Standard Operating Procedure
Protocol Selection for Compliance Activity

1. PURPOSE

To define the procedures utilized to select protocols for the purpose of conducting compliance activities.

2. SCOPE

This procedure applies to all compliance activities performed by the Education and Compliance Office.

3. RESPONSIBILITIES

The IRB Executive Committee, IRB Chair or RCCO leadership will be responsible for notifying the Education and Compliance Office of requested “for cause” audits occurring as a result of known or suspected problems in the conduct of human subject research.

The Office for Investigator-Sponsored IND and IDE Support will notify the Education and Compliance Office of protocols involving investigator-sponsored INDs or IDEs.

The Education and Compliance Coordinators are responsible for selecting protocols for all other compliance activities.

4. PROCEDURES

4.1 For RISE interviews, the Education and Compliance Coordinator will review the list of recently approved protocols using the following criteria for selection:

- Source of funding (federal or internal funding)
- Greater than minimal risk
- Investigator new to the University
- Established investigator who has never undergone a RISE review
- PI is graduate or doctoral student
- Focus of research considered high profile
- Gene transfer intervention
- Radioactive drug research
- Coordinating Center Protocol
- Greater than minimal risk protocol conducted in a transnational setting
4.2 The ECO will base its selections of schools/departments/divisions for full departmental QA audits on information including but not limited to:

- Date of last audit within the respective area
- Number of previous audits performed in the respective area
- IRB protocol reconsideration rate of the respective area
- Recommendations received from the IRB

5. REFERENCES/DOCUMENTATION

NA

Original: 8/1/01
Reviewed/Revised: 11/20/03
Reviewed: 9/3/04
Reviewed/Revised 7/11/05
Reviewed/Revised: 1/17/06
Reviewed/Revised: 2/2/06
Reviewed/Revised: 12/15/2010
Reviewed/Revised: 6/1/11
Reviewed/Revised: 10/5/12
1. PURPOSE

To define the procedure utilized for investigator notification of a RISE interview, randomly selected audit or for-cause audit.

2. SCOPE

This procedure applies to all investigator site compliance activities performed by the Education and Compliance Office.

3. RESPONSIBILITIES

The Education and Compliance Coordinators are responsible for providing written notification to investigators regarding upcoming compliance activities conducted on their protocols.

4. PROCEDURES

4.1. After a protocol is identified for a compliance activity, a written notification will be sent to the principal investigator by the Education and Compliance Office. Examples of compliance activity review notifications are attached. Note “For Cause” audit notifications are only sent after the IRB Executive Committee/IRB Chair has notified the investigator of the audit.

4.2. Notification of a compliance activity will be sent via e-mail with a request for a delivery receipt. The notification will be sent to the e-mail address of the principal investigator and applicable research team members (designated research coordinator and mentor if applicable) listed in the OSIRIS protocol. The notification and the electronic delivery receipt will be saved in the ECO electronic file folder created specifically for each compliance activity.

4.3 For departmental reviews, the dean or the department chair will receive notification of the planned compliance activity. The notification to the dean or department chair will permit the dean or department chair to request a compliance activity of a particular investigator in the respective area.

5. REFERENCES/DOCUMENTATION

Attachments: Example of RISE notification
Example of Randomly selected protocol for audit
Example of For-cause audit notification
Example of departmental audit notification
List of items to be reviewed for audit
MEMORANDUM

To: PI
From: Kelly Dornin-Koss, MPPM, RN, CIP
Director, Education and Compliance Office for Human Subject Research

Date: June 1, 2010
Subject: RISE Review (Research Investigator Start-up Education)
IRB #: PRO000000: Title of study here

The Research Conduct and Compliance Office of the University of Pittsburgh is committed to the improvement of the quality, efficiency, and integrity of our research environment and activities. In pursuit of this commitment, the office supports a quality assurance program to assess the research activities conducted under and in accordance with the University's Assurance Agreement with the Office of Human Research Protections, DHHS.

The objective of this quality assurance program for human subject research is to ensure that proper scientific, ethical and regulatory requirements are followed in Institutional Review Board (IRB) approved protocols. The program is also designed to encourage compliance by detecting errors and/or omissions that might inadvertently occur when implementing research activities. It is felt that this program will serve a very useful educational purpose and enhance academic research practice at the University of Pittsburgh.

At this time, RISE interviews are being conducted on protocols for which IRB approval has recently been obtained. Your study, IRB #PRO000000: Title of study, meets this criterion and has been selected. Although you may not yet have enrolled subjects, the compliance staff would like to review your methods to implement the research protocol. A member of the compliance staff will contact you within the next week to arrange for a mutually agreeable time to conduct the interview.

The interview will be conducted with you, the study coordinator, and any additional personnel you feel would benefit by attending this educational activity. This interview will involve approximately one hour of your time. Availability of a conference room or quiet area for the compliance staff to review associated documents will be necessary. Documents pertaining to your research will be held strictly confidential. Enclosed you will find a brief outline of some of the documentation that may be reviewed during the RISE process. You may wish to refer to our website for additional information.

http://www.ecohsr.pitt.edu/.

I would very much appreciate your cooperation with the RISE quality assurance program.
To: Jane Doe, Ph.D.

From: KDK, Co-Director
Research Conduct and Compliance

Date: February 21, 2001

Subject: Research Quality Assurance Program

Research Protocol: IRB #000000: Title

The Research Conduct and Compliance Office of the University of Pittsburgh is committed to the improvement of the quality, efficiency, and integrity of our research environment and activities. In pursuit of this commitment, the Education and Compliance Office for Human Subject Research supports a quality assurance program to assess the research activities conducted under and in accordance with the University's Assurance Agreement with the Office of Human Research Protections, DHHS.

