of IRB activities to ensure compliance with all applicable regulations and IRB SOPs. The IRB study file of a protocol selected for review at the research site may be selected for review, as well as other randomly selected research studies. The following may be reviewed:

- The entire protocol file to ensure compliance with regulations and IRB SOPs in the initial and ongoing review of the research;
- Informed consent to ensure inclusion of all required and additional elements, risks and study procedures;
- IRB membership lists and meeting minutes;
- Education of RSPP staff and IRB members.

An audit checklist will be used to document proper performance of the audit.

1.6.2 Quality and Efficiency of IRB Function

The Institutional Official, in consultation with others as appropriate, will complete an assessment on the quality and effectiveness of activities an IRB review and function. Quality and effectiveness will be measured on a performance scale of 1 to 5, with 1 indicating "development needed" and 5 indicating "significant strength". Scores will be maintained on file in a secure folder maintained by the RSPP Manager. Quality and efficiency will also be assessed by reviewing:

- Workload of RSPP staff and IRB members, and
- Turn around time from initial submission to IRB review and approval.

1.6.3 IRB Quality Improvement

The Research Quality Assurance Specialist will present an aggregate summary of audit findings to IRB Steering Committee annually for recommendations or improvements as needed.

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Periodic reports will also be submitted to the Research Quality Assurance and Compliance Committee who will be responsible for benchmarking audit findings and making additional recommendations to the Aurora IRB Steering Committee as needed.

The IRB audit findings will be presented to the IRB at least annually with recommendations from the IRB Steering Committee.

2. SCOPE

These policies and procedures apply to all Aurora IRB approved protocols.

3. APPLICABLE REGULATIONS, GUIDELINES, AND STANDARDS

45 CFR. 46

21 CFR. 11

21 CFR 50

21 CFR 54

21 CFR 56

21 CFR 160

21 CFR 312

21 CFR 812

ICH GCP Guidelines

AAHRPP Elements I.5.A, I.5.B, I.5.D

4. REFERENCES TO OTHER APPLICABLE SOPS

SOP RR 403

SOP 601

SOP 602