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ADVERSE EVENT REPORTING

Effective Date: July 1, 2004
Original Approval Date: January 22, 2001
Revision Date: June 15, 2004
July 22, 2004

Approved By: Niels Beck, PhD
Chair, Health Sciences IRB

Table of Contents

1.0 Purpose
To assure knowledge and compliance by documenting the adverse event reporting procedure for the Health Sciences IRB.
2.0 Scope

The SOP applies to all human subject research falling under the purview of the Health Sciences Institutional Review Board.

3.0 Definitions

*Adverse event* - recognized harmful or unfavorable outcome occurring to a participant in a research study. NOTE: It is important to remember that adverse events can be injuries other than physical injuries. Events such as emotional distress, employment/insurance consequences or familial relationship consequences may also be classified as adverse events. It is also important to remember that misplaced records leading to a possible breach in confidentiality also constitutes an adverse event.

*Expected adverse event* – event has been documented in the informed consent as a possible side effect/consequence of participation in the study.

*Related adverse event* – the causality of the event has been determined to be definitely, probably or possibly attributable to the investigational agent.

*Serious adverse event* - event resulting in one of the following outcomes
  - Results in death
  - Life-threatening
  - Requires or prolongs hospitalization
  - Results in persistent or significant disability or incapacity
  - Results in congenital anomaly or birth defect
  - Cancer (secondary or other new cancer in individuals with pre-existing cancer)
  - Drug overdoses
  - Requires treatment to prevent one of the previous medical outcomes

Examples of non-medical events that are classified as serious include, but are not limited to:
  - Suicide
  - Confidentiality breach
  - Loss of employment
  - Loss of insurance
  - Severe emotional distress requiring treatment

*Unexpected adverse event* -
  - Not listed in the informed consent and/or research protocol
  - Increase in severity from that which is described and expected
  - Occurs at greater frequency than that which is described and expected

*Unrelated adverse event* – the causality of the event has been determined to be unlikely attributable or unrelated to the investigational agent.

An unexpected event (not listed in the consent form) should be classified as serious if it meets the definition of serious, otherwise it should be classified as non-serious.
When emerging event patterns show that the event has either increased in severity or frequency from that described in the consent, the unexpected event(s) should be treated and reported using the serious event reporting criteria.

4.0 Policy/Procedure

The monitoring and review of adverse events and the impact they may have on the risk/benefit ratio within a study is an important component in the ethical, safe conduct of a study. The PI, as the point of responsibility for the conduct of the study and the one person with intimate knowledge of the study which they are conducting, must review all documentation of events (both on-site and off-site) to make an informed conclusion as to the impact of the event, or pattern of events, on the risk/benefit ratio of the study and any steps that must be taken to alleviate the identified risks.

The IRB reviews all submitted events to also come to a conclusion of the impact of the event(s) on the risk/benefit ratio of the study. The IRB will recommend any actions that are needed to alleviate identified risks and also to determine if any changes need to be made to the conduct of the study.

The attached HS IRB AE Flowchart (Appendix 1) outlines the reporting requirements to the HS IRB for both events occurring in on-site studies and those occurring off-site.

On-site Adverse Events

Adverse events meeting the following criteria which occur within studies being conducted on-site must be submitted to the HS IRB by completion of a Serious Adverse Event Report form.

Serious, Unexpected, Related
Serious, Expected, Related
Non-serious, Unexpected, Related

Adverse events occurring in on-site studies do not need to be reported to the HS IRB if they meet the following criteria:

Serious, Unexpected, Unrelated
Serious, Expected, Unrelated
Non-serious, Unexpected, Unrelated
Non-serious, Expected, Unrelated

Events that are determined to be Non-serious, Expected, Related do not need to be reported to the IRB if they are listed as a possible side effect in the consent form. The HS IRB AE Cumulative Log form is available as a tool on which to log these events to help determine if the severity or frequency of occurrence pattern may place it into the Serious, Expected, Related category. If the event is listed as a possible side effect in the Investigators Drug Brochure but not the consent form, it must be added to the consent form.

The HS IRB Adverse Event Report form should be completed and submitted to the HS IRB within 5 days of the occurrence of the on-site event. If the participant is enrolled in an on-site study but the event occurred while they were in another location (i.e. on vacation) and the 5-day time-frame can not be met because of the logistics of obtaining the necessary information, the
IRB should be provisionally notified of the occurrence of the event within 5 days of being informed of the occurrence of the event. The completed HS Serious Adverse Event Report form should be submitted as soon the information for completion becomes available.

A separate HS IRB Adverse Event Report form must be completed in its entirety for each on-site event.

**Exception for Pediatric Oncology Trials**

Side effects occurring in pediatric oncology patients are routinely monitored through hospitalization rather than an outpatient basis. Hospitalization is a criteria of an event requiring reporting on a Serious Adverse Event Report form. If the event is listed in the consent form as an expected side effect and information is provided either in the consent form or during the consent discussion processes that the event will be monitored through hospitalization, it does not need to be reported on a Serious Adverse Event Report form. If the hospitalization is an ICU stay, is excessively prolonged or complicated or if the event meets one of the other serious criteria, it must be reported to the HS IRB on a Serious Adverse Event Report form.

**Serious Adverse Event Resulting in Death**

The IRB must be notified **within 24 hours** of any on-site event resulting in the death of a participant. This notification should be by telephone contact followed by the completed HS Serious Adverse Event Report form if there is not sufficient time to complete the paperwork within 24 hours.

If telephone notification of the death is necessary, the following information should be provided at the time of notification:

- project(s) for which death is being reported
- condition under study in project(s)
- brief synopsis of events leading to the death
- causality of the death specifically in relationship to study agent or procedures
- number of other participants enrolled on study at this site
- information on whether other participants need to be immediately notified
- investigator opinion on the risk/benefit analysis of continuing the study or suspending the study
- any extenuating circumstances or additional enlightening information
- contact information of whom to contact to discuss event

A subcommittee comprised of the IRB Chair, Vice-Chairs, IRB Administrator, and a physician member of the Board, or their respective designees, will convene within 1 day of the notification to review the event and make recommendations of any necessary actions. If the death occurs on a weekend or holiday when the 1-day convening would not be possible, the review group will meet on the first workday after the event.

**Death Report Exception**

Because of the inherent nature of the diseases under study on oncology trials, on-site deaths that occur within these studies do not have to be reported to the HS IRB unless thought to be related (definite, probable, possible) to the investigational agent or specific study procedures.
Provisional Notification of Serious Adverse Events

If a serious event occurs which does not result in death but for which the required paperwork submission timeline can not be met, the IRB may be notified of the event by telephone or e-mail. The information that must be provided in that communication includes, but is not limited to,

- project(s) for which event is reported
- condition under study in project(s)
- statement of event
- brief description of event
- causality of event
- any extenuating circumstances or additional enlightening information
- contact information of whom to contact to discuss event

Adverse Event Reports from Off-site Locations

Event reports received from off-site locations that meet the following criteria must be individually reported to the HS IRB on a Serious Adverse Event Report form:

Serious, Unexpected, Related

The HS IRB Serious Adverse Event Report form should be completed and submitted to the HS IRB within 10 days of receipt of notification of the occurrence of the event from the outside entity. A separate HS IRB Serious Adverse Event Report form must be completed in its entirety for each event. If a MedWatch or other sponsor reporting form has been received, this form should be submitted with the AE form. In the case of an off-site event with an attached MedWatch-type reporting form, Sections A-F of the AE Reporting form, minus the complete description of the event, must be completed.

All other event reports received from off-site locations do not have to be reported to the HS IRB on an individual basis unless the Principal Investigator feels the event raises an issue that impacts on participant safety and of which the HS IRB needs to be informed.

All off-site Adverse Event Reports that do not meet the SAE reporting criteria of Serious, Unexpected, Related must be individually reviewed by the Principal Investigator to determine if they contain information identifying an increased risk to the study population of the PI-conducted trial or whether they contain new information regarding unanticipated events. If the PI determines that the reports do not contain information which needs to be communicated to the participant or that impacts the risk/benefit ratio of the study, the PI will complete an AE Certification form to submit at the time of Continuing Review of the study. This Certification form and the attached AE reports will be filed in the HS IRB study file without HS IRB review or acknowledgement.

AE Cumulative Log

The AE Cumulative Log form is a tool that has been developed to aid the study staff in identifying patterns and emerging, previously unexpected adverse events of the investigational agent in question and whether the cumulative number and burden of adverse events are sufficient to shift the balance of the risk/benefit ratio for current and/or future study participants, and whether the informed consent document needs revising. Additionally, the log may be used to log
expected events to help identify when an event may shift to a serious, unexpected event because the severity or frequency is beyond that which is expected and documented in the consent.

At any time that the PI feels that an event or pattern identified on the cumulative log qualifies as an event reportable to the HS IRB, they should complete a Serious Adverse Event Report form and submit it to the HS IRB within the allowable timeframe.

**Follow-up Reports**

If an event report has been submitted to the HS IRB, any follow-up reports generated to that initial report do not need to be submitted to the IRB as a separate Serious Adverse Event Report submission unless information contained in the follow-up changes the risk level of the report.

**Closed/Completed/Terminated Studies**

If an on-site study has been closed/completed/terminated for greater than 30 days, any adverse event reports from other sites do not need to be submitted to the HS IRB for review. If the event is of the magnitude that it requires immediate notification of all past participants, then it should be submitted to the HS IRB.

**Regulatory Reporting Responsibility**

The PI is responsible for reporting the event to the applicable regulatory or sponsor division in accordance with their requirements. Examples of possible entities to which reporting is required include, but is not limited to: Sponsor, OHRP (acting on behalf of the Secretary of DHHS), FDA, and federally funded cooperative research groups.

The requirement to report the event to the institutional officials of the University of Missouri-Columbia is fulfilled with the submission of the report to the HS IRB.

It is the responsibility of the PI and study staff to track the adverse events occurring in relation to a particular study to ensure accurate reporting of events on the Continuing Review Report Form.

**AE Reports Precipitating Informed Consent Revisions**

Adverse events which precipitate a revision to the Informed Consent document should be noted as such. Two copies of the revised consent document, with the revisions highlighted on one copy, should be submitted to the HS IRB along with the AE Report Form.

**IRB Review of Adverse Event Reports**

Each electronically submitted event report will be sent to an HS IRB member for expedited review and action. AEs of a medical nature will be sent to physician members while non-medical events may be sent to any member with expertise in the study and/or event area.

The reviewer packet sent to the IRB reviewer includes:

- event report completed by PI plus attachments
- AE report generated from the HS IRB database listing all received events attributed to the study
- Revised consent, with revisions highlighted, if consent revisions are necessitated
The acknowledged report will be returned to the PI for placement in the study files. If the reviewer has any questions or comments, correspondence between the PI, reviewer and IRB administrative office will occur to satisfactorily resolve the issue.

If the reviewer feels the event warrants it, the event will be presented and reviewed by the fully convened board at the first available opportunity.

5.0 Applicable Regulations

45 CFR 46.103(b)(5)
21 CFR 56.108(b)(1)

6.0 Related SOP

Informed Consent – Types and Elements
Continuing Review Report

7.0 Review Panel

Clinical Trials Office of Ellis Fischel Cancer Center
Office of Clinical Research
Cardiology Research Unit
APPENDIX 1

HS IRB AE Flowchart
HS IRB - ADVERSE EVENT REPORTING

Page 9 of 18

HS IRB AE Flowchart

Did event occur within on-site study?

Yes

Is event serious?

Yes

Is event unexpected?

Yes

Related to agent? (Def, Prob, Poss)

AE

NR

No

Related to agent? (Def, Prob, Poss)

CL

NR

No

Is event unexpected?

Yes

Related to agent? (Def, Prob, Poss)

AE

NR

No

Related to agent? (Def, Prob, Poss)

NR

NR

No

Related to agent? (Def, Prob, Poss)

NR

NR

AE = Serious Adverse Event Report Form

CL = Quarterly submitted cumulative log

NR = No reporting necessary
APPENDIX 2:

HS Serious Adverse Event Report
HS IRB - ADVERSE EVENT REPORTING

Page 11 of 18

HS Serious Adverse Event Report

Project Number: ___________
Review Number: ___________

Section A - Project Information

(1) Project Title
Read only data would go here.

(2) On-Site Principal Investigator / Contact Person

(3) Study Staff

<table>
<thead>
<tr>
<th>Name</th>
<th>Role</th>
<th>Educational Training Date</th>
<th>HS HIPAA Training Date</th>
<th>Primary Contact</th>
</tr>
</thead>
</table>

Section B – On-Site Study Information

(1) Sponsor Protocol Number/Version:

(2) Study Drug Indication/Purpose of Study:

(3) FDA IND # IDE # of Investigational Agents Under Study

(4) Onsite Protocol Status:*

(5) Current study enrollment at this institution:*

Section C - Report Information

(1) Did the event occur at this institution?*
   _____ Yes  _____ No

(2) Different Study
   A. Did the event occur in a different study than the on-site study for which it is being reported?*
      _____ Yes  _____ No
   B. If different study, provide the common investigational agent between the studies:
   C. If different study, condition under study for reported event:

(3) MedWatch
   A. Is MedWatch or other sponsor reporting form attached?
      _____ Yes  _____ No
   B. If yes, Report Tracking Number:
   C. If yes, Report Date:

(4) Is this a follow-up report?
SECTION D - Adverse Event Details

(1) Adverse Event Term(s)*

(2) Onset Date of Event:

(3) Grade of event:

(4) Relationship of event to investigational agent or study procedure:

(5) Action Taken:

(6) Outcome of event:

(7) Did participant die as a result of adverse event?
    _____ Yes  _____ No

SECTION E - Subject Information

(1) Subject Information

A. Study ID:

B. Initials

C. Age:

D. Gender:

E. Diagnosis:

SECTION F - Informed Consent

(1) Informed Consent

A. Does the current consent form address this risk?*
   _____ Yes  _____ No

B. If no to 1A, should the consent form be revised as a result of this event?
   _____ Yes  _____ No

C. If no to 1B, explain why it should not be added to consent:

(2) Notification

A. Will currently enrolled subjects be notified of this event?
   _____ Yes  _____ No

B. If yes to 2A, describe method of notification:
**SECTION G - Adverse Event Description**

(1) If Serious Adverse Event was related to something other than investigational agent or study procedure, please provide details:

(2) Complete Description of Event:

<table>
<thead>
<tr>
<th>Drug Treatment Information</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Agent Name</td>
<td></td>
</tr>
<tr>
<td>Dose</td>
<td></td>
</tr>
<tr>
<td>Route</td>
<td></td>
</tr>
<tr>
<td>Schedule</td>
<td></td>
</tr>
<tr>
<td>Dates Given</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>SECTION H - Drug Treatment Information</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>SECTION I - Device Treatment Information</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Name</td>
<td></td>
</tr>
<tr>
<td>Manufacturer</td>
<td></td>
</tr>
<tr>
<td>Device Class</td>
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</table>

<table>
<thead>
<tr>
<th>SECTION J - Concomitant Medications</th>
<th></th>
</tr>
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<tbody>
<tr>
<td>Medication</td>
<td></td>
</tr>
<tr>
<td>Start Date</td>
<td></td>
</tr>
<tr>
<td>Stop Date</td>
<td></td>
</tr>
<tr>
<td>Relevant to AE?</td>
<td></td>
</tr>
</tbody>
</table>
APPENDIX 3

PI Certification Form
AE Certification Paragraph

The Principal Investigator (PI) of a project has the responsibility to review all adverse event reports occurring in related studies conducted at this institution or other institutions and to use their expertise to determine appropriate actions that need to be taken to protect research participants.

Do the reports, either individually or as a cumulative group

<table>
<thead>
<tr>
<th>Event</th>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td>Occur in a study conducted at another site?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Increase the risk to this study subject population?</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Contain new information regarding unanticipated events?</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Change the magnitude or frequency of expected events?</td>
<td>Yes</td>
<td>No</td>
</tr>
</tbody>
</table>

As PI, I certify that I have reviewed each adverse event report in its entirety and have determined that these reports, either individually or as a cumulative group, do not contain new information that needs to be transferred to the participant and do not impact the risk/benefit ratio of this study.

As such, these reports have not been individually submitted to the HS IRB for review. These reports are being submitted as part of the Continuing Review Report submission packet to be placed in the study file without HS IRB review.