The objective of this quality assurance (QA) program for research is to ensure that proper scientific, ethical and regulatory requirements are followed in Institutional Review Board (IRB) approved protocols. The program is also designed to encourage compliance by detecting errors and/or omissions that might inadvertently occur when implementing research activities. This program is designed to be educational and to enhance academic research practice at the University of Pittsburgh.

Compliance activities are being conducted throughout the six Schools of Health Sciences. Your protocol, IRB #_____ has been selected for (Name the compliance activity). A member of the ECO-HSR staff will contact your office within the next week to arrange for a mutually agreeable time to conduct the (compliance activity).

An interview will be conducted with you, the study coordinator, and any additional personnel you feel should attend, to discuss this research study and related issues. This interview will involve approximately one hour of your time. Your presence during the course of the (name the compliance activity) is not necessary. Availability of a conference room or quiet area for the day for the audit staff to review patient records and other associated documents will be necessary. Documents pertaining to your research will be held strictly confidential. Enclosed you will find a brief outline of some of the documentation that may be reviewed during the (name the activity).

I would very much appreciate your cooperation with the research quality assurance program.

Enclosure (1)
To: John Doe, MD
    Associate Professor of Medicine and Surgery

From: Name(s) of ECO-HSR staff
      Education and Compliance Coordinator(s)

Date: August 20, 2010

Subject: Research Quality Assurance Program

Study to be Audited: IRB #00000: A Randomized Multi-Center, Double-Blind Study Evaluating the Efficacy and Safety of Drug A

The Institutional Review Board Executive Committee has requested that the Education and Compliance Office (ECO) perform an audit of the above-named research study. In compliance with this directive, an ECO staff member will be contacting you to arrange for a time to review the activity on this study. It is the policy of the ECO that audits requested by the Executive Committee be performed within a two week time frame.

The objective of the quality assurance (QA) program for clinical research at our University is to ensure that proper scientific, ethical and regulatory requirements are followed in all Institutional Review Board (IRB) approved clinical protocols. The program is also designed to encourage compliance by detecting errors and/or omissions that might inadvertently occur when implementing research activities.

Your presence during the course of the audit is not necessary. However, before initiating the audit, an interview is necessary to discuss research activities and other related issues. This interview will involve approximately one hour of your time. You may invite members of your research team to attend and participate in the interview/discussion. Availability of a conference room or quiet area for the day to go over research participant’s records and other related issues will be necessary.

Documents pertaining to your clinical research will be held strictly confidential. Enclosed you will find a brief outline of some of the documentation that may be reviewed during the audit. We would like to thank you in advance for your cooperation with the quality assurance program.

If you have questions regarding this notice, please do not hesitate to call us at XXX-XXX-XXXX.

Attachment (1)
The Research Conduct and Compliance Office of the University of Pittsburgh is committed to the improvement of the quality, efficiency, and integrity of our research environment and activities. In pursuit of this commitment, the office supports a quality assurance program to assess the clinical research activities conducted under and in accordance with the University's Assurance Agreement with the Office of Human Research Protections, DHHS.

The objective of this quality assurance program for clinical research is to ensure that proper scientific, ethical and regulatory requirements are followed in Institutional Review Board (IRB) approved clinical protocols. The program is also designed to encourage compliance by detecting errors and/or omissions that might inadvertently occur when implementing research activities. This program is designed to be educational and to enhance academic research practice at the University of Pittsburgh.

At this time, we plan to conduct internal audits on protocols within the School of _________. The above-referenced research studies have been selected for audit. If you have suggestions for any additional investigators/protocols to be audited, please contact Ms. Elizabeth Taylor of the Education and Compliance Office for Human Subject Research at 412-383-0000.

You will be provided with copies of the audit reports. Once the audit process is complete, the staff of the Research Conduct and Compliance Office will be available, upon your request, to provide an educational seminar covering “Good Research Practice.” Thank you in advance for your cooperation with this quality assurance initiative.
SAMPLE INFORMATION REVIEWED DURING QUALITY ASSURANCE REVIEW
(Not all may apply)

**IRB Process**

Dates of approval relative to initiation of research activities
Dates of modification approval relative to implementation
Lapse of approval
Progress reports

**Consent process and documentation**

Correct version of consent form document
Signed and dated by subject and person obtaining consent
Presence of extemporaneous modifications
Correct emergency contact information
Narrative documentation of informed consent process

**Subject Records**

Documentation of all points of eligibility criteria
Documentation of all study activities
Documentation of follow-up activities
Copies of source documents included in research records
Reporting of adverse events to appropriate regulatory offices
Documentation of terms of subject termination from study
Review of data collection tools/procedures

**Test article accountability**

Proper storage of test article
Review of inventory records (dispensing and retrieval)
Review of return or disposal records

**Lab Facilities**

Laboratory site/certification and quality of performance
Disposal of radioactive and biohazardous waste
Records of retained laboratory samples

**Documentation**

Regulatory files/records
IRB files/records
Sponsor correspondence
Monitor visits

Updated 6/1/11
1. PURPOSE

To define the procedure utilized to contact the Principal Investigator prior to conducting a compliance activity.

2. SCOPE

This procedure applies to all compliance activities performed by the Education and Compliance Office.

3. RESPONSIBILITIES

The Education and Compliance Coordinators are responsible for contacting the Principal Investigator to arrange for the compliance activity.

4. PROCEDURES

4.1. The principal investigator will be contacted to make arrangements for the compliance activity. With the investigator’s permission, arrangements can be made through the clinical research coordinator or other designated research staff. This initial contact should take place within one week of the delivery of the e-mail notification.

