

<b>DEPARTMENT:</b> Research Compliance		<b>Reference#</b> IRB.011
<b>Effective Date:</b> 7/19/2007	<b>Page</b> 1 of 11	<b>Replaces Policy Dated:</b> 1/23/2006
<b>Description:</b>	Monitoring and Oversight	

**A. Ensuring Continuing Review Prior to Expiration of Approval**

Ninety days prior to expiration of IRB approval, the PI is notified in writing that continuing review of their research protocol is coming due. A form is provided to submit the required information and documents. Once the completed form and required documents are received, the protocol is reviewed either at a convened meeting of the IRB or through the expedited review procedure as described previously.

When IRB approval expires, the PI is notified that all research activities must stop. Research activities include, but are not limited to, recruitment and enrollment of subjects, collection of specimens, research on previously collected specimens, review of medical records or other health information, data analysis, and performance of research tests/procedures, treatment or follow-up on previously enrolled subjects.

If treatment and/or follow-up of subjects is necessary for subject safety and welfare, the PI must inform the IRB in writing immediately to request permission to continue previously enrolled subjects on study. The IRB Chair is responsible for considering these requests on a case-by-case basis and providing written documentation of permission, when granted.

**B. Ensuring Prompt Reporting to the IRB of Proposed Changes in Research Activities and Ensuring that Changes are not Initiated without IRB Review and Approval, Except Where Necessary to Eliminate Apparent Immediate Hazards**

Federal regulations [45 CFR 46.103\(4\)](#) require IRBs to have written procedures to ensure prompt reporting to the IRB of proposed changes in a research activity, and for ensuring that such changes in approved research, during the period for which IRB approval has already been given, may not be initiated without IRB review and approval except when necessary to eliminate apparent immediate hazards to the subject.

Investigators are required to promptly report to the IRB proposed changes in research for approval prior to initiation of the proposed change. The procedures used by the IRB to ensure compliance with this requirement include the following:

<b>DEPARTMENT:</b> Research Compliance		<b>Reference#</b> IRB.011
<b>Effective Date:</b> 7/19/2007	<b>Page 2 of 11</b>	<b>Replaces Policy Dated:</b> 1/23/2006
<b>Description:</b>	Monitoring and Oversight	

1. Inclusion of statement in the approval letter reminding investigators of requirement to submit any changes to the protocol and/or consent form to the IRB for approval prior to initiation of the change;
2. Inclusion in the required education program for research personnel of requirement to obtain IRB approval of changes to the protocol and/or consent form prior to initiation of changes;
3. Inclusion of statement in the approval letter requiring investigators to use the latest version of IRB-approved and validated consent form(s) when enrolling subjects;
4. Inclusion in the required education program for research personnel of the requirement to use the latest version of IRB-approved and validated consent form(s) when enrolling subjects;
5. Reminder of requirement in educational venues, e.g., research coordinator orientation, lectures, random QI roundtable discussions, focus groups; and
6. Random assessments of investigator's protocol-specific records and files.

Proposed changes during the period of IRB approval are reviewed by the IRB as described previously in this policy.

**C. Ensuring Reporting of Unanticipated Problems Involving Risks to Subjects or Others**

Federal regulations [45 CFR 46.103\(b\)\(5\)](#) require IRBs to have written procedures for ensuring prompt reporting to the IRB, appropriate institutional officials, and the department or agency head of any unanticipated problems involving risks to subjects or others.

Investigators are required to promptly report to the IRB unanticipated problems involving risks to subjects or others. An unanticipated problem involving risks to subjects or others is defined as any unexpected untoward event that involves any aspect of the research and places the subject or anyone else at risk of serious harm. The following are examples of unanticipated events that need to be reported to the IRB if they involve risks to subjects or others.

Examples of unanticipated events (not inclusive):

<b>DEPARTMENT:</b> Research Compliance		<b>Reference#</b> IRB.011
<b>Effective Date:</b> 7/19/2007	<b>Page 3 of 11</b>	<b>Replaces Policy Dated:</b> 1/23/2006
<b>Description:</b>	Monitoring and Oversight	

- Serious unanticipated and related adverse events;
- Events resulting in unplanned changes to the protocol;
- Events resulting in one time planned changes;
- One time inclusion/exclusion changes;
- Interim results;
- Safety monitoring reports;
- Participant complaints;
- Laboratory errors;
- Medication errors;
- Disclosure of confidential information;
- Lost or stolen confidential information;
- Disqualification of investigators; or
- Suspension of investigator.