Signature of Principal Investigator

Date
APPENDIX 4

AE Cumulative Log
HS Cumulative AE Log

Project Number: ____________
Review Number: ____________

Section A - Project Information

1. Project Title
   Read only data would go here.

2. On-Site Principal Investigator / Contact Person

3. Study Staff

<table>
<thead>
<tr>
<th>Name</th>
<th>Role</th>
<th>Educational Training Date</th>
<th>HS HIPAA Training Date</th>
<th>Primary Contact</th>
</tr>
</thead>
</table>

Section B – Cumulative Log Details

Current Event Details

*Please click here to view a table of all the Adverse Events*

<table>
<thead>
<tr>
<th>Event Date:</th>
<th>Report Date:</th>
</tr>
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<tbody>
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</table>

<table>
<thead>
<tr>
<th>Event Term(s):</th>
<th>Causality of Event:</th>
<th>Outcome of Event:</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
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</table>

<table>
<thead>
<tr>
<th>Event Occurred:</th>
<th>Study in which Event Occurred:</th>
</tr>
</thead>
<tbody>
<tr>
<td>On-site; Off-site</td>
<td>Same; Different</td>
</tr>
</tbody>
</table>

SECTION C – Event Discussion

1. Synopsis of above listed events:
   (include discussion of observed patterns and assessment any change to risk/benefit ratio)

2. Consent Revision

   A. Should the consent be revised because of any of the above events?*
      _____ Yes _____ No

   B. If yes, please provide brief overview of necessitated revisions:

3. Notification
   A. Should current participants be notified of any of the events?*
      _____ Yes _____ No

   B. If yes, please document procedure for notification
### Table Format of Cumulative Log Current Event Details

<table>
<thead>
<tr>
<th>Event Terms(s)</th>
<th>Event Date</th>
<th>Report Date</th>
<th>Causality</th>
<th>Outcome</th>
<th>On/Off Site</th>
<th>On/Off Study</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
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</tbody>
</table>
Agenda

Effective Date: October 1, 2004
Original Approval Date: October 1, 2004
Revision Date: N/A

Approved By: Niels Beck, PhD
Chair, Health Sciences IRB

Table of Contents

Purpose
Scope
Definitions
Policy/Procedure
Attachment Agenda

1.0 Purpose

To assure knowledge and compliance by documenting the contents of the board agenda to be distributed prior to a convened meeting.

2.0 Scope

The SOP applies to all human subject research falling under the purview of the Health Sciences Institutional Review Board.

3.0 Definitions

None

4.0 Policy/Procedure

The HS IRB shall prepare an agenda in advance of all convened meetings and distribute proposed agenda to all members prior to the convened meeting. The agenda should include the following:

1. The date of the meeting
2. Introductions
3. Approval of previous minutes
4. Chair Comments  
5. Review of previously contingent CRRs  
6. Review of CRRs (a separate listing of all CRR scheduled for review is attached)  
7. Delinquent CRRs scheduled to be terminated  
8. Emergence use of investigational drug or device  
9. Review of amendment requests to approved projects requiring full-board review  
10. Review of previously deferred projects  
11. Review of new projects  
12. Additional agenda items may be added if necessary, for example, review of a Humanitarian Use Device.

Attachment pages will include a listing of all activities handled through expedited or administrative channels since the last board meeting. They include:

1. Amendments to approved projects  
2. Reported adverse events  
3. Projects approved as exempt status  
4. Projects review through expedited review  

A sample IRB agenda is provided in attachment 1 to this SOP.
AGENDA

Date of Meeting

Introductions

Approval of Minutes

Chair Comments
   List in numerical order

Approval of Continuing Review Reports
   A listing of which is attached

Delinquent Continuing Review Reports Scheduled for Termination
   If applicable, a listing will be attached

Emergency Use of Investigational Drug or Device
   If applicable
   IRB project number – Project title – Principal Investigator

Review of Amendments to Approved Projects
   If applicable
   IRB project number – Project title – Principal Investigator
   Primary Reviewer: Name of assigned primary reviewer

Review of Previously Deferred Projects
   If applicable
   IRB project number – Project title – Principal Investigator
   Primary Reviewer: Name of assigned primary reviewer Lay Reviewer: Name of assigned lay reviewer

Review of New Projects (total number)

Full Board Review (number of projects)

IRB project number – Project title – Principal Investigator
Primary Reviewer: Name of assigned primary review Lay Reviewer: Name of assigned lay reviewer
Amendments to Approved Projects – Expedited Review (xx)

IRB project number – Project Title – Principal Investigator [number of amendment requests submitted]

Review of New Projects

Exempt Projects (xx)

IRB project number – Project title – Principal Investigator – Date exemption granted

Expedited Projects (xx)

IRB project number – Title of Project – Principal Investigator – Date of expedited approval

Adverse Event Reports [xx reports]

Enter IRB project number – Title of Project – Principal Investigator [number of reports associated with project]
1.0 Purpose

To aid in assuring knowledge and compliance of all persons involved in any aspect of human subject research by documenting the requirements for submission and review of amendments.

2.0 Scope

The SOP applies to all human subject research falling under the purview of the Health Sciences Institutional Review Board.

3.0 Definitions

Amendment: Any change to a study from what was previously approved during the period for which approval was given.
Minimal risk: Probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests.

4.0 Policy/Procedure

General Information

45 CFR 46.103(b)(4)(iii) requires that the IRB review and approve all proposed changes in a research study, prior to the initiation of such changes, as new or corrected information is obtained. These amendment requests may be submitted to the IRB administrative office at any time using the online eIRB system.

In certain circumstances, an amendment may need to be implemented immediately to eliminate the apparent immediate hazards to the subjects. In these circumstances, the amendment must be submitted as soon as possible after implementation. Additionally, the IRB must be informed through a phone call or other suitable notification of the need to implement the amendment immediately.

All project amendments should be submitted to the HS IRB office regardless of whether the study sponsor indicated that the amendment requires IRB approval. It is the responsibility of the IRB office/chair(s) to determine whether the amendment is considered administrative in nature and how it should be processed. Submission of all amendments is also required for IRB record keeping and to permit the reconstitution of the history of the project and project-related actions from the IRB file.

The amendment request will be processed by the IRB office in the order in which it is received. The following categories of review will be determined for each request:

- minor/administrative changes
- major changes

If the amendment requires full board review, the amendment will be placed on the next available agenda contingent if a complete submission has been received.

Amendment requirements
Two copies of all amendment materials should be submitted to facilitate review.

Proposed modifications to any study documents must be reviewed and receive IRB approval before they can be implemented. The only exception to this requirement is a protocol amendment/deviation that is necessary to eliminate an apparent immediate hazard to the human volunteers.

The date of approval of an amendment does not change the original approval date or the date by which the regularly scheduled continuing review of the project is to be performed.

Types of amendments include, but are not limited to:

- amendment to the study protocol
- amendment to the informed consent document
- amendment to study personnel
• amendment to the protocol, investigator brochure, or drug brochure
• amendment to the recruitment materials, surveys, questionnaires, etc.

Each amendment is project specific and may not span across multiple studies. Amendments may dictate that revisions be made to more than one project document. For example, a protocol amendment may impact both the protocol and the consent document. Two copies of all revised documents must be submitted for review and approval, in addition to the amendment form being submitted through the online eIRB system.

Requests for amendments should include the following information:
• Study title
• IRB project number
• Principal Investigator
• Contact person (if other than Principal Investigator)
• Complete description of the proposed changes. If the amendment request pertains to the protocol, the protocol amendment summary and the actual amended protocol pages must be submitted. If the amendment changes to the protocol are extensive, a complete new protocol must be submitted with the changes incorporated. A detailed summary of the amendment changes from the sponsor should be submitted, if available.
• If the amendment request requires revisions to the consent document two copies of the revised consent document, one copy which has been highlighted to indicate the revisions, must be submitted.

Once approved by the IRB, the approval will be indicated on the original amendment request which will be returned to the Principal Investigator or contact person for inclusion into the study files. A copy of all materials will be kept in the IRB administrative office files as documentation of the action taken.

Minor/administrative changes

The regulations allow for expedited review of minor/administrative changes in previously approved research in accordance with 45 CFR 46.110(b)(1 and 2). These changes are minor and administrative/editorial in nature and do not impact or change the risk/benefit ratio.

Administrative changes include but are not limited to:
• Change in/addition to study personnel
• Change in Principal Investigator
• Change in current advertisement or request for additional advertisement.
  o Additional advertisement requests will be considered administrative if the method of advertisement/recruitment was previously approved in the application.
  o If a new type of advertisement/recruitment is requested, the request will be reviewed on an individual basis to determine if it merits a higher level of review, based on the allowable expeditable categories and/or the minor changes to previously approved projects outlined in this SOP.
  o National advertising/recruitment materials will be reviewed in relation to the local context. The IRB understands the difficulty in requesting revisions to national recruitment materials; therefore, if the IRB requests revisions which are unable to be resolved with the sponsor, then the national recruitment materials may be disapproved
from being played in the local market. As with any amendment which may be
disapproved, it will first be reviewed by the full board.

- Changes to improve the clarity of statements or to correct typographical errors provided the
  requested change does not alter the content or intent of the statement
- Minor changes requested by the IRB
- Closing to enrollment for planned interim analysis

Additional minor changes include but are not limited to:

- Request inclusion of activities that fall under the categories of allowable expedited review
  set forth in 45 CFR 46.110.
- Changes to minimal risk projects which do not significantly alter the risk/benefit ratio.
- Changes in inclusion/exclusion criteria making the population pool smaller
- Changes in the inclusion/exclusion criteria which do not significantly increase the possible
  study population pool
- Changes in the recruitment/advertising methods which are intended to increase enrollment
  in approved subject categories and in the context of approved inclusion/exclusion criteria
- Increase in study enrollment nationwide, as long as enrollment at this institution does not
  increase from what was previously approved
- New or changes in study documents to be to be distributed to or seen by subjects such as
  surveys, questionnaires, brochures, etc. which are not significantly changed or do not
  change the content or meaning of the previously approved versions.
- Alterations in reimbursement/compensation amount or changes to compensation method
  that are not so great as to change the risk/benefit ratio. Any request to add/change
  compensation to a study must obtain approval from the Accounting Department prior to
  approval from the IRB.
- Increase in study visits to increase safety monitoring
- Decrease in number or volume of sample collections provided it does not change the
  risk/benefit ratio
- Changes in or removal of perceived risks that improve the risk/benefit ratio
- Extension of study enrollment phase, as long as enrollment at this institution does not
  change from what was previously approved
- Reopening enrollment after planned interim analysis, provided it does not change the
  risk/benefit ratio

Minor/administrative changes will be reviewed by the Chair, Vice-Chair, or other qualified board
member. The board member always has the option, upon further review of the request, to request
review of the amendment by the full board. If disapproval of the amendment request is imminent,
the amendment must be reviewed by the full board.

The Board will be notified of any approved amendments with a listing in the attachment pages of
the agenda of each monthly meeting.

Major Changes

In accordance with 45 CFR 46.108(b), all amendment requests which do not meet the criteria set
forth in the expedited categories (45 CFR 45.110) are considered major and must be reviewed by
the full board at a meeting in which a majority of the members are present, with at least one
nonscientific member present.
Full board amendment requests will be reviewed using the primary reviewer system and will be placed on the next available agenda after which a complete submission was received. The primary reviewer for the amendment will receive copies of the amendment request and all supporting or revised documents, a summary of the amendment changes, if available, the original application and the most recent approved consent, and if applicable, any other relevant file materials. All other board members will receive a copy of the amendment request, a summary of the amendment changes, if available, the most recent approved consent and application and, if applicable, a copy of any revised document(s) which will be handed to or viewed by subjects (such as the proposed revised consent document or revised recruitment materials).

Examples of amendment requests considered to be major include:

- Changes that do not meet any of the above criteria
- Changes in the inclusion/exclusion criteria or recruitment method which would significantly increase the possible study population pool
- Alterations in the dosage or route of administration of an administered drug
- Extending the duration of the study
- Addition/deletion of study arms or phases
- New or significantly revised study documents to be distributed to or seen by subjects such as surveys, questionnaires, brochures, etc.
- Deletion of study procedures, visits, or procedures that may adversely impact study safety
- Inclusion of documented risks judged to be substantial, such as newly discovered drug side effects
- Changes in radiation or biosafety

The Board always has the option to request that amendments that substantially change the conduct of the study be presented as separate new proposals.

If disapproval of the amendment request is imminent, the Principal Investigator will be contacted to appear before the board to answer any questions the Board may have. If the IRB decides to not approve an amendment, there is no other appeal process. Higher institutional officials have no authority to approve research which an IRB has disapproved.

The reviewer/Board always has the option to request revision of the informed consent or other study documents if, in their opinion, the amendment request impacts the study in such a way as to necessitate a revision. The IRB will refrain from requesting minor editorial or minor changes to the consent or other study documents that do not have an impact on the study due to the amendment request until the next scheduled continuing review of the study, at which time a thorough revision of the informed consent will take place.

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Authority of the IRB

Effective Date: January 22, 2001
Revised Date: February 24, 2006
Reviewed Date: October, 2005

Approved By: Niels Beck, PhD
Chair, Health Sciences IRB

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1.0 Purpose
To assure knowledge and compliance by documenting the authority of the Health Sciences IRB

2.0 Scope
This SOP applies to all human subject research being conducted which falls under the purview of the Health Sciences Institutional Review Board

3.0 Definitions
None

4.0 Policy/Procedure

The Health Sciences Institutional Review Board (IRB) on the Columbia campus is established as required by regulations of the Department of Health and Human Services (45CFR46.101 et seq.); the Food and Drug Administration (21CFR56.101 et seq.) and by the Federal Wide Assurance (FWA00002876) of the University of Missouri-Columbia. The IRB is an appropriately constituted administrative body established to protect the
rights and welfare of human subjects recruited to participate in research activities conducted under the auspices of the University of Missouri – Columbia.

**MU Divisions Applying to HS IRB**

The Health Sciences IRB reviews all human subjects research conducted by the faculty, staff or students of the following:

- Health Sciences Center
  - Children’s Hospital
  - Columbia Regional Hospital
  - Ellis Fischel Cancer Center
  - Howard A. Rusk Rehabilitation Center
  - Missouri Rehabilitation Center
  - University Hospitals and Clinics
- School of Medicine
- Charles and Josie Smith Sinclair School of Nursing
- School of Veterinary Medicine
- School of Health Professions
- Harry S Truman Memorial Veterans Hospital
- Missouri Institute of Mental Health

The Board reports to and receives administrative support from the Vice-Provost of Research, University of Missouri-Columbia.

**Jurisdiction of HS IRB**

In accordance with the regulations of the Department of Health and Human Services, (DHHS) and the Food and Drug Administration (FDA), the HS IRB has the authority to review and approve research proposals, monitor, require modifications in, or disapprove all research activities involving human research volunteers that fall within its jurisdiction. The jurisdiction of the HS IRB is defined by its binding commitment (FWA 00002876) with the DHHS and by institutional policies to include all human subject research as follows:

1. research to be conducted on the premises of the aforementioned facilities either by staff of the facilities or outside researchers
2. research to be conducted elsewhere that involves faculty, students or staff of the aforementioned facilities
3. research to be conducted elsewhere that utilizes data collected on patients, research subjects or staff of the aforementioned facilities
4. research conducted by an outside researcher involving patients or staff of the aforementioned facilities
5. research funded through the University of Missouri – Columbia or University of Missouri Health Sciences Center or supported by
resources, irrespective of whether the research is directly supported by federal funds

**Authority of HS IRB**

The authority conveyed to the HS IRB includes the following:

1. To review all research projects involving human volunteers prior to initiation of the study and involvement of human volunteers.

2. To require revisions in research protocols, informed consent documents or other study related documents as a condition for initial or continuing approval.

3. To approve new research projects or continuation of previously approved projects.

4. To disapprove the initiation of a new research project.

5. To monitor the activities in approved projects including regularly scheduled continuing review at least every 12 months, amendments, deviations, and adverse events.

6. To suspend or terminate previously approved projects for change in risk/benefit ratio or noncompliance

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1.0 Purpose

To aid in assuring knowledge and compliance of all persons involved in any aspect of human subject research by documenting the requirements for biosafety review.

2.0 Scope

The SOP applies to all human subject research falling under the purview of the Health Sciences Institutional Review Board.

3.0 Definitions

Biosafety: Infectious agents, potentially infectious materials, certain toxins, recombinant products, and other hazardous biological materials which are potentially hazardous to humans, animals, and/or plants (see the MU Biosafety Manual for more detailed definition and examples).
4.0 Policy/Procedure

Administrative

The Institutional Biosafety Committee (IBC) is a separate university entity, under the auspices of Environmental Health & Safety, empowered with the review and approval of all new requests and requests for significant changes in existing approvals of recombinant DNA or biosafety level 2 or 3 materials.