4.2 Departmental audits may be scheduled at a mutually agreeable time, preferably within one month of the audit notification.

4.3 “For Cause” audits should be scheduled within two weeks of receipt of the audit notification. If the investigator is unable to comply with the two-week time frame, the IRB Executive Committee will be notified of problems in scheduling the audit in a timely manner. Unless the Education and Compliance Office is directed otherwise by the IRB Executive Committee, the audit date will be set at the first agreeable date between the investigator and the Education and Compliance Office.

5. REFERENCES/DOCUMENTATION

NA

Original: 11/20/03
Reviewed: 9/3/04
Reviewed/Revised 1/17/06
Review/Revised: 12/15/10
Reviewed: 6/1/11
Reviewed: 10/5/12
1. PURPOSE

To define the procedure utilized to select research participants’ records for review during an audit.

2. SCOPE

This procedure applies to all investigator site audits performed by the Education and Compliance Office.

3. RESPONSIBILITIES

The Education and Compliance Coordinators are responsible for selecting research participants’ records for review during investigator site audits.

4. PROCEDURES

4.1. Prior to the audit, the principal investigator/study coordinator will be requested to provide a list of all study participants to the Education and Compliance Office. To ensure the confidentiality of the research participants, the list will be limited to the research participant’s initials or unique identification number and their date of study enrollment.

4.2. From this list, the Education and Compliance Office will select 20-25% of the participant population. For large studies with enrollment greater than 100, 5-10% of the participant population will be selected. The list of subjects selected for audit will be provided to the PI/coordinator so that all records containing information relevant to the study may be assembled, i.e., research records, clinic charts, hospital records. Access to all selected subjects’ records and associated documents should be provided to the Education and Compliance Office.

At the time of the audit, the ECO staff may request additional records for review. If no problems are identified with the research records or if a systematic error or omission is identified, the ECO may elect to review a square root of the total number of subjects enrolled in lieu of a percentage of subjects enrolled.

4.3. In the case of a “for cause” audit, the Education and Compliance Office may review 100% of the research participants’ records. In cases where the safety of the research subject may be in immediate jeopardy, the Education and Compliance Office may request the research subject’s name and social security number to expedite the review of the subject’s medical record if applicable.
5. REFERENCES/DOCUMENTATION

NA

Original: 8/1/01
Reviewed/Revised: 11/20/03
Reviewed: 9/3/04
Reviewed/Revised 1/24/06
Reviewed: 6/1/11
Reviewed: 10/05/12
Standard Operating Procedure
Review of IRB File in Preparation for a Compliance Activity

1. PURPOSE

To define the procedures utilized to review the IRB file in preparation for a Compliance Activity.

2. SCOPE

This procedure applies to all Compliance Activities performed by the Education and Compliance Office for Human Subject Protection.

3. RESPONSIBILITIES

The Education and Compliance Coordinators are responsible for reviewing the IRB file in preparation for Compliance Activities.

4. PROCEDURES

4.1. Prior to conducting the Compliance Activity, the Education and Compliance Coordinators will review the associated protocol file. During the IRB file review, the Education and Compliance Coordinators will assess:
   a) Dates of initial protocol review and approval by the IRB
   b) Nature and dates of any modifications to the IRB approved protocol, e.g. changes in entrance criteria, study procedures, drug administration, consent form changes (if applicable)
   c) Dates of approval granted by the IRB
   d) Lapse of IRB Approval
   e) Relevant IRB meeting minutes

   This information will be used as a source of reference, which will be used during the course of the compliance activity.

4.2. Any inconsistencies or omissions noted during the file review will be documented and included in the compliance activity report. Inconsistencies will also be recorded in the QA database under the section titled “IRB Issues.” Issues of significant concern noted with the IRB review of the study will be brought to the attention of the Director of the ECO-HSR who will forward the issue to IRB leadership as needed.

5. REFERENCES/DOCUMENTATION

NA

Original: 8/1/01
Reviewed/Revised: 11/20/03
Reviewed: 9/3/04
Reviewed/Revised: 12/15/2010
Reviewed/Revised: 6/1/11
Reviewed: 10/5/12
<table>
<thead>
<tr>
<th>SAMPLE</th>
<th>TIME LINE</th>
<th>SAMPLE</th>
</tr>
</thead>
<tbody>
<tr>
<td>IRB #00110000: Treatment of Post Syndrome: A Placebo, Controlled Randomized Trial of…..</td>
<td>PI: John Doe, MD</td>
<td></td>
</tr>
<tr>
<td>9/22/01</td>
<td>Original submission to IRB</td>
<td></td>
</tr>
<tr>
<td>10/20/01</td>
<td>Reviewed by Committee D. IRB requesting changes and clarifications</td>
<td></td>
</tr>
<tr>
<td>11/3/01</td>
<td>Changes and clarifications submitted to IRB – consent form changes – re consent required.</td>
<td></td>
</tr>
<tr>
<td>11/14/01</td>
<td>IRB approval.</td>
<td></td>
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<tr>
<td></td>
<td>• Approval Date: October 20, 2001</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Renewal Date: October 19, 2002</td>
<td></td>
</tr>
<tr>
<td>9/20/02</td>
<td>Renewal request received by the IRB. No date on submission. No mods. 12 subjects enrolled.</td>
<td></td>
</tr>
<tr>
<td>10/1/02</td>
<td>Reviewed by Committee A. Full approval given.</td>
<td></td>
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<tr>
<td></td>
<td>• Approval Date: October 1, 2002</td>
<td></td>
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<tr>
<td></td>
<td>• Renewal Date: September 30, 2003</td>
<td></td>
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<tr>
<td>8/26/03</td>
<td>Renewal with modifications submitted. 16 subjects enrolled. Modifications are:</td>
<td></td>
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<tr>
<td></td>
<td>• Addition of co-investigator</td>
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<td></td>
<td>• Increase in total number of subjects to be enrolled from 20 to 25</td>
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<td></td>
<td>• Addition of 6 week follow-up visit</td>
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<tr>
<td>9/21/03</td>
<td>Reviewed by Committee C. Changes/clarifications requested by IRB</td>
<td></td>
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<tr>
<td>10/12/03</td>
<td>Changes/clarifications submitted to IRB.</td>
<td></td>
</tr>
<tr>
<td>10/18/03</td>
<td>IRB approval given.</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Approval Date: September 21, 20003</td>
<td></td>
</tr>
<tr>
<td></td>
<td>• Renewal Date: September 20, 2004</td>
<td></td>
</tr>
<tr>
<td>8/20/04</td>
<td>Reminder from IRB to renew.</td>
<td></td>
</tr>
<tr>
<td>9/21/04</td>
<td>IRB terminated study due to failure to submit renewal request.</td>
<td></td>
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<tr>
<td>10/6/04</td>
<td>Memo to IRB from study coordinator, stating that protocol is no longer active.</td>
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</tr>
<tr>
<td>10/15/04</td>
<td>Chosen for audit. Notification sent to PI.</td>
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</tbody>
</table>
Standard Operating Procedure
Development of Compliance Activity Worksheets