The Sunrise Health IRB has developed specific guidelines and forms for investigators to use when reporting adverse events and protocol deviations, exceptions and violations. All other unanticipated problems involving risks to subjects or others should be reported in writing by letter or email to the IRB.

Consistent with the Adverse Event Reporting Guidelines and guidance on Protocol Deviations, Exceptions and Violations, unanticipated or serious problems involving risks to subjects or others must be reported to the SHIRB within ten (10) working/fourteen (14) calendar days of discovery of the problem or event. The only exception to the time frame for reporting is deaths. Deaths must be reported immediately, within 24 hours of discovery of the event.

The IRB Chair/Designee is responsible for reviewing and determining whether the subject(s) participating in the research or others were placed at risk of serious harm and whether the problem or event is unanticipated. If the reported problem is unanticipated and involves risks to subjects or others, the report is referred to the IRB for review at a convened meeting. The SHIRB is responsible for the review of the unanticipated problem and by majority vote may take one or more of the following actions:

- Accept the report and approve the proposed changes, if any, with no further action required;
- Require additional information;
- Require modifications to the protocol and/or consent form;

<b>DEPARTMENT:</b> Research Compliance		<b>Reference#</b> IRB.011
<b>Effective Date:</b> 7/19/2007	<b>Page</b> 4 of 11	<b>Replaces Policy Dated:</b> 1/23/2006
<b>Description:</b>	Monitoring and Oversight	

- Require that subjects currently on protocol be notified of the event;
- Require that subjects whose participation has ended be notified of the event;
- Require that subjects currently on protocol be re-consented;
- Modify the continuing review schedule;
- Suspend the research;
- Terminate the research;
- Request a directed audit by the Office of Research Compliance; or
- Other actions deemed appropriate by the IRB.

The IRB staff is responsible for preparing a description of the problem and recording the findings and actions of the IRB in the Minutes. The principal investigator is notified in writing of the actions of the IRB as described previously.

In addition, when applicable, the Chair of the IRB is responsible for preparing a report to the Institutional Official within 30 days of the IRB meeting. Copies of the report are sent to the following, when applicable:

- Principal Investigator
- Department Head (chair/chief);
- Institutional Representatives of the institution relying on SHIRB review;
- Food and Drug Administration (FDA-regulated research);
- Office for Human Research Protections; and

**In addition, Serious Adverse Events, as defined by SHIRB Guidance GUI.001 Adverse Event Reporting Guidelines, that occur within a facility under the jurisdiction of the SHIRB will be reported by SHIRB staff to the appropriate Quality Management and/or Risk Management Department**

**D. Noncompliance with Human Subject Protection Regulations or IRB Requirements and Determinations**

**Non-compliance** means any action or activity associated with the conduct and oversight of human subjects research that is at variance with these Policies & Procedures and the relevant federal regulations on which they are based. Non-compliant actions may range from minor to serious; they may be unintentional or willful; and they may occur only once or several times.

<b>DEPARTMENT:</b> Research Compliance		<b>Reference#</b> IRB.011
<b>Effective Date:</b> 7/19/2007	<b>Page</b> 5 of 11	<b>Replaces Policy Dated:</b> 1/23/2006
<b>Description:</b>	Monitoring and Oversight	

**Serious non-compliance** means non-compliance that affects the rights and welfare of participants, or compromises the integrity or validity of the research.

**Continuing non-compliance** means a pattern of non-compliance that indicates a lack of understanding about the regulations or ethical requirements that may affect the rights and welfare of participants, or compromise the integrity or validity of the research. The pattern of non-compliance is assessed by the number of incidents occurring during the course of a protocol, and whether the same noncompliant action was repeated or many different noncompliant events occurred.

The frequency of non-compliance is assessed mainly by the number of incidents occurring during the course of a protocol, and would also take account of whether the same noncompliant action was repeated or many different noncompliant events occurred.

**1. Reporting concerns**

Reports of non-compliance in human subjects research may come from many sources including, but not limited to, an investigator (as a self-report); a study monitor, auditor or sponsor; a research subject; or a person not directly involved with the research.

**2. Responding to concerns**

To the extent that an instance of non-compliance may be covered by procedures established by the Sunrise Health System policies, any investigation of non-compliance with requirements of the human research protection program conducted by the IRB as well as any remedial action required or recommended by the IRB must be coordinated with the Vice President of Quality.

Similar provisions will be made for coordinating any investigation with the Compliance Officer of Sunrise Health as appropriate.

In cases of noncompliance involving investigators subject to other corporate compliance programs, the IRB chair will seek advice from the Legal Department and the Compliance Officer about how to interact with the corporate compliance officers.