Review and approval by the IBC is REQUIRED for any IRB study or amendment which involves the use of biosafety materials REQUIRED for the protocol, even if it is not part of the research question. This requirement comes directly from the IBC and the regulations which it must follow. The IRB only serves as a flow-through of information.

The review of biosafety related issues is beyond the expertise of the Board; and therefore, the IRB will defer its opinion on biosafety issues to the Institutional Biosafety Committee per 45 CFR 46.107(f). The IRB will hold its final approval until approval from the IBC has been received in the IRB office.

Procedure

1) If the question on the IRB application which states, “Is any agent to be used in this study considered a biohazard?” is marked “Yes,” the HS IRB office will forward to the IBC a copy of the project application, consent form, and protocol or drug brochure on the biologic (information which was provided to the IRB as part of the required number of copies). The HS IRB office staff will also provide the Biosafety office information to which IRB meeting a particular project was assigned and when the IRB packets are delivered to board members.

2) The Biosafety office will directly contact the investigator if there are any biological hazard-related questions and issues, as well as requests for additional information and/or materials.

3) The Biosafety office will make every effort to provide to the HS IRB its administrative and scientific review and approval in a timely fashion, preferably before the IRB meeting when a particular project will be discussed.

4) The HS IRB will make its approval contingent upon receiving approvals from the IBC, unless otherwise indicated by IBC for a specific project.

5) The following paragraph will be placed in the HS IRB “received application pending letter/e-mail”:

Please note that it is the researcher responsibility to make sure that all protocols needing Radiation Safety Committee (RSC) and Institutional Biosafety Committee (IBC) approvals receive such approvals prior to protocol initiation. The HS IRB will not issue the final project approval if RSC and/or IBC approval is not on file in the HS IRB office. To assist in the review process, the IRB office will forward a copy of the relevant study materials to the RSC or IBC for review, when needed. The RSC or IBC will directly contact the investigator with any questions or request for follow-up. Please contact the Radiation Safety Office at 573-882-7221 for more information on RSC requirements or the Institutional Biosafety Committee office at 882-7018 for more information on IBC requirements.
**Board Education**

Effective Date: February 16, 2001
Original Approval Date: February 16, 2001
Revised Date: July 23, 2002  February 24, 2006
Reviewed Date: October, 2005

Approved By: Niels Beck, PhD
Chair, Health Sciences IRB

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- Purpose
- Scope
- Definitions
- Policy/Procedure

1.0 **Purpose**
To aid in assuring knowledge and compliance of all persons involved in any aspect of human subject research by documenting the policy for Board education.

2.0 **Scope**
The SOP applies to all human subject research falling under the purview of the Health Sciences Institutional Review Board.

3.0 **Definitions**
None

4.0 **Policy/Procedure**

The Health Sciences Institutional Review Board (“HS IRB”) is established pursuant to and in accordance with the regulations of the Department of Health and Human Services (45 CFR46.101); the Food and Drug Administration (21 CFR 56.101); the Belmont Report; and the FederalWide Assurance (FWA00002876) of the University of Missouri-Columbia. The HS IRB is an appropriately constituted administrative body established to protect the rights and welfare of human subjects that are recruited to participate in research activities conducted under the auspices of the University of Missouri-Columbia.
The HS IRB has a duty to ensure that all members possess the professional qualifications and experience to adequately review the degree of protocol complexity and risk to human subjects. All members are required to:

- Complete the HS IRB Education and Training requirement prior to serving on the Board, reviewing or voting on any research project that is under the jurisdiction of the University of Missouri-Columbia, at a convened IRB meeting.
  - The HS IRB Education and Training requirement includes:
    - Attending an HS IRB Education and Training Seminar for the certified period; or
    - Completing the web-based training module
    - Complete continuing education and training requirements during regularly scheduled meetings
    - Complete continuing education every two (2) years from the date of the first training seminar, video, or web-based module.

The HS IRB highly recommends all members attend continuing educational events on an ongoing basis to maintain the professional qualifications and experience necessary to adequately review and meet the degree of protocol complexity, to assure adequate protection of human subjects involved in research.

The HS IRB office has some funds in the budget to send one or two board members to regional and/or national training events each year.
Purpose and Function of the IRB

Effective Date: January 22, 2001
Original Approval Date: January 22, 2001
Revised Date: Presented at IRB meetings on 8/29/01 and 9/12/01,
Approved on 8/29/01 and 9/12/01,
Revisions suggested by IRB members on 8/29/01 have been incorporated into the policy
Reviewed: October, 2005

Approved By: Niels Beck, PhD
Chair, Health Sciences IRB

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Purpose
Scope
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1.0 Purpose
To aid in assuring knowledge and compliance of all persons involved in any aspect of human subject research by documenting the purpose and function of the Board.

2.0 Scope
The SOP applies to all human subject research falling under the purview of the Health Sciences Institutional Review Board.

3.0 Definitions
None

4.0 Policy/Procedure

The purpose of the Health Sciences Institutional Review Board is to assure that the rights and welfare of human research volunteers are adequately protected in research being conducted in conjunction with the University of Missouri Health Sciences Center and its affiliates. The principles which govern the IRB in assuring that the rights and welfare of
subjects are protected are those principles embodied in the regulations and the Federal Wide Assurance.

To accomplish this purpose, a group deliberation process is used to review and approve protocols and related materials (i.e. informed consent document, investigator brochures, recruitment materials, test article information, etc.) to determine:

1) the level of risk category into which each proposal falls

2) that the level of risk is minimized by procedures consistent with sound research design that do not unnecessarily expose the research volunteer to risk

3) that the risks to research volunteers are reasonable and are outweighed by the anticipated benefit and the knowledge that may be expected to be gained

4) the evaluation of risks and benefits considers only the risk/benefits which may result from the research (risk/benefit of standard of care procedures are not taken into account except as relating to research).

5) the risk/benefits are not considered in light of long-range effects of applying research knowledge gained effecting public policy

6) the participant selection pool is equitable

7) the human subject volunteers are adequately informed of the risk and benefits of participation in the research study, what is involved in participation in the research study

8) informed consent is adequate and obtained from each prospective volunteer and appropriately documented in accordance with and to the extent required by federal regulations and HS IRB policies

9) the privacy and confidentiality of each research volunteer and the corresponding data is adequately protected

10) the inclusion of appropriate additional safeguards to protect the rights and welfare of research volunteers who may be vulnerable to coercion or undue influence (those individuals considered as members of vulnerable populations, (e.g. children, prisoners, incompetent persons, or economically or educationally disadvantaged individuals)

The Board carries out the purpose and function in its review of all newly submitted projects, amendment requests, adverse event notification and continuing review.

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Certificates of Confidentiality

Effective Date: July 1, 2004
Original Approval Date: July 1, 2004
Revision Date: 

Approved By: Niels Beck, PhD
Chair, Health Sciences IRB

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1.0 Purpose

To aid in assuring knowledge and compliance of all persons involved in any aspect of human subject research by documenting the requirements for obtaining a Certificate of Confidentiality.

2.0 Scope

The SOP applies to all human subject research falling under the purview of the Health Sciences Institutional Review Board.

3.0 Definitions

Identifying information: Broadly defined as any item or combination of items in the research data that could lead directly or indirectly to the identification of a research subject.

Sensitive: Disclosure of identifying information could have adverse consequences for subjects or damage their financial standing, employability, insurability, or reputation.
4.0 Policy/Procedure

General Information
Certificates of Confidentiality (COC) are issued to protect the privacy of research subjects by protecting investigators and institutions from being compelled to release information that could be used to identify subjects with a research project.

Certificates of Confidentiality are issued to institutions or universities where the research is conducted. Certificates of Confidentiality are project specific. It is intended that they allow the investigator and others who have access to research records to refuse to disclose identifying information in any civil, criminal, administrative, legislative, or other proceeding, whether at the federal, state, or local level.

Certificates can be used for biomedical, behavioral, clinical or other types of research that are sensitive. A Certificate may be granted:
- For studies collecting information that if disclosed could have adverse consequences for subjects or damage their financial standing, employability, insurability, or reputation.
- To help achieve the research objectives and promote participation in studies by assuring confidentiality and privacy to participants.

Examples of sensitive research activities include but are not limited to the following:

* Collecting genetic information;
* Collecting information on psychological well-being of subjects;
* Collecting information on subjects' sexual attitudes, preferences or practices;
* Collecting data on substance abuse or other illegal risk behaviors;
* Studies where subjects may be involved in litigation related to exposures under study (e.g., breast implants, environmental or occupational exposures).

A Certificate of Confidentiality protects personally identifiable information about subjects in the research project while the Certificate is in effect. Generally, Certificates are effective on the date of issuance or upon commencement of the research project if that occurs after the date of issuance. The expiration date should correspond to the completion of the study. The Certificate will state the date upon which it becomes effective and the date upon which it expires. A Certificate of Confidentiality protects all information identifiable to any individual who participates as a research subject (i.e., about whom the investigator maintains identifying information) during any time the Certificate is in effect. An extension of coverage must be requested if the research extends beyond the expiration date of the original Certificate. **However, the protection afforded by the Certificate is permanent.** All personally identifiable information maintained about participants in the project while the Certificate is in effect is protected in perpetuity. If a COC is obtained after a study has already started, the COC covers the entire study period, not just from the point at which the COC was obtained.
Applying for a Certificate of Confidentiality
An investigator may choose to apply for a Certificate of Confidentiality on his or her own, or the IRB may require that an investigator obtain a Certificate prior to conducting the research. The IRB may grant a conditional approval of the research study while the COC process is ongoing. However, approval of the Certificate must be submitted to the IRB before any research may take place. Even after a study has been approved, a COC may be required by the IRB due to a change in the risk:benefit ratio of the study (for example, an amendment may request to include a questionnaire that asks subjects highly sensitive information). If a COC is obtained after a study has already started, the COC covers the entire study period, not just from the point at which the COC was obtained.

If NIH funds the research project for which a COC is requested, an investigator may apply through the funding Institute. Investigators who intend to apply for a Certificate of Confidentiality should contact the Human Subjects Office regarding procedural steps regarding obtaining a Certificate of Confidentiality. Complete information is available on the NIH Office of Extramural Research web site (http://grants.nih.gov/grants/policy/coc/).

Studies involving an IND or IDE require that the investigator apply to the FDA for the COC. Studies that do not involve an IND or IDE require that the investigator apply to the appropriate NIH institutes for the COC.

Involuntary Disclosure
While Certificates are intended to protect against involuntary disclosure, investigators should note that research subjects might voluntarily disclose their research data or information. Subjects may disclose information to physicians or other third parties. They may also authorize in writing the investigator to release the information to insurers, employers, or other third parties. In such cases, researchers may not use the Certificate to refuse such disclosure. Moreover, researchers are not prevented from the voluntary disclosure of matters such as child abuse, reportable communicable diseases, or subjects threatening violence to self or others. However, if the researcher intends to make any voluntary disclosures, the consent form must specify such disclosure.

Documentation of Certificate of Confidentiality in Informed Consent
In the Informed Consent Document, investigators should tell research subjects that a Certificate is in effect. Subjects should be given a fair and clear explanation of the protection that it affords, including the limitations and exceptions noted above.

The HS IRB has developed suggested language for the informed consent document regarding Certificates of Confidentiality. Investigators should use this language when appropriate:

To help keep information about you confidential, we have obtained [applied for] a Confidentiality Certificate from the Department of Health and Human Services (DHHS). The Confidentiality Certificate adds special protection for research information about you. The Confidentiality Certificate says that the investigator is protected from being forced, even under a court order or subpoena, to release information that could identify you. You should be aware, however, that the investigator may release identifying information in some circumstances. For example, medical information may be disclosed in cases of medical necessity, or
take steps (including notifying authorities) to protect you or someone else from serious harm, including child abuse. Also, because this research is sponsored by [insert appropriate agency], staff from that and other DHHS agencies may review records that identify you for audit or program evaluation [include only if federally funded]. This Certificate does not imply that the Secretary, DHHS, approves or disapproves of the project. [any other exceptions (e.g., communicable disease reporting if you test for a communicable disease) should be included as steps the researchers may take voluntarily]

You should understand that a Certificate of Confidentiality does not prevent you or a member of your family from voluntarily releasing information about yourself or your involvement in this research. Also, if an insurer, employer, or other person obtains your written consent to receive research information, then the researchers may not use the Certificate to withhold that information.

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Conflict of Interest

Effective Date: June 1, 2004
Original Approval Date: June 1, 2004
Revision Date: December 12, 2005

Approved By: Niels Beck, PhD
Chair, Health Sciences IRB

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1.0 Purpose
2.0 Scope
3.0 Definitions

1.0 Purpose

To aid in assuring knowledge and compliance of all persons involved in any aspect of human subject research by documenting the requirements for conflict of interest.

2.0 Scope

The SOP applies to all human subject research falling under the purview of the Health Sciences Institutional Review Board.

3.0 Definitions

Conflict of Interest (COI) - University employees shall faithfully discharge their duties and shall refrain from knowingly engaging in any outside matters of financial interest incompatible with the impartial, objective, and effective performance of their duties. They shall not realize personal gain in any form which would influence improperly the
conduct of their University duties. They shall not knowingly use University property, funds, position or power for personal or political gain. They shall inform their supervisors in writing of reasonably foreseen potential conflicts.

*Financial (Direct) Interest* – Financial interest includes but is not limited to consulting, speaking or other fees; honoraria; gifts; or licensing revenues, and equity interests or stock options.

*Non-financial (Indirect) Interest* - Private interests include unpaid leadership positions, membership on the board of directors, companies, clubs, societies and organizations such as trade unions and voluntary organizations, which members of the public might reasonably think could influence the decision-making process.

### 4.0 Policy/Procedure

#### General Information

An institution may face a conflict among its multiple duties to protect human subjects. To ensure the integrity of research and its compliance with applicable laws and regulations, and the institution’s legitimate interest in the financial health and economic viability of the enterprise, institutions should ensure that the responsibility for human subjects research does not overlap or coincide with responsibility for those institutional financial interests that may be directly affected by the outcome of the research. Institutions should ensure that the functions and administrative responsibilities related to human subjects research are separate from those related to investment management and technology licensing.

Conflicts of Interest may include either financial (direct) or non-financial (indirect) interests. COI are not prohibited because not all interests cause conflicts that impact research. When there are specific financial relationships or other non-financial interests in research the disclosure must be forwarded to the Conflict of Interest committee for review [http://www.research.missouri.edu/complia/coi.htm](http://www.research.missouri.edu/complia/coi.htm).

#### Direct Financial Relationships

Institutions and individuals involved in human subjects research may establish financial relationships related to or separate from particular research projects. Those financial relationships may create financial interests of monetary value, such as payments for services, equity interests, or intellectual property. When such direct financial interests are disclosed, the disclosure is forwarded to the Conflict of Interest committee for review.

#### Indirect Non-financial Interests

Private interests in outside organizations can result in COI. Examples of private interests include unpaid leadership positions, membership on the board of directors, companies, clubs, societies and organizations such as trade unions and voluntary organizations, which members of the public might reasonably think could influence the decision-making...
process. When such indirect, non-financial interests are disclosed, the disclosure is forwarded to the Conflict of Interest committee for review.

**Board member conflict:**
The regulations state (45 CFR 46.107e and 21 CFR 56.107e) that no IRB member may participate in the IRB’s initial or continuing review of a project in which the member has a conflicting interest, except to provide information requested by the IRB. Any member (including chairs) that may have a conflict of interest with any research reviewed by the Board, will be excused from the meeting prior to any discussion of the project and during the vote. The member may be invited into the meeting to answer questions, however they will be excused during the Board deliberations. If a chair is excused from the meeting due to a possible COI, a board member will take over the deliberations for that particular project in the absence of the chair. Chairs that oversee the conduct of a meeting routinely do not vote on projects except in the case of a tie; however, they do count towards quorum.

If a member is excused from the meeting due to a conflict of interest, a valid quorum must be present or the meeting must be terminated from further action until a valid quorum is obtained.

**Investigator conflict:**
Any investigator that may have a conflict of interest with any proposed research will be forwarded to the Conflict of Interest Committee. Each investigator shall disclose to the COI committee all interests

1. that would reasonably appear to be directly and significantly affected by the funded research or educational activities; or

2. in entities whose financial interests would reasonably appear to be directly and significantly affected by such activities.

This information must be disclosed:

a. at the time the IRB proposal is submitted;

b. on an annual basis during the project annual renewal; and

c. immediately as new significant interests are obtained.

The Conflict of Interest Committee, under the auspices of the Deputy Chancellor, independently determines whether the COI can be effectively managed, reduced or eliminated, working with the investigator and the IRB. The COI committee notifies the IRB of final determination in the case. Final approval of a study is held pending determination by the COI committee.