1. PURPOSE

To define the procedures utilized to prepare protocol specific worksheets for a compliance activity.

2. SCOPE

This procedure applies to all compliance activities performed by the Education and Compliance Office for Human Subject Research.

3. RESPONSIBILITIES

The Education and Compliance Coordinators are responsible for preparing worksheets for all compliance activities.

4. PROCEDURES

4.1 Prior to conducting the compliance activity, the Education and Compliance Coordinator will develop worksheets specific to the research protocol. These worksheets will include data points outlined in the IRB approved protocol, which are deemed to be pertinent to the conduct of the study such as:

- Eligibility criteria
- Screening procedures
- Study procedures
- Follow-up procedures

In addition, prior to the compliance activity the lead Education and Compliance Coordinator will inquire whether or not the research team developed study specific data collection forms. In those instances where forms have been developed by the team, the lead Education and Compliance Coordinator will request a copy of the forms and review them for accuracy and completeness. During the compliance activity recommendations will be made regarding the forms to ensure compliant study documentation in accordance with the approved protocol.

5. REFERENCES/DOCUMENTATION

Audit table of Inclusion criteria attached.

Original: 8/1/01
Reviewed/Revised: 11/20/03
Reviewed: 9/3/04
Reviewed/revised: 12/15/10
Reviewed/revised: 6/1/11
Reviewed: 10/5/12
### INCLUSION CRITERIA

<table>
<thead>
<tr>
<th>Criteria</th>
<th>Criteria Met/Documented??</th>
<th>Y or N</th>
</tr>
</thead>
<tbody>
<tr>
<td>Subject is &gt; 18 years of age</td>
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</tr>
<tr>
<td>Must have the following laboratory values prior to surgery:</td>
<td></td>
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<tr>
<td>• WBC &gt; 2000/mm³</td>
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<tr>
<td>• Platelet count &gt; 50,000</td>
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<td></td>
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<tr>
<td>• Bilirubin &lt; 2 mg/dl</td>
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<tr>
<td>• Creatinine &lt; 2 mg/dl</td>
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<tr>
<td>Women of childbearing potential must have a negative pregnancy test prior to entering study</td>
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<tr>
<td>Subjects must be free of the following conditions:</td>
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<td>• MI within the past 12 months</td>
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<td>• Current lung cancer or history of lung cancer</td>
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<tr>
<td>• Current unstable angina</td>
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<tr>
<td>• Clinically active heart failure</td>
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<tr>
<td>• Active respiratory infection</td>
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<tr>
<td>• History of clinical depression defined as any hospitalization for clinical depression or suicide attempt in the past 10 years, or a CESD score &gt; 17</td>
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<tr>
<td>Subject <strong>does not have</strong> a history of allergy or intolerance to medications “A”, “B” or “C”</td>
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</tbody>
</table>
1. PURPOSE

To define the procedures necessary to conduct a pre-compliance activity interview.

2. SCOPE

This procedure applies to all investigator compliance activities performed by the Education and Compliance Office for Human Subject Research.

3. RESPONSIBILITIES

The Education and Compliance Coordinators are responsible for preparing for and conducting an interview prior to the compliance activity.

4. PROCEDURES

4.1. The interview is to be held prior to the conduct of a compliance activity with a member or members of the respective research staff.

This interview is performed to evaluate the plans to implement the conduct of the study and identify the individual(s) responsible for various protocol related activities, such as:

- Preparing IRB protocol submissions
- Training study staff
- Recruiting study participants
- Implementing and documenting the informed consent process
- Maintaining study documentation
- Monitoring data
- Reporting adverse events/Unanticipated Problems (UAPS)
- Collection, preparation and storage of biological samples
- Analyzing study data

4.2. During the interview, information is also obtained regarding:

- Number of subjects screened and enrolled into the study
- Number of sites involved, if the study is multi-center
- Review of reported adverse events/UAP – status and resolution
- Occurrence of site monitoring visit(s)
- Adherence to data and safety monitoring plans
- Difficulties in subject recruitment or in study conduct
- Maintenance and security of research data

4.3. The pre-compliance activity interview is to be utilized as an opportunity to clarify any questions or issues that the Education and Compliance Coordinators may have regarding the conduct of the study.
5. REFERENCES/DOCUMENTATION

Attached example of interview form.