<b>DEPARTMENT:</b> Research Compliance		<b>Reference#</b> IRB.011
<b>Effective Date:</b> 7/19/2007	<b>Page</b> 6 of 11	<b>Replaces Policy Dated:</b> 1/23/2006
<b>Description:</b>	Monitoring and Oversight	

Concerns disclosed to the Compliance Officer will be investigated according to procedures described in Sunrise Health and HCA Policy. The Compliance Officer may refer the matter to the IRB for further investigation.

All concerns disclosed to the chair of the IRB will be disclosed immediately to the Compliance Officer of Sunrise Health, as appropriate. Unless the Compliance Officer indicates that the matter must be investigated under the guidelines set out in the Compliance Program, the IRB chair will initiate an investigation as soon as practicable. In cases of very serious non-compliance, eg when a subject's safety has been compromised or when a subject may have been injured due to non-compliance, the investigator's Department Chair/Chief and/or superior may be notified at an early stage of the investigation.

The chair may conduct the investigation personally, delegate the matter to another IRB member who may have particular expertise or insight into the matter, or assemble an ad hoc committee, which may include persons who are not IRB members but have necessary expertise to evaluate the matter.

The time frame for beginning the investigation will generally be determined by the seriousness of the non-compliance, with investigations of the most serious allegations being initiated with greatest alacrity. In general, it is to be expected that most investigations should begin within 30 days of being reported to the IRB chair. The IRB Chair, or whoever was designated by the Compliance Officer, will communicate the results of the investigation, in writing, to the IRB office and it will be distributed to all members for consideration at the next convened meeting. At the discretion of the Chair, brief reports of continuing investigations may be made verbally at convened meetings and documented in the minutes.

### **3. Evaluation**

- a. Non-compliance is not serious or not continuing. If an IRB Chair who becomes aware of non-compliance and can determine that (1) the non-compliance was clearly not serious and not continuing, (2) the research staff recognized the non-compliance, and (3) the research staff took appropriate corrective actions, then the Chair

<b>DEPARTMENT:</b> Research Compliance		<b>Reference#</b> IRB.011
<b>Effective Date:</b> 7/19/2007	<b>Page</b> 7 of 11	<b>Replaces Policy Dated:</b> 1/23/2006
<b>Description:</b>	Monitoring and Oversight	

may make a note to the file, and he or she need take no further action.

- b. Non-compliance is serious or continuing. If serious or continuing non-compliance is demonstrated, the Institutional Review Board must make a determination at a convened meeting of the seriousness and frequency of the non-compliance, and such determination will be made on a case-by-case basis. In general, the seriousness of the non-compliance is gauged by the extent to which research subjects are harmed or put at increased risk. Willful disregard for the welfare of research subjects would be considered particularly egregious, however, frequent instances of minor non-compliance would also be considered cause for concern. The IRB will determine the appropriate way to remedy the non-compliance.

#### 4. Notifications

- a. IRB staff notes the results of the IRB's determinations in the meeting minutes.
- b. The IRB chair notifies the investigator in writing of the results of the investigation and of any remedial actions required by the IRB. At the discretion of the IRB chair, the report to the investigator might exclude identities of persons who raised concerns or participated in the investigation. The IRB includes in the notification a request for the investigator to respond in writing. The convened IRB will review the response.
- c. After review by the convened IRB, the IRB chair drafts a report that includes a description of the nature of the event, the findings of the organization, actions taken by the organization or IRB, reasons for the organization's or IRB's actions, and plans for continued investigation or action. The report is approved by the Vice President of Quality, signed by the IRB chair, filed in the protocol file and sent to the IRB with the next agenda packet.
- d. If the non-compliance is determined after investigation to be serious or continuing, then copies of the report are sent, as appropriate, to:
  - (1) The IRB in the next agenda packet.

<b>DEPARTMENT:</b> Research Compliance		<b>Reference#</b> IRB.011
<b>Effective Date:</b> 7/19/2007	<b>Page 8 of 11</b>	<b>Replaces Policy Dated:</b> 1/23/2006
<b>Description:</b>	Monitoring and Oversight	

- (2) Institutional Compliance Officer.
  - (3) Sponsor, if the IRB determines at a convened meeting that the sponsor of the research should be notified. If the sponsor has already established a reporting policy for the type of event, then those guidelines will be considered.
  - (4) Principal investigator's Department Chair/Chief and/or superior, if the IRB determines at a convened meeting that he or she should be notified.
  - (5) OHRP. At the discretion of the Vice President of Quality, an initial notification may be made by telephone within 48 hours.
  - (6) FDA, if the research is FDA regulated. At the discretion of the Vice President of Quality, an initial notification may be made by telephone within 48 hours.
- e. At the discretion of the Vice President of Quality, copies of the report may also be sent to the legal department of the relevant institution.
  - f. Consistent with the Compliance Programs of Sunrise Health, the person who made the initial allegation or reported a concern will be apprised of the results of the investigation.