Examples of how conflicts of interest might be addressed include the following:
• Public disclosure of significant interests
• Monitoring of research by independent reviewers
• Modification of the research plan
• Disqualification from participation in all or a portion of the research
• Divestiture of significant interests

Additional information
The University of Missouri-Columbia has several policies governing COI:
• Business Policy and Procedures on COI:
• Collected Rules and Regulations on COI:
• Collected Rules and Regulations on conflict with federal grant agencies:
Continuing Review Report (CRR)

Effective Date: July 1, 2004
Original Approval Date: July 1, 2004
Revision Date: August 23, 2005

Approved By: Niels Beck, PhD
Chair, Health Sciences IRB

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1.0 Purpose

To assure knowledge and compliance by documenting the continuing review procedure of approved projects for the Health Sciences IRB.

2.0 Scope

The SOP applies to all human subject research falling under the purview of the Health Sciences Institutional Review Board.
3.0 Definitions

**CRR** – Continuing Review Report, the annual report required by the FDA and OHRP

**Primary Contact** – may be any person designated by the Principal Investigator for the completion of administrative paperwork

**Consented** – indicates all participants who signed the consent form whether or not eligibility requirements were met.

**Enrolled** - indicates all participants who signed the consent form and met eligibility requirements.

4.0 Policy/Procedure

Continuing review of research must be substantive and meaningful. Continuing review by the convened IRB, with recorded vote on each study, is required unless the research is otherwise appropriate for expedited review under 45 CFR 46.110.

Regulations codified at 45 CFR 46.111 set forth the criteria that must be satisfied in order for the IRB to approve research. These criteria include, but are not limited to, determinations by the IRB regarding risks, potential benefits, informed consent, and safeguards for human subjects. Not only must the IRB ensure that these criteria are satisfied at the time of initial review, but also at the time of continuing review.

Requirements

At the time of initial review and approval of a research proposal, the Board establishes a time interval by which continuing review of the project must occur. This interval can be set for any length of time but must be no longer than 12 months from the initial approval or continued approval date. The Board may request a separate review or change the review interval at any time they deem it necessary because of revised information from an amendment, adverse event, or information obtained during a scheduled continuing review.

Principal Investigators will be informed in the project approval letter of the scheduled continuing review interval for the project. It is the responsibility of the Principal Investigator to submit the CRR even without notification from the HS IRB office. Continuing review is mandatory for all currently active research projects; including those that have been closed to subject accrual but are still involved in data collection and analysis or are in long-term follow-up.

The information requested on the Continuing Review Report (CRR) includes:

- Description of current consent process
- Verification that informed consent was obtained from all subjects and that all signed consent forms are on file (unless requirements have been waived)
- Verification that consent form has not been translated without IRB approval
- Current project status, if the study is closed to enrollment, the date that the study closed to enrollment
- Current funding status
- Current funding source
- Number of subjects enrolled study-wide since the original approval of the study
- Number of subjects enrolled study-wide since the last continuing review
• Number of subjects enrolled on-site (since original approval and since last continuing review
  o Breakdown of information into number of subjects that did not meet eligibility requirements, number of subjects that withdrew from the study, number of subjects currently on active treatment or long term follow-up, number of subjects who have completed the study, number of subjects whose participation was terminated by the investigator, number of subjects lost to follow-up
• Reasons for withdrawal of participation
• Reasons for termination of subjects
• Current progress of enrollment
• Subject complaints
• Special subject population information
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• Brief narrative of study summary
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• Subject compensation information
• Information regarding unanticipated problems
• Number of Adverse Events
• Description of Adverse Events
• Number of Amendments
• Description of Amendments (protocol and CIDB)
• Change in study personnel
• Description of risk/benefit ratio
• Progress of research
• Changes in literature
• Description of preliminary findings
• DSMB information and reports
• Sponsor Monitoring information and reports
• Federal Agency audit information and reports
• Certificate of Confidentiality information and report
• Form 1572 information
• Conflict of Interest Disclosure

All CRRs will be acted upon by the full board unless they meet the expedited review requirements as codified in 45 CFR 46.110 (please see section on Expedited Review for additional information). All continuing reviews will be conducted using a primary reviewer system of review.

The IRB must still receive and review reports of local, on-site adverse events and unanticipated problems involving risks to subjects or others and any other information needed to ensure that its continuing review is substantive and meaningful.

Changing the Status of a Study on a CRR form
A CRR form may be used to change the status of a study yearly as necessary. If a study is “Active-open to enrollment” one year, but over the course of the following year, has changed to “Closed-data analysis only,” this change should be reflected on the CRR.
If a study has been completed, but a Completion/Termination/Withdrawal Form has not yet been submitted at the time of study expiration, a CRR form must be submitted in lieu of the Completion Form. This eliminates the confusion often caused by submitting a Completion Form at CRR time and expedites the approval of the form.

**Submission**

A query is run on the first working day of the month for all studies where the approval expires two months later. EXAMPLE: On April 1, 2004, a query is run to find all studies where the approval expires in June 2004. From this query the first notice of expiration is sent to the Primary Contact for the study and a CRR form is made available in the electronic submission system for completion. It is the responsibility of the Principal Investigator to submit a CRR even without notification from the HS IRB office.

The complete CRR submission is due on the last working day of the month that the first notice of expiration was sent. Before the CRR is reviewed in the HS IRB office, it must be submitted online and a complete hardcopy CRR submission is required.

A complete CRR submission consists of two copies of each of the following where applicable:

1. Completed CRR form
2. Clean copy of the consent form – if the study is active, open to enrollment
3. Complete copy of current protocol (if not already on file)
4. Group Meeting Information (CALGB, GOG, ASCOG, COG, etc.)
5. Data Safety & Monitoring Report
6. Grant application – if not previously submitted
7. Certificate of Confidentiality
8. Form 1572
9. Statement of Compliance

Numbers 2-9 are considered “attachments” by the HS IRB office and will be referred to as such throughout this SOP.

If a CRR has not been submitted by the requested date, a second notice of expiration is sent to the Primary Contact as well as the Principal Investigator, if different than the Primary Contact. This email details the expiration date, and the last possible date that the CRR can be received in the IRB office before the study will be terminated. This due date is measured in terms of the last convened board meeting prior to the study’s approval expiration. In order to be reviewed at a particular board meeting, the CRR must be submitted no later than three weeks prior to the board meeting for adequate preparation for review. EXAMPLE: The approval for a study expires on May 3, 2004. The last board meeting at which this study can be approved is April 28, 2004. Three weeks before this board meeting is April 7, 2004. Therefore, the last possible date that the CRR can be submitted to the IRB office is April 7, 2004. If the CRR has not been submitted by the due date, the study will be terminated by the IRB on its expiration date. In rare occasions, CRRs submitted after the final due date are looked at on a case-by-case basis to determine if there is adequate time to prepare the CRR for review, otherwise the study will be terminated.

**Processing and Review**

The IRB office staff review each CRR for accuracy, completeness and whether it qualifies for full board or expedited review. Any questions or clarifications on the project status, progress report,
enrollment, etc. are handled via communication with the Principal Investigator or Study Coordinator. All CRR forms will be acted upon by the full board unless they meet the expedited review criteria as codified in 45 CRF 46.110.

**Expeditied Review**

CRR forms received in the office that meet the criteria codified in 45 CFR 46.110 (8-9) may be expedited.

8) Continuing review of research previously approved by the convened IRB as follows:
   a. Where (i) the research is permanently closed to the enrollment of new subjects; (ii) all subjects have completed all research-related interventions; and (iii) the research remains active only for long-term follow-up of subjects; or
   b. Where no subjects have been enrolled and no additional risks have been identified; or
   c. Where the remaining research activities are limited to data analysis.

9) Continuing review of research, not conducted under an investigational new drug application or investigational device exemption where categories two (2) through (8) do not apply but the IRB has determined and documents at a convened meeting that the research involves no greater than minimal risk and no additional risks have been identified.

For a multi-center protocol, an expedited review procedure may be used by the IRB at a particular site whenever the conditions of category (8)(a), (b), or (c) are satisfied for that site.

With respect to category 8(b), while the criterion that “no subjects have been enrolled” is interpreted to mean that no subjects have ever been enrolled at a particular site, the criterion that “no additional risks have been identified” is interpreted to mean that neither the investigator nor the IRB at a particular site has identified any additional risks from any site or other relevant source.

The continuing reviews will be conducted using a primary reviewer system of review. As each CRR form is received and categorized as expedited, it will be assigned to a primary reviewer for review (typically the IRB chairs for expedited reviews). The primary reviewer will receive a detailed Project History Report, a current copy of the protocol and, if applicable, the Cumulative AE Log and Amendment Log in addition to the completed CRR form. With these documents, the primary reviewer will be provided with a clear picture of the file; however, the primary reviewer always has the option to view the file in the HS IRB office to clarify any questions that may arise. The primary reviewer may request that the IRB office staff resolve any problems or questions. The primary reviewer may also determine that the CRR does not qualify for expedited review and must be reviewed by the convened Board. The Board will be notified through attachments to the agenda of all CRRs that were reviewed at the expedited level.

**Full Board Review**

The continuing reviews will be conducted using a primary reviewer system of review. As each CRR form is received, it will be assigned to a board meeting using the thirty (30)
Each CRR will also be assigned to a primary reviewer for review. The Primary Reviewer will receive the following information:

- Completed CRR form and all attachments
- Copy of current protocol
- Detailed Project History report
- Cumulative AE Log (if applicable)
- Amendment Log (if applicable)
- Copies of all previously reviewed CRRs

With these documents, the primary reviewer will be provided with a clear picture of the file; however, the primary reviewer always has the option to view the file in the HS IRB office to clarify any questions that may arise.

All other Board members will receive only copies of each completed CRR form and other attachments that will be presented and acted upon at the convened meeting.

The primary reviewer will present to the Board any problems or questions found during the continuing review. Also, any Board member may indicate for discussion any issues they found during their review of the CRR. The minutes of IRB meetings will document separate deliberations, actions, and votes for each protocol undergoing continuing review by the convened IRB.

If no issues are raised the project will be approved to continue for another year (or whatever the originally indicated approval period).

If minor issues are raised (e.g. minor consent changes, obtaining national numbers, etc.), the board may approve the study for one year (or other stated period to be decided by the Board) pending said changes. In such cases, the administrative staff will contact the Principal Investigator or Primary Contact to obtain the necessary information. The Principal Investigator or Primary Contact has 90 days to provide the office with the requested information. If the information is not obtained within 90 days, the study will be placed on-hold until the requested information has been received.

If substantial issues are raised or the Board needs information for further review, the Board may approve the continuation of the project for a period of time, to be decided by the Board, until clarification can be made on said issues. The administrative staff will contact the Principal Investigator or Primary Contact to obtain the necessary information. Once the requested clarification has been received, the Board will review the CRR again prior to the expiration date set forth by the Board. If the Board approves the continuation of the study, approval will be granted for the remainder of the approved review interval from the date of CRR board review, thereby keeping the anniversary date.

EXAMPLE: The expiration date of Study XYZ is June 27, 2004 and it will go before the convened Board on June 16, 2004. The Board approves it for one month so that some areas of concern can be resolved. A stamp will be put on the CRR stating that it has been approved from June 16, 2004 until July 16, 2004. At their meeting on July 14, 2004, the Board approves the study for the remainder of the one-year time period.
Another stamp is placed on the CRR stating that it was approved from July 14, 2004 until June 27, 2005.

If the issues raised are substantial enough to warrant Board concern that the risks/benefits ratio has been altered and if the opinion of the Board it is necessary, the Board may disapprove the continuation of the project. The Principal Investigator may be invited to the board meeting to answer questions.

**CRR approval**

Once continuing approval has been granted the IRB Chair, indicating the date of review, the date of approval, and the approval expiration date, will sign the completed CRR. When the continuing review occurs annually and the IRB performs continuing review within 30 days before the IRB approval period expires, the IRB may retain the anniversary date as the date by which the continuing review must occur. The new expiration date is calculated from the last approval date plus 12 months (or other time frame as specified by the Board).

EXAMPLE: A CRR was reviewed by the convened IRB on April 14, 2004 and it expires on May 10, 2004. The review date would be April 14, 2004. The approval date would be May 10, 2004 and the approval expiration date would be May 10, 2005.

This review and approval system is in accordance with the guidelines set forth by OHRP on July 11, 2002.

If the IRB deems that the study is not being conducted in accordance with requirements, or a change has occurred in the risk/benefit ratio necessitating placing the study on hold or termination of the approval, the Principal Investigator will be promptly notified with written justification.

Failure to return the completed CRR or to inadequately complete the CRR prior to the deadline set by the IRB office will result in termination of the project by the IRB. The Principal investigator will be notified first via email, then in writing by the IRB, that the project has been terminated due to noncompliance with the continuing review regulations. A courtesy copy of this termination letter will also be provided to the relevant Dean or Department Chair, IRB Chair, and appropriate sponsor or oversight authority (if applicable). A listing of projects scheduled for termination because of CRR noncompliance will be documented in the meeting minutes as an attachment.

**Approval Expiration**

The IRB and investigators must plan ahead to meet required continuing review dates. If an investigator has failed to provide continuing review information to the IRB or the IRB has not reviewed and approved a research study by the continuing review date specified by the IRB, the research must stop, unless the IRB finds that it is in the best interests of individual subjects to continue participating in the research interventions or interactions. Enrollment of new subjects cannot occur after the expiration of IRB approval. The regulations make no provision for any grace period extending the conduct of research beyond the expiration date of IRB approval.

When continuing review of a research protocol does not occur prior to the end of the approval period specified by the IRB, IRB approval expires automatically. Such expiration of IRB approval does not need to be reported OHRP as a suspension of IRB approval under HHS regulations.
5.0  Applicable Regulations
     OHRP Guidance July 11, 2002

6.0  Related SOP
Databases

Effective Date: September 1, 2004
Original Approval Date: September 1, 2004
Revision Date: September 8, 2004

Approved By: Niels Beck, PhD
Chair, Health Sciences IRB

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- Definitions
- Policy/Procedure
  - General Information
  - Consent
  - Review of databases

1.0 Purpose

To aid in assuring knowledge and compliance of all persons involved in any aspect of human subject research by documenting the requirements for maintaining databases.

2.0 Scope

The SOP applies to all human subject research falling under the purview of the Health Sciences Institutional Review Board.

3.0 Definitions

Database – Any collection of records, information, or data, either in electronic or written form.

Prospective - The information (data, documents, specimens, etc.) do not exist at the time the IRB request is made.

Publicly available – Available to the general public, in the form of records, documents, files, etc. Many organizations make data available to researchers at a reasonable cost. These materials
generally are not available to the general public. If data is obtained from any of these sources the data cannot be assumed to be “publicly available.”

Retrospective – The information (data, documents, specimens, etc.) already exist, have been collected and are “on the shelf” at the time the IRB request is made.

Policy/Procedure
General Information
Databases can generally be broken into two categories: research databases and clinical databases. Review of databases by the HS IRB will be considered necessary when:

- The information is collected primarily for research purposes, to act as a repository for current or future analysis or data extraction.
- The information was previously collected for clinical purposes, and now the information, or a subset of information, is proposed for use to investigate a research question.

Generally speaking, departmental registries used to maintain clinical information on patients are not subject to IRB review. However, if there is intent to use various database elements for a specific research project then IRB approval is necessary.

The creation of databases for third parties, such as sponsors, requires IRB review regardless of the intent.

Consent
Prospective enrollment into a research database requires written consent of the subject. Requests for waiver of consent for prospective enrollment into a research database generally do not meet the criteria set forth in the waiver requirements (45 CFR 46.116(d)).

Retrospective review of clinical databases may require written consent, if subjects are readily available through a clinic, doctor’s office, etc. However, waiver of consent may be requested depending on the nature and type of research and if the elements for waiver of consent are met. If a subject has retrospective data that were included in the database review, and attends the clinic, doctor’s office, etc. for a future visit, written consent must be obtained from that subject for inclusion of subsequent data into the database.

Many times studies wish to look at both retrospective and prospective data. A waiver of consent must be requested for the previously existing data and written consent is necessary for all prospectively collected data.

Review of databases
Generally speaking, research studies involving data collected for non-research purposes are eligible for expedited review under category 5. Some database research may qualify for exempt review if it meets the criteria in 45 CFR 46.101(b)(4). Many times data that is publicly available falls under the exempt criteria.

All other prospective collection of data, compiled in a database, must be reviewed by the full board, unless the research meets the criteria for expedited review set forth in 45 CFR 46.110.
Emergency Use of a Test Article

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1.0 Purpose
   To aid in assuring knowledge and compliance of all persons involved in any aspect of human subject research by documenting the policy/procedure for Emergency Use of a Test Article.