Original: 8/1/01
Reviewed/Revised: 6/1/11
Reviewed: 10/5/12
IRB #_________________  QA#_________________

Principal Investigator

Previous Principal Investigators

Study Coordinator

Previous Study Coordinators

Number of subjects screened to date: ______  Number of subjects enrolled to date: ______

If multi-center – number of centers: ______  Number of multi-center subject enrollment: ___

<table>
<thead>
<tr>
<th>Procedure</th>
<th>Responsibility / Comment</th>
</tr>
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<tbody>
<tr>
<td>IRB Submissions</td>
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<tr>
<td>Recruitment Measures</td>
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<tr>
<td>Advertising</td>
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<tr>
<td>Screening</td>
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<tr>
<td>Informed Consent</td>
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<tr>
<td>Randomization</td>
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<tr>
<td>Physical Exam</td>
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<td>Blood Draw</td>
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<td>Lab Used</td>
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<tr>
<td>Blood Storage</td>
<td></td>
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<tr>
<td>Questionnaires</td>
<td></td>
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<tr>
<td>Record Keeping</td>
<td></td>
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<tr>
<td>Regulatory Records</td>
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<tr>
<td>Storage of Records</td>
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<tr>
<td>Drug Accountability</td>
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<tr>
<td>Data Security</td>
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<tr>
<td>Data Analysis</td>
<td></td>
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<tr>
<td>Data monitoring</td>
<td></td>
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<tr>
<td>Staff education</td>
<td></td>
</tr>
</tbody>
</table>
To define the procedures utilized to review the informed consent documents maintained in the investigator’s research records. This procedure is to verify that documentation of informed consent is performed according to Federal Policy (45 part 46) and where applicable FDA (21 CFR 50) as well as the University of Pittsburgh Policy as stated in the Reference Manual for the use of Human Subjects in Research.

2. SCOPE

This procedure applies to all compliance activities performed by the Education and Compliance Office for Human Subject Research.

3. RESPONSIBILITIES

The Education and Compliance Coordinators are responsible for verifying the appropriate documentation of informed consent for research studies.

4. PROCEDURES

4.1. The informed consent document will be reviewed for the presence of the following documentation:

- The signature of the subject or the signature of the subject’s legally authorized representative
- Documentation of assent, if applicable
- The signature of the investigator. *If the study involves a drug, device or surgical procedure, the signature should be that of a physician investigator*
- Dates written adjacent to each signature, in the hand of the signatory
- Narrative documentation in the case history regarding the informed consent process (Required for research regulated by the FDA. Recommended for ALL research protocols.)

4.2. Additional items to be assessed during the review of the informed consent documents include but are not limited to:

- Presence of the IRB approval and expiration dates
- Utilization of the correct version of the IRB approved consent form for each subject
- Placement on appropriate letterhead
- Consistency between the type and frequency of side effects listed in the informed consent document and protocol to those that actually occurred
- Presence of any extemporaneous modification to the informed consent document
- Determination that informed consent was obtained prior to the initiation of any research-related procedures
5. REFERENCES/DOCUMENTATION

Attached: Consent form data table
      Documentation of Informed Consent Process Template Form

Original:  8/1/01
Reviewed/Revised:  6/1/11
Reviewed: 10/5/12
Documentation of the Informed Consent Process

IRB # ______________________________       PI ________________________________
Subject ID__________________________

<table>
<thead>
<tr>
<th>Point Addressed</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>List the persons present during the informed consent discussion</td>
<td></td>
</tr>
<tr>
<td>Who explained the details of study participation?</td>
<td></td>
</tr>
<tr>
<td>Were all risks and benefits of study participation presented to the subject (and family)?</td>
<td></td>
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<tr>
<td>Were all questions answered to the subject’s (and family’s) satisfaction?</td>
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<tr>
<td>Does the subject appear to understand all terms of participation and agree to enrollment?</td>
<td></td>
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<tr>
<td>How was comprehension assessed?</td>
<td></td>
</tr>
<tr>
<td>Was the consent document signed by all parties prior to the performance of any study related procedures?</td>
<td></td>
</tr>
<tr>
<td>Was a copy of the consent document provided to the subject?</td>
<td></td>
</tr>
</tbody>
</table>

Signature and Date of Investigator/Co-Investigator (or IRB approved delegate) who administered the consent process and completed this form.

________________________________   _____________  _____________
Signature       Date    Time

Version 10/05/12

Copyright 2001, 2006 - University of Pittsburgh
<table>
<thead>
<tr>
<th>Subject</th>
<th>IRB Approval Date</th>
<th>Date Research Begun</th>
<th>Signed by Subject</th>
<th>Dated by Subject</th>
<th>Signed by Investigator</th>
<th>Dated by Investigator</th>
<th>Narrative Note of Consent</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
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</table>
Standard Operating Procedure
Review of Research Participant Records and Source Documentation

1. PURPOSE

To define the procedures utilized to review research records maintained by the investigator for research study participants.

2. SCOPE

This procedure applies to all compliance activities performed by the Education and Compliance Office for Human Subject Research.

3. RESPONSIBILITIES

The Education and Compliance Coordinators are responsible for conducting reviews of research participant’s research records.