**5. Protection for whistleblowers**

Persons expressing concerns or making allegations about a protocol involving human participants will not be subject to retaliation or disciplinary action if they act in good faith. This protection holds even if the concerns or allegations are found, upon investigation, to be without merit.

**6. Actions that the IRB may take in Responding to Concerns or Allegations of Non-Compliance**

Remedial action will be determined by the degree of seriousness of the non-compliance, the willfulness of the action, and the number of times it

<b>DEPARTMENT:</b> Research Compliance		<b>Reference#</b> IRB.011
<b>Effective Date:</b> 7/19/2007	<b>Page 9 of 11</b>	<b>Replaces Policy Dated:</b> 1/23/2006
<b>Description:</b>	Monitoring and Oversight	

may have occurred. The following list indicates the range of actions the IRB may take.

- a. No action
- b. Modification of the research protocol
- c. Modification of the information disclosed during the consent process
- d. Additional information provided to past participants
- e. Notification of current participants (required when such information may relate to participants' willingness to continue to take part in the research)
- f. Requirement that current participants re-consent to participation
- g. Modification of the continuing review schedule
- h. Monitoring of the research
- i. Monitoring of the consent
- j. Suspension of the research. (Such action will activate the procedures described in Section E below.)
- k. Termination of the research. (Such action will activate the procedures described in Section E below.)
- l. Obtaining more information pending a final decision
- m. Referral to other organizational entities (e.g., legal counsel, risk management, institutional official)
- n. Other actions deemed appropriate by the IRB

### **Minor Noncompliance (Minor Violation)**

Minor violations are violations that do not impact subject safety, compromise the integrity of the study data and/or affect the subject's willingness to participate in the research.

When the noncompliance is considered minor, the noncompliance (or violation) is to be reported at continuing review.

Minor violations are reviewed at the time of continuing review either at a convened meeting or, as appropriate to the research activities, through the expedited review procedure. If the IRB or IRB Chairperson finds the violation to be serious, the review and reporting requirements for serious and continuing noncompliance are followed, as described above.

<b>DEPARTMENT:</b> Research Compliance		<b>Reference#</b> IRB.011
<b>Effective Date:</b> 7/19/2007	<b>Page</b> 10 of 11	<b>Replaces Policy Dated:</b> 1/23/2006
<b>Description:</b>	Monitoring and Oversight	

**E. Suspension or Termination of Research**

The Sunrise Health IRB may suspend or terminate a research protocol involving human subjects for reasons including, but not limited to:

- Unanticipated problems involving risks to subjects or others; or
- Serious or continuing noncompliance with the research.

When the Sunrise Health IRB votes to suspend or terminate a research protocol, the IRB considers whether the suspension or termination requires that subjects be withdrawn from the study and/or places subjects at risk of harm.

When subjects must be withdrawn from an interventional study, the IRB considers and determines necessary termination procedures for the safety and welfare of those subjects, e.g., drug taper, final visit, lab tests, other follow-up, and arrangements for continued care by the subject's physician or through appropriate referrals.

If the IRB determines that the suspension or termination will place subjects at risk of harm, the IRB must determine what subjects are to be told and the manner in which they are to be notified, e.g., in writing or by telephone.

Depending upon the reasons for the suspension or termination and the design of the protocol, the SHIRB may require that the following subjects be notified of the suspension or termination:

- All subjects who have been or are enrolled;
- Subjects currently on protocol; or
- Subjects who participated in a certain aspect of the protocol.

Whenever the SHIRB suspends or terminates a research protocol involving human subjects, the following individuals, when appropriate, are notified by the IRB Chair of the suspension or termination within 10 working days of the suspension/termination:

- Study participants;
- Principal investigators, co-investigators and study staff;
- Department Head (chair/chief);
- Departments involved in the conduct of the research;

<b>DEPARTMENT:</b> Research Compliance		<b>Reference#</b> IRB.011
<b>Effective Date:</b> 7/19/2007	<b>Page 11 of 11</b>	<b>Replaces Policy Dated:</b> 1/23/2006
<b>Description:</b>	Monitoring and Oversight	

- Institutional Official
- Institutional representatives of institutions relying on SHIRB;
- Food and Drug Administration (FDA); and
- Office for Human Research Protections (OHRP)

Expiration of IRB approval is not considered termination of research and is not subject to the reporting requirements outlined above.