2.0 Scope
   The SOP applies to all human subject research falling under the purview of the Health Sciences Institutional Review Board.

3.0 Definitions
   Emergency Use: The use of a test article on a human subject in a life-threatening situation in which no standard acceptable treatment is available and in which there is insufficient time to obtain IRB approval.

   Test Article: Any drug for human use, biological product for human use, medical device for human use, human food additive, color additive, electronic product, or any other
article subject to regulation under the act or under sections 351 or 354-360F of the Public Health Service Act.

Life Threatening: Includes the scope of both life-threatening and severely debilitating, as defined below:

- Life-threatening means diseases or conditions where the likelihood of death is high unless the course of the disease is interrupted and diseases or conditions with potentially fatal outcomes, where the end point of clinical trial analysis is survival. The criteria for life-threatening do not require the condition to be immediately life-threatening or to immediately result in death. Rather, the subjects must be in a life-threatening situation requiring intervention before review at a convened meeting of the IRB is feasible.
- Severely debilitating means diseases or conditions that cause major irreversible morbidity. Examples of severely debilitating conditions include blindness, loss of arm, leg, hand or foot, loss of hearing, paralysis or stroke.

4.0 Policy/Procedure

The FDA regulations for the protection of human subjects and patients allow for an investigational drug or device to be used in emergency situations without prior IRB approval [21 CFR 56.102(d), 21 CFR 56.104(c)]. The emergency use provision in the FDA regulations is an exemption from prior review and approval by the full IRB. All the following conditions for emergency must be met:

- Subject is facing a life-threatening condition, for which there is no conventional treatment
- There is insufficient time to obtain IRB approval prior to administration
- The subject to receive the test article will not be enrolled in a research study involving the test article
- The physician has legitimate access to a test article and believes that there is reasonable likelihood that its use may be advantageous to the life-threatening condition

Approval of an emergency use of an investigational drug will be granted for only one (1) patient. If subsequent use of the test article is contemplated on the same subject or others, a complete IRB application must be submitted for full board review prior to any additional use of the test article. An investigator cannot carry out a research project on a case-by-case basis under an emergency use premise.

Procedure to Obtaining Emergency Use approval

1. Prior to administration of the test article, the investigator must notify the Chair and/or IRB administrative office of the request for Emergency Use approval and the intention to use an investigational test article.
2. The IRB will provide the investigator with written information and procedures for obtaining approval for emergency use of a test article. (The instructions will be consistent with this SOP). Attachment 1 contains the written information and procedures. Required information:
   a. Written request outlining the necessity for Emergency Use
   b. Subject’s name
   c. Name and IND # (investigational new drug identification number) of test article
   d. Explanation of subject’s history and rationale for use of drug
   e. Informed consent document

3. No review or action will occur until receipt of the items requested in 2.

4. The Chair and IRB administrative office will review the request for emergency use and the provided consent document for acceptability.

5. If the request is approved, a memorandum documenting the approval will be prepared for the investigator. (See Attachment 2)

6. The investigator will be required to sign the approval memorandum signifying their understanding of and agreement of the reporting requirements.

7. A copy of the completed memorandum and approved consent document will be provided to the investigator. A full copy of all documents and information will be kept in a file in the IRB administrative office.

8. The Emergency Use exemption will be valid for a period of 30 days from the date of exemption. If the investigational test article is not administered within 30 days of the approval, the approval will be rescinded and any subsequent request for emergency use will need to be requested following the documented procedures of requesting an Emergency Use approval.

**Reporting Requirements**

A report must be received in the IRB office within 5 days of issuance of the approval. The report must be a written status of the emergency use including information on the administration of the test article. If a report is not received within 5 days, a member of the IRB staff will contact the investigator on day 5 to obtain the status of the emergency use and reiterate reporting procedures to the investigator.

A full report is due again by 30 days. If a report has not been received in the IRB office within 30 days of issuance of the approval, a member of the IRB staff will contact the investigator on day 30 to obtain the status of the emergency use and reiterate reporting procedures to the investigator.

All adverse events associated with the emergency use exemption must be reported to the IRB within 5 days of the adverse event occurrence.

If the Chair or IRB administrative office can not be contacted in advance, the investigator may administer the drug as long as s/he obtains informed consent from the subject, and
provided written notification to the IRB within five (5) days of the test article administration.
Attachment 1:

REQUIREMENTS AND PROCEDURES FOR THE EMERGENCY USE OF AN UNAPPROVED INVESTIGATIONAL DRUG, BIOLOGIC OR DEVICE

The FDA regulations for the protection of human subjects and patients allow for an investigational drug or device to be used in emergency situations without prior IRB approval. Emergency use is defined as the use of a test article (e.g. investigational drug or biologic) on a human subject in a life-threatening situation in which no standard acceptable treatment is available and in which there is insufficient time to obtain IRB approval.

Requirements for Emergency Use

Each of the following conditions must exist to justify the emergency use of an unapproved investigational drug (including biologic) or device:

1) the patient has a life-threatening condition that requires immediate treatment
2) no generally acceptable alternative for treating the patient is available
3) because of the immediate need to use the drug or device, there is not sufficient time to submit for full IRB review and action

Exemption from full IRB approval for Emergency Use of an investigational drug will be granted for only one (1) patient. If subsequent use of the test article is contemplated on the same subject or others, a full application packet submitted for full board review will be required prior to any additional administration of the test article. An investigator can not carry out a research project on a case-by-case basis under an emergency use premise.

University policies require that the IRB chair or IRB administrative office be notified prior to the emergency use of an investigational drug or device, however, this notification should not be construed as IRB approval. Notification is required by the IRB to ensure that the conditions described in the respective FDA regulations are met and to reinforce the OHRP directives prohibiting the designation of such use as a research activity.

Procedure for obtaining exemption from full IRB approval for Emergency Use of a test article is as follows:

1) Prior to administration of the test article, the investigator should notify the Chair and/or the IRB administrative office of the request for Emergency Use exemption and the intention to use an investigational test article.
2) Written request of an exemption from full IRB approval for Emergency Use of a test article must be provided to the IRB administrative office outlining the necessity for Emergency Use including:
   a) Subject’s name
   b) name and IND # of test article
   c) explanation of patient’s history and rationale for use of drug
3) Proposed informed consent document must be submitted to the IRB administrative office for review.

4) No review or action will occur on the Emergency Use request until the IRB has received the items requested in 2) and 3).

5) The Chair and IRB administrative office will review the request for exemption from approval for Emergency Use and the informed consent document for acceptability.

6) If exemption from full board approval for an Emergency Use is granted, a memorandum documenting this action will be provided to the investigator. The investigator will also be required to sign this memorandum documenting that s/he has read and agrees to comply with the documentation and reporting requirements for Emergency Use of a test article.

The physician is required to notify the IRB administrative office within 5 days and again within 30 days of the date of approval for exemption from IRB approval. This notification must be a written report of the status of the emergency use including information on the administration of the test article.

Any adverse events associated with the Emergency Use of the test article must be reported to the IRB within five (5) days of their occurrence.

The Emergency Use exemption will be valid for a period of 30 days from the date of exemption. If the investigational test article is not administered within 30 days of the approval, the approval will be rescinded and any subsequent request for emergency use will need to be requested following the documented procedures of requesting an Emergency Use exemption from full board approval.

If the Chair or IRB administrative office can not be contacted in advance, the investigator may administer the drug as long as the criteria stipulating emergency use are met, informed consent is obtained from the subject, and the physician provides written notification to the IRB within (5) days of the test article administration.

Federal regulations allow the waiver of informed consent under certain circumstances (20 CFR 50.23 (a)). The criteria that must be met in order to waive informed consent are:

1) the subject is confronted by a life-threatening situation necessitating use of the investigational drug

2) informed consent cannot be obtained because of an inability to communicate with, or obtain legally effective consent from the subject

3) there is insufficient time to obtain consent from the subject’s legal representative

4) no alternative method of approved or generally recognized therapy is available that provides an equal or greater likelihood of saving the life of the subject

If there is insufficient time to obtain an independent physician’s determination that the above four conditions apply, and immediate use of the drug is required to preserve the patient’s life, the drug may be given to the patient. However, within five (5) working days of the administration of the
drug, an independent physician must submit in writing to the IRB a review and evaluation of the
decision to use the drug. An independent physician is a physician who is not otherwise
participating in the treatment of the patient.

These procedures apply only to clinical use of investigational drugs. Use of FDA-approved drugs
for an unlabeled use in a treatment setting is considered part of clinical judgment and is not
subject to regulation unless the investigator wishes to research an unlabeled use.
MEMORANDUM

DATE: <current date>

TO: name of doctor

FROM: L. Wayne Hess, M.D.
Chair
Institutional Review Board

RE: emergency protocol

The Chair of the Institutional Review Board has reviewed the information provided regarding this patient’s condition and has approved the consent form provided by the physician. An Emergency Use exemption from full board approval has been granted after a review of the situation and the informed consent document. This approval is valid only for this patient in this situation at this time.

A full report is due back to the IRB by calendar date 5 days hence and again by calendar date 30 days hence.

Failure to submit reports as requested constitutes a breach in IRB compliance.

PHYSICIAN ASSURANCE

I agree to accept responsibility for the scientific conduct of this project.

I agree to report back to the IRB by calendar date 5 days hence and by calendar date 30 days hence.

I agree to report any adverse events to the IRB within 5 days of their event.

Signed: ________________________________

Date: ________________________________
1.0 Purpose
To aid in assuring knowledge and compliance of all persons involved in any aspect of human subject research by documenting procedure for exempt review.

2.0 Scope
The SOP applies to all human subject research falling under the purview of the Health Sciences Institutional Review Board.

3.0 Definitions
None

4.0 Policy/Procedure
All applications submitted to the IRB administrative office will be reviewed at one of three levels: 1) Exempt, 2) Expedited, or 3) Full Board.
Prior to final approval being granted on any project, it must be determined that the Principal Investigator has completed the educational training requirement. If the requirement has been met, the project will proceed with notification of the action taken. If the requirement has not been met, the Principal Investigator will be notified of the requirement and means to meet the requirement. The project will not proceed be decided upon until training has been completed.

All studies or individuals from outside the University of Missouri-Columbia must have an advisor or collaborator from MU on the project.

**Exempt**

The exempt application will be submitted to the IRB administrative office for review. The Compliance Officer will review the application to determine if it meets the criteria set forth in 46.101(b). If the application meets the criteria for an exempted application, the Compliance Officer will sign the application in the appropriate place indicating approval. The original approved application will be returned to the Principal Investigator for inclusion into the study file. The project number, the title and the Principal Investigator’s name will be included in the information attachments to the agenda and minutes of the next board meeting.

If the application does not meet criteria for an exempted project, the Principal Investigator will be contacted that approval was not granted for the exemption of the project and will be requested to submit a full board/expedited application.

**Project Approval**

The Principal Investigator will be notified in writing (attachment 5) of the approval of the project.

**Case Report Exception**

Retrospective case reports of 3 or less individuals are not interpreted to meet the definition of research as this small number does not contribute to “generalizable knowledge”. Therefore, an exempt application request is not required to be submitted to the HS IRB Office unless identifiable information is being collected.

A completed Waiver of HIPAA Authorization form must be submitted to the HS IRB, regardless of number of subjects, prior to accessing medical information to complete the case report.

Any prospective case reports or case reports of more than 3 individuals must still be submitted to the HS IRB Office on an exempt application request. Also, the HS IRB Office should be contacted for additional guidance if there are any unique aspects to the case report or any questions as to whether an exempt request should be submitted.
Expirations

Effective Date: 10-2002
Original Approval Date: 10-2002
Revision Date: 6-28-04
8-01-04

Approved By: Niels Beck, PhD
Chair, Health Sciences IRB

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Purpose
Scope
Definitions
Policy/Procedure

1.0 Purpose

To aid in assuring knowledge and compliance of all persons involved in any aspect of human subject research by documenting the necessary elements of the expiration dates on consent forms for the Health Sciences IRB.

2.0 Scope

The SOP applies to all human subject research falling under the purview of the Health Sciences Institutional Review Board.

3.0 Definitions

Expiration date: The date at which the approval period for the project ends. (See CRR SOP for detailed information on how to determine the expiration date).

4.0 Policy/Procedure

In order to comply with OHRP’s recommendations in their common findings of July 10, 2003 (http://www.hhs.gov/ohrp/compliance/findings.pdf), the HS IRB requires that each written informed consent document contain both the approval and expiration dates of a study. Copies of these dated documents must be used in obtaining informed consent. The expiration date on the informed consent documents are taken from the original or continuing review expiration of a study.
It is the primary investigator’s responsibility to ensure that the latest approved consent, with a valid expiration date, be used for each study subject. Using a consent form which has passed the expiration date, or which is not the latest approved version, constitutes a protocol deviation and should be reported to the HS IRB using the deviation form on the eIRB website.

The expiration date on the informed consent document does not mean that a subject’s consent to participate in a study expires once the expiration date has passed. Rather, this procedure helps ensure that only the current, IRB approved informed consent documents are presented to subjects and serves as a reminder to the investigators of the need for continuing review. If a subject’s consent was obtained on an approved IRB consent form, with a valid expiration date, then that consent is valid. Subjects do not need to be consented every year on a new consent form with a new expiration date.

In certain circumstances, an amendment, protocol deviation, or adverse event may necessitate a change to the informed consent document. These changes may change the risk:benefit ratio and/or may constitute new findings regarding the study. Per 45 CFR 46.116(b)(5), subjects should be informed of these new findings, and hence, may need to be consented on the revised consent forms.

A ‘clean’ copy (without IRB approval signature and dates) of each approved consent form must be submitted with the continuing review report (CRR). This is to ensure that the latest approved consent is reviewed with the CRR and that the consent form(s) receive the new expiration date (as determined by the CRR review). The new expiration date is calculated from the last approval date plus 12 months (or other time frame as specified by the Board) (see CRR SOP for more details).
Health Insurance Portability and Accountability Act (HIPAA) Research Policy

Effective Date: April 14, 2003
Original Approval Date: April 14, 2003
Revised Date: January 20, 2005
December 9, 2005

Approved By: Niels Beck, PhD
Chair, Health Sciences IRB

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   - Notice of Privacy Practices
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1.0 Purpose

To clearly define the circumstances under which protected health information (PHI) may or may not be either used internally or externally disclosed in connection with research.

2.0 Scope

This policy covers all PHI, which is used or disclosed, which is or may be created, through and/or during research activities. This policy applies to all faculty, staff (including student employees),
students, residents, post-doctoral fellows, and non-employees (including visiting faculty, courtesy, affiliate and adjunct faculty, industrial personnel, fellows, etc.) who conduct research, assist in the performance of research, or otherwise use or disclose PHI in connection with research activities at the University of Missouri- Columbia. This policy applies to the following covered components, the employees within them, and anyone receiving PHI from one of these entities:

Health Sciences Center
   Children’s Hospital
   Ellis Fischel Cancer Center
   Howard A. Rusk Rehabilitation Center
   Missouri Rehabilitation Center
   University Hospitals and Clinics
   University Physicians

Columbia Regional Hospital
School of Medicine
School of Health Professions
Charles and Josie Smith Sinclair School of Nursing
Missouri Institute of Mental Health
Student Health Center
Psychological Science
Education & Counseling Psychology

3.0 Definitions

Business Associate Agreement: An agreement between an entity or person who performs a function involving the use or disclosure of Protected Health Information (PHI) on behalf of a covered entity or provides certain specified services where the provision of the service involves the disclosure of PHI for a covered entity.

Disclosure: The release, transfer, provision of, access to, or divulging in any other manner of information outside the entity holding the information.

Health Information: Any information whether oral or recorded in any form or medium that (1) is created or received by a health care provider, health plan, public health authority, employer, life insurer, school or university, or health care clearinghouse; and (2) relates to the past, present, or future physical or mental health or condition of an individual; the provision of health care to an individual; or the past, present or future payment for the provision of health care to an individual.

Individually Identifiable Health Information (IIHI): Is information that is a subset of health information (as defined above), including demographic information collected from an individual that identifies the individual or with respect to which there is a reasonable basis to believe the information can be used to identify the individual.

Protected Health Information (PHI): Individually identifiable health information that is (1) transmitted by electronic media; (2) maintained in electronic media; or (3) transmitted or maintained in any other form or medium. There are several exclusions to PHI such as employment or school records.

Use: With respect to individually identifiable health information, the sharing, employment,
application, utilization, examination, or analysis of such information within an entity that maintains such information.