4. PROCEDURES

4.1. The Education and Compliance Coordinators will review the research records of human subjects enrolled into the respective research study. This review will:

a) Evaluate the investigator’s methods of documenting research data in terms of their organization, condition, completeness, and legibility

b) Determine whether there is adequate documentation to assure that all subjects did exist and were alive and available for the duration of their stated participation in the study.

c) Compare the investigator’s research participant records, [i.e. the case report form(s)/data collection tool(s)], with the source documentation to verify the accuracy of the participant’s records relative to the source documentation.

d) Determine whether each record contains documentation of:
   • Eligibility criteria met (or not met) for each subject
   • Screening, study and follow-up procedures implemented per the IRB-approved protocol
   • Adverse events and UPA reported in accordance with IRB and sponsor requirements
   • Observations, information, and data on the condition of the subject at the time the subject entered into the research study as well as throughout participation and study closure
   • Records of exposure of the subject to the test article, if applicable
   • The identity of all persons/departments responsible for the performance and analysis of all study-related procedures and dates the procedures were performed.
SOP #: I-A-9
SOP Area: Investigator Compliance Activity
University of Pittsburgh
Education and Compliance Office for Human Subject Research

4.2 Record review findings will be documented on the audit worksheets to assess compliance with the IRB approved protocol.

4.4 In addition to the items outlined above, the ECO coordinator will evaluate:
   - Consistency of procedures as outlined in the protocol and consent document
   - Whether the protocol and consent document reflect “actual practice”
   - Whether any modifications were implemented prior to IRB approval
   - Whether any additional procedures are being performed that were omitted from the protocol and/or consent document

5. REFERENCES/DOCUMENTATION

   NA

Original: 8/1/01
Reviewed/Revised: 11/20/03
Reviewed 9/3/04
Reviewed/Revised: 12/15/10
Reviewed/Revised: 6/1/11
Reviewed: 10/5/12
1. PURPOSE

To define the procedures utilized to review the regulatory files maintained by the investigator.

2. SCOPE

This procedure applies to all compliance activities performed by the Education and Compliance Office for Human Subject Research.

3. RESPONSIBILITIES

The Education and Compliance Coordinators are responsible for conducting reviews of investigator regulatory file(s) for research studies selected for a compliance activity.

4. PROCEDURES

4.1. During a compliance activity, the Education and Compliance Coordinators will review the regulatory files maintained by the investigator in accordance with the list of the required Regulatory File Documents (attached) and in accordance with the study design and funding source. A brief summary will be included in the written report to address the status of the regulatory file and actions necessary to ensure the records are complete.

5. REFERENCES/DOCUMENTATION

Attached Review of Regulatory File Management

Original: 8/1/01
Reviewed/Revised: 11/20/03
Reviewed/Revised: 9/3/04
Reviewed/Revised: 12/15/10
Reviewed/Revised: 6/1/11
Reviewed: 10/5/12
Review of Regulatory File Management

It is recommended that all principal investigators maintain a regulatory binder or file system, which contains all supportive study documentation. These records may be reviewed at the time of an audit. Following is a list of recommended items to be maintained within the regulatory binder. Items that would only be applicable for studies involving an IND/IDE, are under the purview of the FDA or are federally funded are listed separately at the bottom of the page.

1. Protocol
2. Informed Consent
3. IRB Correspondence
4. Sponsor Correspondence
5. Sponsor Monitoring Log/Reports
6. Serious and Unexpected Adverse Events
7. Data and Safety Monitoring Reports
8. Delegation of Authority Signature List
9. Drug / Device Accountability
10. Laboratory Certification
11. Range of Normal Values
12. Investigator’s CV
13. Training Certifications
14. Final Study Report

In addition, the following files should be maintained for research requiring an IND/IDE, are under the purview of the FDA or receive federal funding:

1. FDA correspondence, i.e. for investigator-sponsored INDs and IDEs (Note per IRB policies, a copy of all investigator IND correspondence must be submitted to the O3IS Office)
2. Investigator’s brochure
3. Form FDA-1572
4. Form FDA-1571
1. PURPOSE

To define the procedures utilized to review test article accountability during a compliance activity.

2. SCOPE

This procedure applies to all compliance activities involving a test article performed by the Education and Compliance Office for Human Subject Research.

3. RESPONSIBILITIES

The Education and Compliance Coordinators may request the assistance of the Investigational Drug Service or may personally conduct the review of test article records at the investigator site.

4. PROCEDURES

4.1 The Education and Compliance Coordinators may assess the following information (depending on the nature of the study):

- Appropriate storage methods
- Physician dispensing orders written
- Test article administered or dispensed by a qualified person authorized according to the UPMC policies
- Inventory log maintained for the test article to include:
  - drug name
  - dosage form and strength
  - date and quantity of receipt
  - lot number
  - expiration date
  - quantity and date dispensed
  - identification of the study participant
  - date(s) and quantity returned by the study participant
  - date(s) and quantity returned to the sponsor/ or onsite destruction
  - amount transferred or wasted
  - name, address, and telephone number of the sponsor
- Inventory records are consistent with subject research records
- Test article preparation instructions available. Documentation of preparation of each drug administration including date and name of preparer.
4.2 If there is a problem or concern with the test article accountability managed by the Investigational Drug Service, the ECO staff may contact the IDS to clarify or address the problem.

5. REFERENCES/DOCUMENTATION

Original: 8/1/01
Reviewed/Revised: 11/20/03
Reviewed: 9/3/04
Reviewed/Revised: 2/2/06
Reviewed/Revised: 12/15/10
Reviewed/Revised: 6/1/11
Reviewed: 10/5/12
1. PURPOSE

To define the procedures utilized to review electronic research records.

2. SCOPE

This procedure applies to compliance activities where use of electronic research records is involved.

3. RESPONSIBILITIES

The Education and Compliance Coordinators are responsible for reviewing electronic research records where the use of such records are involved in research records selected for a compliance activity.