4.0 Policy/Procedure

General Information
The Health Sciences IRB is the designated Privacy Board for research at the University of Missouri-Columbia. As such, the Health Sciences IRB is committed to conducting research in compliance with all applicable laws, regulations, and University of Missouri policies. The Health Sciences IRB will apply the ‘minimum necessary’ standard of the HIPAA regulations to all research, taking into account any allowable exclusions. The ‘minimum necessary’ standard states, “a covered entity must make reasonable efforts to limit protected health information to the minimum necessary to accomplish the intended purpose of the use, disclosure, or request.”

Research Use or Disclosure of PHI With Authorization

1. As a general rule, a researcher must obtain an Authorization from all participants in research prior to the internal use or external disclosure of PHI for any research related purpose that is not otherwise permitted or required under this policy.

2. The researcher must complete the Authorization Form and submit it to the IRB.

See Authorization Form and Guidance
http://www.research.missouri.edu/assets/forms/HIPAA_Authorization.pdf

3. An authorization must be in plain language and must contain all of the following elements:
   a. A specific and meaningful description of the information to be used or disclosed;
   b. The name or identification of the persons or class of persons authorized to make disclosures of PHI and to use PHI for research related purposes;
   c. The name or identification of the persons or class of persons authorized to receive disclosures of the PHI and to use the PHI for research related purposes;
   d. A description of each purpose of the use or disclosure;
   e. An expiration date or event, or a statement ‘end of research study’ or ‘none’ when appropriate;
   f. The individual’s signature (or that of his/her authorized representative as determined by Missouri Law) and date;
   g. A statement that the individual may revoke the authorization if done in writing to the principal investigator; however, the researcher may continue to use and disclose, for research integrity and reporting purposes, any PHI collected from the individual pursuant to such Authorization before it was revoked;
   h. A statement that an individual’s clinical treatment may not be conditioned upon whether or not the individual signs the research Authorization. However, participation in research may be conditioned on a signed Authorization;
   i. A statement that information disclosed under the Authorization could potentially be redisclosed by the recipient and would no longer be protected under HIPAA;
   j. The individual must be provided with a copy of the signed Authorization.

4. Signing an Authorization
   a. Adults
i. A competent individual, 18 years of age or older, should always sign the authorization to use or disclose his/her PHI.

ii. If the individual is competent but unable to sign the authorization, the person witnessing the form may write in “Patient unable to sign due to __________. Patient gave verbal permission.” The authorization must be witnessed.

iii. If the patient is not conscious, coherent, or not competent for whatever reason, a legally recognized proxy must sign the Authorization. Missouri law recognizes the following order of individuals capable to serve as proxies for incompetent individuals being treated by MU Healthcare:
   - The consent of a legal guardian, attorney in fact, or a family member in the following order of priority:
     - Spouse
     - Adult son or daughter
     - Either parent
     - Adult sibling
     - Adult relative by blood or marriage.

Waiver of Authorization by the IRB

1. In some circumstances, Research Authorizations, otherwise required under this policy, may be waived or altered by the IRB provided the following criteria are satisfied and documented:
   a. The use or disclosure of PHI involves no more than a minimal risk to the privacy of individuals, based on the presence of at least the following elements:
      i. An adequate plan to protect the identifiers from improper use and disclosure;
      ii. An adequate plan to destroy the identifiers at the earliest opportunity consistent with the conduct of research, unless there is a health or research justification for retaining the identifiers or such retention is otherwise required by law and;
      iii. Adequate written assurances that the protected health information will not be reused or disclosed to any other person or entity, except as required by law, for authorized oversight of the research project, or for other research for which the use or disclosure of PHI would be permitted by this Policy.
   b. The research could not practicably be conducted without the waiver; and
   c. The research could not practicably be conducted without access to and use of the PHI.

2. A request for Waiver of Authorization must be completed by the researcher and submitted to the IRB for prior review and approval.

3. The IRB will maintain the following documentation about the waiver;
   a. A statement identifying the IRB and the date on which the waiver request was approved (see approval stamp below);
b. A statement that the IRB determined that the waiver satisfied the criteria for waiver;
c. A statement that the waiver has been reviewed and approved under either normal or expedited review procedures; and
d. The documentation is signed by the IRB chair or his/her designee.

See Waiver of Authorization Guidance and Form

Use and Disclosure of PHI Without Authorization Preparatory to Research

1. Physicians, and other healthcare providers, may contact their own patients for purposes of recruiting them to participate in a research study without an Authorization.
2. Individuals responding to an advertisement regarding participation in a research study may be given an explanation of the study prior to obtaining an Authorization.
3. An investigator (employed by MU healthcare) may use and disclose PHI without authorization ‘preparatory to research’ to identify potentially qualifying subjects. Any contact with subjects must be through their own treatment provider and authorization obtained from the investigator prior to obtaining PHI from the subject.
4. An Authorization must be obtained from an individual who has indicated interest in participating in a study prior to asking the individual any screening questions that involve PHI.
5. Researchers may use or disclose PHI without an Authorization or IRB waiver of Authorization for the development of a research protocol, provided that the researcher documents that all the following criteria are satisfied:
   a. The use or disclosure of PHI is solely to prepare a research protocol, or to identify prospective research participants for purposes of seeking an Authorization;
   b. The researcher shall not record or remove the PHI from the covered entity (MU Healthcare); and
   c. The PHI sought is necessary for the purpose of the research.

See Review Preparatory to Research Form and Guidance
http://www.research.missouri.edu/assets/forms/Preparatory_to_Research_Guidance.pdf
http://www.research.missouri.edu/assets/forms/Preparatory_to_Research_Assurance.pdf

Use and Disclosure of Decedent’s PHI Without Authorization

1. Researchers may use and disclose a decedent’s PHI for research without an Authorization or IRB waiver, provided the researcher documents that all the following criteria are satisfied:
   a. The use will be solely for research on the PHI of a decedent;
   b. The researcher has documentation of the death of the individual about whom information is being sought; and
   c. The PHI sought is necessary for the purpose of the research.
2. The researcher will provide documentation to the IRB Office that all the above criteria are met.

See Use and Disclosure of Decedent’s Information
http://www.research.missouri.edu/assets/forms/Research_on_Decedents.pdf
Use or Disclosure of De-Identified Health Information

1. De-Identified health information is exempt from HIPAA and may be used or disclosed for research purposes without Authorization or IRB waiver.

2. Researchers must provide documentation to the IRB Office that the health information has been de-identified by one of the following two methods:

   a. **Statistical Method:** The IRB may determine that health information is de-identified for purposes of this policy if an independent, qualified statistician:

      i. Determines that the risk of re-identification of the data, alone or in combination with other data, is very small;
      ii. Documents the methods and results by which the health information is de-identified, and the expert makes his/her determination of risk. **THE EXPERT MAY NOT BE THE RESEARCHER OR ANYONE DIRECTLY INVOLVED IN THE RESEARCH STUDY.**

   b. **Removal of All Identifiers:** Identifiers concerning the individual, the individual’s employer, relatives, and household members that must be removed include:

<table>
<thead>
<tr>
<th>Name</th>
<th>Social Security number</th>
<th>Account numbers</th>
</tr>
</thead>
<tbody>
<tr>
<td>Geographic information smaller than state</td>
<td>Electronic mail address</td>
<td>Certificate or license numbers</td>
</tr>
<tr>
<td>Elements of dates including birth date, admission date, date of death, and all ages &gt;89 years of age</td>
<td>Fax numbers</td>
<td>Vehicle identifiers and serial numbers including license plate</td>
</tr>
<tr>
<td>Telephone numbers</td>
<td>Health plan beneficiary number</td>
<td>Device identifiers and serial numbers</td>
</tr>
<tr>
<td>Medical Record number</td>
<td>Full face photographic images and comparable images</td>
<td>Web Universal Resource Locators (URL’s)</td>
</tr>
<tr>
<td>Internet Protocol (IP) address numbers</td>
<td>Biometric identifiers, including finger and voice prints</td>
<td>Any other unique identifying number, characteristic, or code</td>
</tr>
</tbody>
</table>

3. Re-Identification: The de-identified information may be assigned a code that can be affixed to the research record that will permit the information to be re-identified if necessary, PROVIDED that, the key to such a code is NOT accessible to the researcher requesting to use or disclose the de-identified health information.

   See De-Identification Form
   [http://www.research.missouri.edu/assets/forms/De-Identification.pdf](http://www.research.missouri.edu/assets/forms/De-Identification.pdf)

Limited Data Set

1. A researcher may use a Limited Data Set for any research purpose without an Authorization or Waiver of Authorization.

2. A Limited Data Set is defined as PHI that may include any of the following direct identifiers:
   a. Town, city, State, and zip code;
   b. All elements of dates directly related to an individual, including birth date, admission date, discharge date, and date of death.
3. A Limited Data Set must exclude all of the direct identifiers listed above except those allowed in #2 of this section, related to the individual, the individual’s employer, relatives or household members of the individual.

4. A Limited Data Set may be used or disclosed only if there is a Data Use Agreement between the University and the recipient of the limited data set.

See Data Use Agreement, External, Internal
http://www.research.missouri.edu/assets/forms/Data_Use_Agreement.pdf

Accounting of Disclosures
1. As a general rule, an individual has the right to an accounting of all disclosures of his/her PHI for research purposes, unless such disclosure was made pursuant to an Authorization, or is part of a Limited Data Set.
2. Records of disclosures of PHI must be kept in the following circumstances:
   a. Disclosures pursuant to an IRB waiver.
   b. Disclosures of PHI used in preparation of a research protocol.
   c. Disclosures of a decedent’s PHI used for research.
3. A simplified accounting procedure may be used if the research use or disclosure involves the PHI of more than 50 people. Under the simplified procedure:
   a. The individual must be provided a list of research protocols in which the individual’s PHI may have been used.
   b. The list must provide the following:
      i. The name of the protocol or other research activity;
      ii. A description of the purpose of the study and the type of PHI disclosed; and
      iii. The timeframe during which such disclosures occurred.
   c. The Privacy Officer will be notified and may assist the individual in contacting those researchers to whom it is likely that the individual’s PHI was actually disclosed.

Notice of Privacy Practices
1. A notice of Privacy Practices must be provided to a research participant when an Authorization is signed. These may be obtained through docushare https://docs.hsc.missouri.edu or on the MU Healthcare website.

See Notice of Privacy Practices
https://docs.hsc.missouri.edu/dscgi/ds.py/Get/File-2590/Notice_of_Privacy_Practices.doc

Business Associate Agreement (BAA)
1. A Business Associate is an entity or person who performs a function involving the use or disclosure of PHI on behalf of a covered entity such as claims processing, data analysis, case management, utilization review, quality assurance, billing, benefit management, practice management, or repricing.
2. A Business Associate may also provide certain specified services where the service involves the disclosure of PHI for a covered entity, such as legal, actuarial, accounting, consulting, data aggregation, management, administrative, accreditation, or financial services.
3. In some cases a covered entity may serve as a Business Associate of another covered entity.
4. For review of BAA, contact the University of Missouri Business Office, Lisa Wimmenauer, 882-4097, 319 Jesse Hall.
5. The terms of a BAA cover the obligations and Activities of Business Associate, Permitted Uses and Disclosures by Business Associate, Term and Termination, Effect of Termination and
other miscellaneous issues.
Humanitarian Use Device

Effective Date: April 19, 2002
Original Approval Date: April 19, 2002
Review Date: October, 2005

Approved By: Niels Beck, PhD
Chair, Health Sciences IRB

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  - Informed Consent

1.0 Purpose
To aid in assuring knowledge and compliance of all persons involved in any aspect of human subject research by documenting the policy for Board education.

2.0 Scope
The SOP applies to all human subject research falling under the purview of the Health Sciences Institutional Review Board.

3.0 Definitions
Definition/Background of a Humanitarian Use Device: A Humanitarian Use Device (HUD) is a device that is intended to benefit patients in the treatment and diagnosis of diseases or conditions that affect or are manifested in fewer than 4,000 individuals in the United States per year. A device manufacturer's research and development costs could exceed its market returns for diseases or conditions affecting small patient populations. Therefore, the Food and Drug Administration (FDA) developed and published the HUD regulation to provide an incentive for the development of devices for use in the treatment or diagnosis of diseases affecting these populations.

The FDA makes the determination that the disease or condition affects or is manifested in fewer than 4,000 individuals in the United States per year at the time of the request for HUD designation.
On June 26, 1996, FDA issued a final rule to carry out provisions of the Safe Medical Devices Act of 1990 regarding Humanitarian Use Devices (HUDs). This regulation became effective on October 24, 1996.

4.0 Policy/Procedure

IRB review and approval
The statute and the implementing regulation [21 CFR 814.124(a)] require IRB review and approval before a HUD is used. There is an exception to this rule for emergency situations in which the physician determines that approval cannot be obtained in time to prevent serious harm or death to the patient. IRBs are responsible for initial as well as continuing review of the HUD. For initial review of the HUD, IRBs are required to perform a full board review. In order to accomplish this, the principal investigator must submit the following:

1. A full IRB application, or
2. A letter or documentation from the sponsor that documents the following 10 items:
   • The generic and trade name of the device
   • The FDA HDE number (this is a 6 digit number preceded by the letter H)
   • The date of HUD designation
   • Indications for use of the device
   • A description of a device
   • Contradictions, warnings, and precautions for use of the device
   • Adverse effects of the device on health
   • Alternative practices and procedures
   • Marketing history
   • Summary of studies using the device

Please note that the HDE application contains the above listed sections and it is routine for the sponsor of a HUD to send a document with this information to IRBs.

Additional information required for submission:

1. Any other documents and/or information about the device.
2. Device labeling developed for patient use, if available.

The HUD application will be reviewed and approved by the convened IRB and processed as any new project. The application will be assigned a primary and lay reviewer and will be discussed at a convened IRB meeting.

The IRB does not need to review and approve individual uses of a HUD. As long as the use of the HUD is within the FDA approved indication, the IRB may approve use of the device without any further restrictions, use of the device under a protocol, or use of the device on a case-by-case basis. In reviewing use of the HUD, IRBs should be cognizant that the use of the device should not exceed the scope of the FDA approved indication.
Although the use of HUDs has to be approved by IRB, there is usually no protocol, since the use is not considered a research project; there are no reporting guidelines provided; it is up to the IRB to decide whether to require a consent form and whether continuing review should be carried out by the full board or under expedited review. It is also up the IRB to decide about reporting requirements.

**Informed consent**

The Federal Food, Drug, and Cosmetic Act (the Act) and the Humanitarian Device Exemption (HDE) regulation do not require informed consent because an HDE provides for marketing approval, and so use of the HUD does not constitute research or an investigation which would normally require informed consent. Although neither the Act nor the regulation requires informed consent, decision is left to the discretion of the IRB and it is highly recommended. The HS IRB office recommends that a consent document is submitted at the time of HUD submission in case during the review process the IRB requires consent.

Most HDE holders, have developed patient labeling that incorporates information to assist a patient in making an informed decision about the use of the device. That is, the patient labeling contains a discussion of the potential risks and benefits of the device, as well as any procedures associated with the use of the HUD. It also states that the device is a humanitarian use device for which effectiveness for the labeled indication has not been demonstrated. If the IRB does not require the consent, the labeling information should be used instead.

[Return to Table of Contents]
1.0 Purpose

To aid in assuring knowledge and compliance of all persons involved in any aspect of human subject research by documenting the necessary elements of the informed consent process for the Health Sciences IRB.

2.0 Scope

The SOP applies to all human subject research falling under the purview of the Health Sciences Institutional Review Board.
3.0 **Definitions**

**Assent:** A minor’s affirmative agreement to participate in research. Mere failure to object should not, absent affirmative agreement, be construed as assent.

**Guardian:** Individual who is authorized under applicable state or local law to consent on behalf of a child to general medical care.

**Informed Consent:** An ongoing process whereby a subject voluntarily agrees, based upon adequate knowledge and understanding of relevant information, to participate in research or to undergo a diagnostic, therapeutic, or preventive procedure. The subject must not feel coerced or perceive undue influence that results in the agreement to participate. In giving informed consent, subjects may not waive or appear to waive any of their legal rights, or release or appear to release the investigator, the sponsor, the institution or agents from liability for negligence.

**Legally Authorized Representative (LAR):** Individual or judicial or other body authorized under applicable law to consent on behalf of a prospective subject to the subject’s participation in the procedure(s) involved in the research. For research conducted by University of Missouri Healthcare, Missouri state statute (MO revised statute 431.064) allows as legally authorized representative;
1. Legal guardian
2. Attorney in fact (person appointed by durable power of attorney
3. Family member in the following order of priority
   a. Spouse (unless the patient has no spouse, or is separated, or the spouse is physically or mentally incapable of giving consent, or the spouse’s whereabouts is unknown or the spouse is overseas
   b. Adult child
   c. Parent
   d. Brother or sister
   e. Relative by blood or marriage

**Minimal risk:** Probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests.

**Minor:** Persons who have not attained the legal age for consent to treatments or procedures involved in the research under the applicable law of the jurisdiction in which the research will be conducted.