4. PROCEDURES

4.1. For research studies that involve the use of electronic records, the Education and Compliance Office staff will ascertain the following information, where applicable:

a) Who was responsible for the software/hardware installation?
b) Are staff required to complete training prior to receiving access and is training documented?
c) Who has access to the data and is access password-protected?
d) Were there any record-keeping problems experienced during the course of the study?
e) What is the source of the data entered into the computer, e.g. direct, case report form, office record, other?
f) Who enters data and when?
g) How are changes made to previously entered data?
h) How are data submitted to the sponsor (i.e. modem, network, fax, hard disk, electronic transfer, mail, and messenger)?
i) If the sponsor discovers an error, omissions, etc., in the data received, what contacts are made with the investigator? How are corrections implemented, and how are they documented?
j) Does the investigator retain a copy of the electronic data for the appropriate time period?
k) Where is it stored, on a server or laptop or both?
l) How is data backed-up?
m) Is it stored with or without identifiers?
n) Is encryption software utilized?

5. REFERENCES/DOCUMENTATION

Original: 8/1/01
Reviewed/Revised: 11/20/03
Reviewed: 9/3/04
Reviewed/Revised: 12/15/10
Reviewed: 10/5/12
1. PURPOSE

To define the procedures utilized to prepare a compliance activity report and disseminate the report findings.

2. SCOPE

This procedure applies to all investigator compliance activities performed by the Education and Compliance Office for Human Subject Research.

3. RESPONSIBILITIES

The Education and Compliance Coordinators are responsible for preparing reports for each compliance activity performed and disseminating the report findings.

4. PROCEDURES

4.1. The heading of the report should include the following information:

a) The type of compliance review
b) The IRB number and the title of the research study
c) The name of the principal investigator
d) The name of the research coordinator
e) The date (s) on which the activity was conducted
f) The date of the report
g) The source of funding
h) The level of risk of the research study
i) The name(s) of the Education and Compliance Office staff involved in the activity
j) The name(s) of the Education and Compliance Office staff responsible for preparing the report

4.2. The introduction of the report should include but not be limited to the following:

a) The reason for the review
b) A brief summary of the research study
c) The number of subjects enrolled in the study
d) The source of subject recruitment
e) The time period over which the subjects were enrolled
f) A summary of the pre-activity interview

4.3. The body of the report should include a summary of the following:

a) IRB correspondence as described in the SOP for IRB protocol file review
b) The number of research records reviewed for the audit
c) The review of informed consent documentation and the outcome of the review
d) Screening procedures reviewed and the outcome of the review
e) Inclusion/exclusion criteria reviewed and the outcome of the review  
f) Study procedures reviewed and the outcome of the review  
g) The occurrence and reporting of adverse events / UAPs  
h) Data and Safety Monitoring Plan and findings  
i) Research data collection and research documentation

Recommendations shall be made for each of the summaries as indicated or if necessary, the investigator shall be requested to provide written clarification(s) or outline a plan of corrective procedures.

4.4 Before the report is distributed to the investigator, it must be reviewed by the compliance sub-committee as outlined in SOP #I-A-15.

4.5 Each compliance activity reports will be sent to the:

- Principal investigator (PI)  
- Study coordinator  
- PI’s immediate supervisor  
- PI’s mentor for student researchers  
- Director of the Education and Compliance Office for Human Subject Research

Others, e.g. the Director of Research, the PI’s Department Chairman or the Dean of the School may be copied on the report as deemed necessary.

4.6 A transmittal letter shall be included with each report.

4.7 The principal investigator shall be given approximately two weeks to provide a written response to the IRB Executive Committee. If there are extenuating circumstances, the principal investigator may request an extension of the response due date.

4.8 Compliance activity reports requiring review by the IRB EC will be reviewed as outlined in SOP #I-A-15. For all other compliance activity reports, the ECO-HSR will assess the adequacy of the investigator’s response and take the appropriate steps to ensure the appropriate resolution of the identified issues.

4.9 When all issues are resolved, the lead auditor will prepare a brief audit summary report. The audit summary will be included in the quality assurance database. If the audit was requested by an IRB Committee, the summary report will be provided to the vice chair of the requesting committee.

4.10 When the audit process is complete, a copy of the audit summary and related, pertinent correspondence will be placed in the respective IRB protocol file or uploaded into OSIRIS by a member of the ECO.

5. REFERENCES/DOCUMENTATION

For the purpose of maintaining confidentiality, a copy of the report is not included in this section. Reports may be accessed with the assistance of the Education and Compliance Office staff or the systems analyst.

Original: 8/1/01  
Reviewed/Revised: 11/20/03  
Reviewed: 9/3/04  
Revised: 5/18/05  
Reviewed/Revised: 6/1/11  
Reviewed: 10/5/12
1. PURPOSE

To define situations wherein issues identified during compliance activity reviews must be immediately reported by the principal investigator to the IRB.

2. SCOPE

This procedure applies to all Compliance Activity Reviews performed by the ECO-HSR.

3. RESPONSIBILITIES

The Education and Compliance Office Coordinators are responsible for instructing the principal investigator to report to the IRB any event that may represent serious non-compliance, continuing non-compliance or an unanticipated problem involving risks to human subjects or others.