**Parent:** Minor’s biological or adoptive parent.

**Qualified study personnel:** Research team members who have undergone the required HS IRB educational and HIPAA training and are knowledgeable and involved in the conduct of the study on which they are listed as part of the study staff.

**Witness:** Impartial 3rd party to observe the consent process whose role it is to ensure that the information presented orally to the participant is the same as that presented in the written document, to ensure no coercion has occurred and/or ensure that in the event the participant cannot personally sign the consent, they witnessed affirmation on the part of the participant.
4.0 Policy/Procedure

The HS IRB is charged with adequately safeguarding all human subjects involved in research. The informed consent process assures that prospective human subjects receive the information necessary to help them understand the nature of the research so they can knowledgeably and voluntarily decide whether or not to participate. As needed, the IRB office works with the Office of Sponsored Programs to clarify language in the consent such as publication, dissemination of information and participant language.

Board Review

The Board is charged with the review and approval of the consent procedure to be used. The Board must review and document approval of the timing and place at which the consent process will occur. In addition to the language contained in the consent form, the consent procedure process may not lead to possible coercion of the potential participant. Coercive influences may include:

1) person obtaining consent
2) location of consent discussion
3) timing of consent discussion
4) interval allowed for review of consent and discussion
5) content language of consent discussion outside of consent document

Additionally, the Board must review and document approval that the consent contains all of the required elements or there is adequate justification for a waiver of the elements. The Board must also review the consent to determine and document that it is written in understandable language and format.

In addition to the review of the consent process, the Board must review the consent document, written summary and/or oral consent checklist to determine the appropriateness of the presented material. The Board may review the consent process and document at any time but must review the process and/or document at initial review, continuing review and at any time that an adverse event, amendment or other actions may have changed the risk/benefit ratio to necessitate revision of the consent procedure or document.

Any suggestions or revisions to the consent that are requested by the Board will be communicated by the Board to the IRB administrative office who will then forward the requests to the Principal Investigator.

The Board has the authority to request to be present and witness the consent process as performed with a potential participant at any time after indicating the desire to the Principal Investigator and study staff. Additionally the Board may delegate to the HS IRB Administrative office the authority to be present at an informed consent process discussion on the Board’s behalf.

Administrative Office Review

To assist the Board in their duties, the Administrative Office of the IRB will also review all consent documents to determine if they contain all of the required elements or include adequate justification for a waiver of the elements. The administrative office will also review the consent to determine that it is written in understandable language and format.

The Administrative Office will review all submitted consent forms, written summaries and/or oral consent checklists to determine if they are written in appropriate language and format and also to determine if they adhere to federal regulations regarding required content. The information in the consent form will be compared with information provided in the application and study protocol to determine if all information
necessary to enable the participant to make an informed decision about the study is being conveyed to the potential participant.

The Administrative Office will conduct this review of the consent at any time but must review the document at initial review, continuing review and at any time that an adverse event or amendment may have changed the risk/benefit ratio to necessitate revision of the consent procedure or document.

Any issues found during the administrative review of the consent will be forwarded to the IRB reviewer.

**Child Assent/Parent Consent**

Whenever minors are recruited as research subjects, the IRB must decide and document whether child assent is required for this project and determine that adequate provisions are made for soliciting the assent of the child when, in the judgment of the IRB, the children are capable of providing assent. The HS IRB has historically decided that the age at which a child will understand and be able to communicate assent by signature is the age of seven (7). However the HS IRB looks at each individual study and what is required of the child and also relies on the judgment of the investigator to determine the understanding and maturity level of the child in obtaining verbal assent.

Per §46.408, in determining whether children are capable of assenting, the IRB shall take into account the ages, maturity, and psychological state of the children involved. This judgment may be made for all children to be involved in research under a particular protocol, or for each child as the IRB deems appropriate. The IRB may waive the requirement for child assent if it deems the children’s capability is limited to the point they can not reasonably be consulted or that the intervention or procedure involved in the research holds out a prospect of direct benefit that it is important to the health or well-being of the children and is available only in the context of the research. Even when the IRB determines the participants are capable of assent, the IRB may still waive the assent requirements under the same circumstances as outlined for waiver or alteration of informed consent.

The IRB must also determine that adequate provisions are made to solicit the consent of the child’s parent(s) or guardian(s). There are four categories of research involving children. Each level has a parental/guardian signatory requirement.

If assent is required, the child must sign the consent form signifying understanding of the project and assent to participate in the research project. The IRB must also determine the child risk category of the proposed research which determines the parental signatory authority. The child category definitions and corresponding parental signatory requirements are as follows:

45 CFR 46.404 Research not involving greater than minimal risk - 1 parent  
45 CFR 46.405 Research involving greater than minimal risk but presenting the prospect of direct benefit to the individual subjects – 1 parent  
45 CFR 46.406 Research involving greater than minimal risk and no prospect of direct benefit to individual subjects, but likely to yield generalizable knowledge about the subject’s disorder or condition – 2 parent  
45 CFR 46.407 Research not otherwise approvable which presents an opportunity to understand, prevent, or alleviate a serious problem affecting the health or welfare of children – 2 parent  

For those category requiring consent of 2 parents, it is required unless one parent is not reasonably available, deceased, unknown, incompetent or when only one (1) parent has legal responsibility for the care and custody of the child.
Per §46.408(c), the IRB may waive the requirements for parental consent if a determination is made that a research protocol is designed for conditions or subject population for which parental/guardian permission is not a reasonable requirement to protect the subjects (i.e. neglected or abused children). This waiver is only allowed if consistent with all applicable federal, state and local laws. Additionally, an appropriate mechanism to protect the participating children must be substituted.

A plan should be outlined to reconsent individuals who turn 18 while participating in research. At that time, they must be afforded the opportunity to consider their continued participation and to provide or deny consent.

**Research Personnel Obtaining Consent**

University of Missouri HealthCare policy (1-A-00) requires physicians to obtain consent for any medical or surgical procedure. Consent for research participation should be no less stringent. Therefore, for any significant risk, medical treatment study which would require that consent was obtained by a licensed physician outside the scope of research, consent for participation in the research study must be obtained by a physician listed and active as part of the study personnel. The types of research falling into this category includes medical or surgical intervention and dispensation of investigational or prescription drugs.

For significant risk, non-medical treatment studies, consent may be obtained by the non-physician PI or other qualified, active member of the study personnel. For all other types of research, such as minimal risk studies, consent must be obtained by a qualified, active member of the study personnel. For all studies, the person obtaining consent must be qualified and knowledgeable about the study to be able to answer any and all questions asked by the potential participant.

For those studies requiring that consent be obtained by a physician, the **physician must at least** present an overview of the project and answer any questions that the potential participant may have before the consent is signed. A coordinator working with the physician on the study may also be involved in the consent process and perform the detailed explanation of the study to the participant.

**Under no circumstances should anyone who is not listed as study personnel and current with IRB training requirements obtain consent, interact with or access data of a potential study participant.**

**Passive Consent**

The Federal Regulations do not recognize passive consent as an allowable consent option. Therefore, passive consent is not a viable consent option and should be avoided. If a passive consent process is felt to be in the best interest of the potential participant, a detailed description of the passive consent process and justification for its use must be submitted to the HS IRB for review on a case by case basis.

**Telephone Consent**

Consent obtained over the telephone is allowable but only under certain conditions. There are two viable options for obtaining telephone consent:

1) If written consent is required by the IRB, the IRB must look at the request for telephone consent and determine if it would be allowable. As a general rule with telephone consent and written documentation, the consent document must be sent (certified mail or fax) to the potential participant and then the consent process is conducted over the telephone with both parties reviewing the written documentation. The consent signed by the participant or participant’s LAR must be received by the study before enrollment proceeds.
2) If waiver of documentation of consent is approved by the IRB, the information may be verbally presented to the potential participant over the telephone. Written documentation must still be entered in the records indicating the participant’s verbal consent to participate in the research. No witness is required for this process.

Faxed Consent

The use of a facsimile machine in obtaining written consent is allowable as long as it is used as a part of the complete consent process. The written consent document may be faxed to the potential participant for review. The participant must be contacted by telephone to allow the opportunity for questions. Once all information has been obtained to the satisfaction of the participant, the participant signed and dated consent form may be returned via fax.

Minors Consenting to Research

As stated previously, the regulations require legally effective informed consent be obtained prior to allowing an individual to participate in research. The General Counsel’s office of the University of Missouri has interpreted “legally effective” to predicate with the legal competency to enter into contracts. Under Missouri Statutes, competency to contract is bestowed at the age of majority, eighteen (18). Missouri law does not recognize “emancipated” minors because of estrangement, marriage or becoming a parent. Therefore a person under the age of 18 may not consent to participation in research for themselves or their child. University of Missouri Healthcare policy allows for a minor to consent to medical treatment or procedures for themselves or their child.

Consent by Legally Authorized Representative

When a person is incompetent to adequately understand the nature of the research and to provide full informed consent, the consent to participate in research may be obtained by a legally authorized representative for that person.

For research conducted within the University of Missouri Healthcare system or research conducted at an outside entity by a healthcare provider of the University of Missouri Healthcare system (referred to in the statute as medical teaching facility), consent may be obtained from either a court appointed legal guardian or, in the event no guardian has been appointed, by an attorney in fact or a family member in the priority order of spouse, adult child, parent, sibling or relative by blood or marriage.

Research conducted at entities not a part of the University of Missouri Healthcare system may obtain consent only from a court appointed legal guardian.

Witness to Consent

A witness to the consent process is only required under the International Code of Harmonization guidelines. However, if a potential participant is competent to understand the consent but is not able to read or sign his/her name, and independent witness must be present to view the consent process and obtaining of the consent. The witness must also sign the consent form as documentation of the witnessing.

Surrogate Consent

Occasional situations arise where an individual may be incapacitated at the time of consent and may not be able to consent for themselves. Examples of this type of situation might be research conducted in the ICU.
or research conducted in the ER. If the potential participant is temporarily incapacitated, consent for participation in research must be obtained from a legally authorized representative, either in person or by telephone consent. The incapacitated participant must be provided with information about the study and allowed to consent to continue participation in the study once they are able.

If time is not sufficient to obtain consent from a legal representative, research with FDA regulated articles may occur (cited under 45 CFR 50.23) if the following criteria are met:
1. the participant is confronted with a life-threatening situation necessitating the use of the test article.
2. informed consent cannot be obtained from the subject.
3. time is not sufficient to obtain informed consent from a legally authorized representative.
4. there is no approved or generally recognized therapy available that provides an equal or greater likelihood of having the life of the participant.

To proceed without consent, both the investigator and a physician not involved in the approved clinical investigation must certify in writing how the above four criteria are met prior to administration of the test article. If there is not sufficient time to consult with an independent physician before administration of the test article, the investigator must certify in writing how the four criteria are met followed by a written review and evaluation by an independent physician within 5 days of the administration of the test article.

All documentation as required above must be submitted to the IRB within 5 days of the administration of the test article.

This may only be used for research on research articles regulated by the FDA and is only an emergency exception to written informed consent to a project that has undergone review and the conduct of the study has been previously approved by the IRB with written consent. This procedure is not to be confused with the emergency use of a test article.

FDA regulations 45 CFR 50.24 set forth special procedures to be followed when it is known in advance that research will be conducted in an emergency situation with no possibility of participant consent or surrogate consent. To meet this exemption from consent in an emergency situation, there are several steps that must be followed including public informational meetings and dissemination in public forums such as newspapers, the intent to conduct this emergency research without consent.

**Determination of Competency to Consent**

When submitting a proposal to the HS IRB which includes incompetent individuals or when research is performed in a population where competency may be in question, the investigator must provide to the IRB a detailed plan to determine competency of the potential participant to offer valid informed consent or whether consent must be obtained from the participant’s legally authorized representative. If the risk of the research outweighs the potential benefit, consideration should be given to include a determination of competency from an uninvolved physician, counselor, etc.

**Consent within a Veteran’s Hospital Facility**

When research is to be conducted using hospital or clinic patients in the Harry S Truman Memorial Veteran’s Hospital, special consent procedures must be used. The consent document must be on the VA 10-1086 consent form. The standard HS IRB consent template may be used with revisions to sections “What are the Costs?”, “What if I am Injured?” and the “Patients Bill of Rights and signature” to include language required to be included in all VA consents. Additionally, all participant signatures on a VA consent are required to be witnessed by an uninvolved third party.
Special Consent Considerations of FDA Regulations

The FDA does not recognize waiver of documentation of consent or waiver of consent as viable consent options. Therefore for all research studies that would fall under compliance with FDA regulations 21 CFR 50, a written consent form with signatures must be used.

5.0 Related SOP

Informed Consent – Types and Elements
Hospital Policy I-A-1

6.0 Review Panel
INFORMED CONSENT – TYPES and ELEMENTS

Effective Date: December 12, 2005
Original Approval Date: December 12, 2005
Revision Date:

Approved By: Niels Beck, PhD
Chair, Health Sciences IRB

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1.0 Purpose

To aid in assuring knowledge and compliance of all persons involved in any aspect of human subject research by documenting the necessary elements of the informed consent process for the Health Sciences IRB.

2.0 Scope

The SOP applies to all human subject research falling under the purview of the Health Sciences Institutional Review Board.

3.0 Definitions

Assent: A minor’s affirmative agreement to participate in research. Mere failure to object should not, absent affirmative agreement, be construed as assent.
**Guardian:** Individual who is authorized under applicable state or local law to consent on behalf of a child to general medical care.

**Informed Consent:** An ongoing process whereby a subject voluntarily agrees, based upon adequate knowledge and understanding of relevant information, to participate in research or to undergo a diagnostic, therapeutic, or preventive procedure. The subject must not feel coerced or perceive undue influence that results in the agreement to participate. In giving informed consent, subjects may not waive or appear to waive any of their legal rights, or release or appear to release the investigator, the sponsor, the institution or agents from liability for negligence.

**Legally Authorized Representative (LAR):** Individual or judicial or other body authorized under applicable law to consent on behalf of a prospective subject to the subject’s participation in the procedure(s) involved in the research. For research conducted by University of Missouri Healthcare, Missouri state statute allows as legally authorized representative;

1. Legal guardian
2. Attorney in fact (person appointed by durable power of attorney
3. Family member in the following order of priority
   a. Spouse (unless the patient has no spouse, or is separated, or the spouse is physically or mentally incapable of giving consent, or the spouse’s whereabouts is unknown or the spouse is overseas
   b. Adult child
   c. Parent
   d. Brother or sister
   e. Relative by blood or marriage

**Minimal risk:** Probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests.

**Minor:** Persons who have not attained the legal age for consent to treatments or procedures involved in the research under the applicable law of the jurisdiction in which the research will be conducted. The age of majority in Missouri is 18 years of age.

**Parent:** Minor’s biological or adoptive parent.

**Witness:** Impartial 3rd party to observe the consent process whose role it is to ensure that the information presented orally to the participant is the same as that presented in the written document, to ensure no coercion has occurred and/or ensure that in the event the participant can not personally sign the consent, they witnessed affirmation on the part of the participant.

### 4.0 Policy/Procedure

The HS IRB is charged with adequately safeguarding all human subjects involved in research. The informed consent process is one way the HS IRB assures prospective human subjects receive the information necessary to help them understand the nature of the research so they can knowledgeably and voluntarily decide whether or not to participate.

Except in limited circumstances where a waiver of consent has been approved, any research involving human subjects that is under the jurisdiction of the University of Missouri-Columbia must educate and provide the subject with Informed Consent requirements pursuant to the federal regulations and guidelines embodied in the HS IRB SOPs, Federal Policy §46.116 and §46.117 and the checklist as provided below:
Informed consent is required to contain (§46.116):

1) a written statement (unless an oral statement approved by the IRB) in language understandable to the volunteer, that the study involves research, an explanation of the purposes of the research, and the expected duration of the subject’s participation;
2) identification of any procedures that are experimental;
3) description of any reasonable foreseeable risks or discomforts to the subject;
4) description of any benefits to the subject or to others which may reasonably be expected from the research;
5) disclosure of appropriate alternative procedures, or courses of treatment, if any, that might be advantageous to the subject;
6) statement describing the extent to which confidentiality of records identifying the subject will be maintained;
7) for research involving more than minimal risk, an explanation as to whether any compensation or any medical treatments are available, if injury occurs and, if so, what they consist of, or where further information may be obtained;
8) an explanation of whom to contact for answers to pertinent questions about the research;
9) an explanation of whom to contact for answers to pertinent questions about the research subjects’ rights;
10) an explanation of whom to contact in the event of a research-related injury to the subject;
11) a statement that participation is voluntary, refusal to participate will involve no penalty or loss of benefits to which the subject is otherwise entitled, and the subject may discontinue participation at any time without penalty or loss of benefits, to which the subject is otherwise entitled.