4. PROCEDURES

4.1. The Education and Compliance Coordinators will instruct the principal investigator to promptly report to the IRB any events identified during a compliance activity review that may represent serious non-compliance, continuing non-compliance or an unanticipated problem that may involve risks to human subjects or others. Examples of which include the following:

- Evidence of a serious adverse event or unexpected adverse event of moderate or greater severity appearing to be associated with the research intervention and not reported to the IRB.
- Evidence of the performance of research procedures of greater than minimal risk not previously approved by the IRB on multiple subjects.
- No documentation or evidence of informed consent for multiple subjects enrolled in research activities of greater than minimal risk.
- Evidence that the majority of the research subjects audited did not meet the eligibility criteria as written in the IRB approved protocol.
- Deviation from IRB approved experimental procedures observed in the majority of the research subjects audited.
- IRB-approved follow-up procedures not performed on the majority of the research subjects audited.
4.2. Any of the above findings should also be reported by the ECO coordinator via email to the Director of the Education and Compliance Office, the IRB Chair and the Adverse Events Coordinator for the IRB within 72 hours of their identification with subsequent discussion and follow-up as mandated.

Reviewed/Revised: June 16, 2011
Reviewed/Revised:10/05/12
1. PURPOSE

To define the procedures utilized to review compliance activity reports and to describe which reports will be forwarded to the IRB Committee F for review.

2. SCOPE

This procedure applies to all investigator compliance review activities (RISE Interviews, Audits and Monitoring Site Visits) performed by the Education and Compliance Office for Human Subject Research (ECO-HSR).

3. RESPONSIBILITIES

The Director of the Education and Compliance Office for Human Subject Research and the Director for the Office for Investigator Sponsored IND and IDE Support¹ will be responsible for evaluating compliance reports and for determining, which findings may represent serious non-compliance, continuing non-compliance, an unanticipated problem involving risks to human subjects or others, or require further review by the IRB Adverse Events Coordinator, and the IRB Chair or the IRB Medical Director.

4. PROCEDURES

After the compliance activity report is prepared as outlined in SOP I.A.13, the report will be reviewed by the Director of the Education and Compliance Office for Human Subject Research and the Director for the Office for Investigator Initiated IND and IDE Support¹.

If the individuals conducting the review determine that no response to the report is required from the research team or that the report requires a response with minor corrective actions (e.g., placement of notes to file in the research record, enhancement of research documentation or clarification of discrepant information) then the ECO-HSR will be responsible for ensuring the identified issues are handled appropriately. This determination will be documented as outlined in the QA Database under the “CARs” tab and will also be sent in the email correspondence sent in association with the comments on the report. The compliance activity report will be sent to the investigator by the ECO-HSR. IRB Committee F will be notified that a compliance review was performed. The notification will include the protocol number, the protocol title, the name of the investigator and the determination category. The entire report will be available to the IRB upon

¹ In the absence of either the Director of the Education & Compliance Office for Human Subject Research or the Director of the Office for Investigator Sponsored IND & IDE Support, reviews may be conducted by the Assistant Director of the IRB or the Director of the Human Stem Cell Research Oversight Office (hSCRO)
request and the ECO-HSR staff will address any questions that the IRB may have regarding the ECO-HSR activity. A summary of the visit will be uploaded into OSIRIS system.

4.2 If the report identifies an issue that requires evaluation by an MD or if the report identifies findings which may represent serious non-compliance, continuing non-compliance or an unanticipated problem report involving risks to human subjects or others, the report will be brought to the attention of the Adverse Events Coordinator and the IRB Chair or IRB Medical Director for further review or discussion. This discussion will occur at the regularly scheduled CARs meeting or sooner as deemed necessary.

4.3 The determination by the reviewers identified in section 4.2 will be documented in the CARs meeting minutes, which will also document which ECO-HSR reviews should be assigned for review by the IRB Committee F. Information provided to the Committee will consist of the compliance activity report, the investigator’s response to the report, all associated reportable events and other information deemed necessary for the review.

4.4 The IRB staff will notify the investigator that the compliance activity report and the response to the report will be reviewed by the IRB Committee F.

5. REFERENCES/DOCUMENTATION

Review of Compliance Activity Report

Original: 4/28/11
Reviewed: 6/10/11
Reviewed/Revised: 10/5/12
## Review of Compliance Activity Report

<table>
<thead>
<tr>
<th>PI: __________________</th>
<th>Protocol #: __________________</th>
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<tbody>
<tr>
<td>Report Date: __________</td>
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**Individuals Performing the Review**

- ____ Director, ECO-HSR
- ____ Assistant Director of the IRB
- ____ Co-Director, O3IS
- ____ Director, HSCRO

### Determination

<table>
<thead>
<tr>
<th>Category</th>
<th>Check all that apply</th>
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<tbody>
<tr>
<td>A.</td>
<td>No further action necessary, compliance activity complete – no possible serious non-compliance, continuing non-compliance or unanticipated problem involving risks to human subjects or others.</td>
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<tr>
<td>B.</td>
<td>Minor issues identified during the visit. The ECO-HSR will correspond with the research team until all items resolved - No serious non-compliance, continuing non-compliance or unanticipated problem involving risks to human subjects or others</td>
</tr>
<tr>
<td>C.1</td>
<td>Item / medical issue identified in the report requires a response from the PI and review by the IRB Chair or the IRB Medical Director but does not need review by convened Committee</td>
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<tr>
<td>C.2</td>
<td>Item / medical issue identified in the report requires a response from the PI and review by the IRB Chair or the IRB Medical Director and may require review by the convened Committee</td>
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<td>D.</td>
<td>Findings may represent serious non-compliance</td>
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<tr>
<td>E.</td>
<td>Findings may represent continuing non-compliance</td>
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<tr>
<td>F.</td>
<td>Findings may represent unanticipated problem involving risk to human subjects or others</td>
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<tr>
<td>G.</td>
<td>Other</td>
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### Determination after Discussion with Adverse Events Coordinator and IRB Chair or Medical Director