When appropriate, one or more of the following elements of information shall also be provided to each subject.

Additional Elements of Informed Consent (§46.117):

1) a statement that the particular treatment or procedure may involve risks to the subject (or to the embryo or fetus, if the subject is or may become pregnant), which are currently unforeseeable;
2) anticipated circumstances under which the subject’s participation may be terminated by the investigator without regard to the subject’s consent;
3) any additional costs to the subject that may result from participation in the research;
4) the consequences of a subject’s decision to withdraw from the research, and procedures for orderly termination of participation by the subject;
5) a statement that significant new findings developed during the course of the research, which may relate to the subject’s willingness to continue participation, will be provided to the subject;
6) the approximate number of subjects involved in the study;
7) incentives for participation in the study

The HS IRB has developed certain items that are felt to enhance the consent document. The following elements shall also be included in the consent document.
Additional HS IRB requested elements:

When appropriate, one or more of these required elements shall be included:

1) study title;
2) name of Principal Investigator;
3) statement that consent may contain language/information that may not be understandable to potential participant and encouragement to ask questions about information;
4) statement that written consent is necessary for participation, if applicable to consent type;
5) schema or timeline description of project events (optional);
6) explanation of randomization (if applicable)
7) statement of reproductive risks and contraception (if applicable)
8) explanation of mechanism or availability of mechanism to unblind study
9) contact information to discuss symptoms of possible side effects;
10) statement that improvement in condition is not guaranteed;
11) MU statement of liability;
12) VA statement of liability (if applicable because of inclusion of VA participants)
13) signature page

In certain instances, when it is appropriate to the project, and with proper explanation/justification from the investigator, the IRB may grant a waiver to inclusion of some of the required elements. This waiving of elements may be done if a certain element is not applicable to the project such as waiving the statement of alternative treatments if there is no alternative treatments or if the study is not a treatment study. The waiving of elements may also be done if it is documented that inclusion of an element may harm a potential subject rather than add to the benefit and explanation.

Consent Types

There are three types of consent processes that can be requested and/or granted by the HS IRB. They are:

1. **Written Consent**

Written consent process is the most common and preferred consent method. This is a written document that contains all of the elements (delineated previously) of the informed consent document and fully explains the project. A template incorporating all of the elements and providing suggested language has been developed by the HS IRB. The template can be accessed at [www.research.missouri.edu/hsirb/forms](http://www.research.missouri.edu/hsirb/forms). This document is presented in its written form to the potential subject or subject’s legally authorized representative (LAR) as part of the informed consent process interaction between the investigator and the potential participant. The signatory requirements for this document are Principal Investigator/study personnel obtaining the consent and the potential subject or LAR. A witness signature is not required on this document unless the potential subject or LAR is able to understand but is not able to read or sign their name to the document. The IRB does have the authority to require a witness if they feel the project warrants one.

2. **Waiver of documentation of informed consent**

Written documentation of informed consent may be waived by the IRB if either of the following apply:
a) the research presents no more than minimal risk of harm to subjects and involves
no procedures for which written consent is normally required outside of the
research context;
b) the informed consent is the only record linking the subject to the research and the
harm from the possible breach of confidentiality is the principal risk to the
subject

When the documentation of consent is waived by the IRB, the investigator or study
representative has to present the project and the elements of consent to the subject or
LAR and obtain a verbal consent to participate. No signatures are required to document
consent; however, if applicable, the investigator must document the consent and the
consent process with a note in either the research records or the subject’s medical record.
In cases in which the documentation of informed consent has been waived, the IRB
usually requires the investigator to provide the subjects with a written statement
containing the elements of consent which describes the research and subject rights.

The Principal Investigator has to provide to the IRB for review and approval the written
version of what will be presented orally to the subject or LAR or provided to them. In
cases in which the IRB requires the investigator to provide the subjects with a written
statement regarding research, such statement has to be submitted, reviewed and approved
by the IRB as well.

The HS IRB has developed a template incorporating the necessary information and
elements to be provided to the potential participant when using waiver of documentation
of consent. The template can be accessed at www.research.missouri.edu/hsirb/forms

The following Consent Checklist should be used to assure that all necessary aspects of
the project and elements of consent are presented to the subject or LAR:

1) statement that the study will involve research and investigational procedures;
2) statement that participation is voluntary and that refusal to take part will not
   involve any penalty or loss of benefits;
3) an explanation of the nature and purpose of the research;
4) information on how many people will participate in the study;
5) detailed information on what is involved in the study (procedures, tests, drugs,
   surveys, interviews, etc.) and the timeline of all study events;
6) information on the length of time participation in the study will last;
7) a statement that the investigator may withdraw the participant from the study at
   any time;
8) a statement that the participant may withdraw from the study at any time without
   losing any medical care and/or benefits;
9) detailed description of reasonably foreseeable risks and discomforts.
10) a description of potential benefits to the study participant and/or to others;
11) description of appropriate alternative procedures and courses of treatment, if any,
    that might be advantageous to the participant
12) statement describing the extent to which confidentiality of records identifying the
    participant will be maintained;
13) statement whether the participant will be charged for any tests, procedures,
    medications or devices used in the research;
14) description of compensation for participating in the study, if any;
15) information regarding compensation for any injury sustained while participating
    in the study;
16) statement regarding participant’s rights: reiteration that participation in the study is voluntary and that the participant may withdraw at any time;
17) detailed information who to contact with problems and questions;
18) an offer to answer questions

Some research falling into this category may not involve a face-to-face consent process, such as distribution and request for completion of a survey. In those instances, the waiver of documentation of consent script may be in the form of the letter or other type of applicable document. Also in those instances, consent to participate may be documented by receiving the completed survey instead of a verbal affirmation to participate.

3. Waiver of informed consent or request for alteration of the required elements

An IRB may waive informed consent provided the IRB finds the justification provided by the investigator meets all of the following criteria. Simply reciting the elements is not proper justification; it must be clearly explained how the criteria are met.

1) the research involves no more than minimal risk to the subjects;
2) the waiver or alteration will not adversely affect the rights and welfare of the subjects;
3) the research could not practicably be carried out without the waiver or alteration;
4) whenever appropriate, the subjects will be provided with additional pertinent information after participation

The IRB must fully document its findings for waiver or alteration of informed consent in the meeting minutes or on the review sheet for the project. Protocol specific information must be included which justifies the IRB finding.

The IRB may require the Principal Investigator to include whatever information it deems necessary to assure the safety and welfare of the human subject involved in research.

4. Other consent form options

The regulations allow for an additional type of consent process called the “short” form. This consent type has very limited utility as a viable consent process and its use should be discussed with the HS IRB on a case by case basis.

Informed Consent

A key element of the consent form process is the consent document. To this end, the consent form must be written in language and format and content to be easily understandable to the reader.

The consent form should

1) be targeted for comprehension at a 6th grade reading level
   a) use brief paragraphs
   b) use section headers to introduce topics
   c) use simple sentence structure
   d) use second person tense
   e) use a type size readable to a person who may have poor vision
f) limit use of complex terms or provide a parenthetical definition/description of the term

2) provide complete and adequate description of how each participant will be involved

3) contain all of the elements required by §46.116 and additionally contain any additional elements which the Board deems necessary and any of the preferred elements required by the Board

4) not include language that may be coercive
   a) not make the subject waive or appear to waive any of their legal rights or release or appear to release the investigator, the sponsor, the institution or agents from liability or negligence.
   b) limit use of complex terms or provide a parenthetical definition/description of the term

5) provide complete and adequate description of how each participant will be involved

6) contain all of the elements required by §46.116 and additionally contain any additional elements which the Board deems necessary and any of the preferred elements required by the Board

7) not include language that may be coercive

8) not make the subject waive or appear to waive any of their legal rights or release or appear to release the investigator, the sponsor, the institution or agents from liability or negligence.

5.0 Related SOP
   Informed Consent – Process and Issues

6.0 Review Panel
Initial Review

Effective Date: September 1, 2004
Original Approval Date: September 1, 2004
Revision Date: December 9, 2005

Approved By: Niels Beck, PhD
Chair, Health Sciences IRB

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1.0 Purpose

To aid in assuring knowledge and compliance of all persons involved in any aspect of human subject research by documenting the procedure for review of new applications for the Health Sciences IRB.

2.0 Scope

The SOP applies to all human subject research falling under the purview of the Health Sciences Institutional Review Board.
3.0 Definitions

Compensation – Any payment to a study participant which may be in the form of cash, credit, voucher, or gift. Alternative forms of compensation can include items such as free medical care, extra vacation time, and academic rewards (in the form of a grade or a letter of recommendation).

Investigational Product - A pharmaceutical form of an active ingredient or placebo being tested or used as a reference in a clinical trial, including a product with a marketing authorization when used or assembled (formulated or packaged) in a way different from the approved form, or when used for an unapproved indication, or when used to gain further information about an approved use.

Key Personnel – All persons who will be obtaining consent, acquiring data, performing data analysis, generating a final report, or other duties related to the study must be listed as study personnel and have the appropriate training that is up-to-date.

Research - A systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge.

4.0 Policy/Procedure

General Information
In conducting the initial review of proposed research, IRBs must obtain information in sufficient detail to make the determinations required in 45 CFR 46.111. IRBs must determine that:

(1) Risks to subjects are minimized: (i) by using procedures which are consistent with sound research design and which do not unnecessarily expose subjects to risk, and (ii) whenever appropriate, by using procedures already being performed on the subjects for diagnostic or treatment purposes.

(2) Risks to subjects are reasonable in relation to anticipated benefits, if any, to subjects, and the importance of the knowledge that may reasonably be expected to result.

(3) Selection of subjects is equitable.

(4) Informed consent will be sought from each prospective subject or the subject's legally authorized representative, in accordance with, and to the extent required by 45CFR46.116.

(5) Informed consent will be appropriately documented, in accordance with, and to the extent required by 45CFR46.117.

(6) When appropriate, the research plan makes adequate provision for monitoring the data collected to ensure the safety of subjects.

(7) When appropriate, there are adequate provisions to protect the privacy of subjects and to maintain the confidentiality of data.

Submission Requirements
Materials required to assist the IRB in its review of proposed research should include the required number of copies (three) of the relevant information, including:

- Application form (submitted electronically through the eIRB)
• Signature page
• Protocol
• Proposed informed consent document (this should include one or more of the following: Written Consent Form Documentation, Verbal Script, Written Request for Other Types of Consent)
• Any relevant grant application(s) – accepted in lieu of protocol in most cases
• HIPAA Documentation
• Letters of permission or support from other participating institutions
• Clinical Investigator’s Drug Brochure
• Any recruitment materials, including advertisements intended to be seen or heard by potential subjects
• Questionnaires, handouts, or any other applicable instruments
• HHS-approved consent and protocol (for multi-centered trials)
• Vulnerable population worksheets

IRB Administrative Review
All applications submitted to the IRB office will be reviewed in the order they are received. The IRB administrative office staff will conduct a preliminary review of the submission materials to determine the completeness of the packet; to determine if, in their opinion, the project may qualify for expedited or full-board review; and to request clarification and/or additional materials so as to provide the reviewer with a complete application that meets all regulations and university policies.

Any incomplete submissions will be left in pending status until all required materials are received. The PI or designated contact person will be notified via e-mail that the packet is incomplete and a list of the materials necessary to complete the packet. A project that is incomplete will not be forwarded for review by the IRB until all the necessary elements and clarifications have been received.

Expedited Review
The expedited review process is conducted by a single IRB board member. The HS IRB office will select a primary reviewer based on their area of expertise in relation to the proposed research project. A copy of the complete submission packet is sent to the selected reviewer, along with any additional clarifications. The primary reviewer will conduct an in-depth review of all pertinent documentation (see submission requirements above) to ensure compliance with the applicable regulations permitting expedited review (45 CFR 46.110).

The primary reviewer generally reviews requests for expedited review within two weeks of receipt of the materials, and will return the review recommendation to the IRB administrative office for final processing. If the primary reviewer requests any revisions or modifications, the HS IRB office will notify the investigator of the revisions. Please see the section below on “Revisions and Modifications.”

The primary reviewer always has the option to request the project be reviewed by another reviewer or the full board if the reviewer 1) feels the project does not meet the requirements for expedited review, or 2) is more comfortable having the project reviewed by the full board even if the study meets the expedited review criteria.

The ‘expedited reviewer sheet’ documents the specific permissible expedited category, a description of the review, a description of the action taken by the reviewer, and any additional findings required under the HHS regulations.
For studies approved via expedited review the project number, title and principal investigator’s name will be included in the attachments to the agenda and minutes of the next board meeting.

**Full Board Review**

Once each submission packet is finished with IRB administrative review, it will be assigned to a specific board meeting based on the date of submission of the materials. Typically, most applications are reviewed by the IRB within approximately one month of receipt. Projects which are submitted between the 5th and 19th of the month will be reviewed at the next mid-month IRB meeting. Projects submitted between the 20th and the 4th will be reviewed at the next end-month IRB meeting. If a project requires extensive follow-up and/or clarifications by the IRB office, it will be held over until the next available agenda after all clarifications have been received.

The applications for full-board review are conducted using a primary reviewer system of review. Both a primary and lay reviewer are assigned to studies reviewed by the full board. A copy of the complete submission packet (see submission requirements above) is sent to the primary reviewer, along with any additional clarifications. The primary reviewer will conduct an in-depth review of all pertinent documentation to ensure compliance with the applicable regulations. The lay reviewer receives a copy of the completed application, any clarifications, proposed consent documents, and any materials to be seen or heard by the subjects (such as advertisements/recruitment materials, surveys, etc.). All other Board members will receive copies of the completed application, proposed consent form and any materials which will be seen or heard by the subjects (such as advertisement/recruitment materials, surveys, etc.). The lay member will present any concerns or questions noted from their review of the consent document or other materials. Also, any board member may indicate for discussion any issues they found during their review of the application or proposed consent. Once all discussion has ceased on a project, a vote on the motion on the table will be taken.

The following items will be included in the recommended action motion:

- Approval, approval with documented modifications, disapproval, or defer
- Level of risk - minimal risk or significant risk
- Type of consent - written consent, waiver of consent, or waiver of documentation of informed consent
- Parental consent and minor assent, if applicable
- Child risk category, if applicable
- Continuing review interval

All motions, discussions and actions taking place during the convened Board meeting will be documented in the written minutes of the meeting.

**Revisions and Modifications**

Many times the IRB will request clarifications or revisions to projects. Any member may request changes to any project materials during the review of a study. For expedited studies, members may request to review the study and its changes when they are notified of the expedited study through the attachments to the agenda.

If the request for modifications are of such magnitude that they are directly relevant to the determinations by the IRB under 45 CFR 46.111, the project and clarifications will be requested by the IRB office and the project will be re-reviewed by the primary reviewer (for expedited

If the requests for clarifications are specifically documented for each project or revisions that are minor (such as documented changes to the consent document) and requires simple concurrence by the investigator, then the IRB administrative office may request and review those additions when they are received without the project being re-reviewed by the primary reviewer (if
reviewed by expedited review) or reviewed at the next convened board meeting. The clarifications are subsequently reviewed and approved by the IRB chair or another designee under an expedited review procedure.

If, however, the investigator makes additional changes other than what the IRB specifically requested, or for some reason (i.e. sponsor insistence) the investigator did not make certain revisions, justification must be provided to the IRB and the revisions must be reviewed by the primary reviewer (if reviewed by expedited review) or by the full board.

Additional Review Requirements
Several other reviews are necessary for studies involving prisoners, devices, drugs, accounting, conflict of interest, veterans, and radiation or biosafety. Several questions within the application itself serve as a guide to the IRB office in determining whether additional reviews are needed. Most of the additional reviews will be required prior to final IRB approval being granted. In many cases, the reviews take place prior to the study being reviewed by the full board; however, some reviews may take place after the IRB has conducted their review. Rarely is it necessary to prolong an approval for a study due to an additional review, however, it can occur. Documentation of each additional review will be entered into the eIRB database. Please review the individual SOPs for each type of review for additional information or requirements.

1. If the project includes prisoners as subjects, a copy of the complete submission packet (see submission requirements above) will be sent to the designated prisoner reviewer. Additionally, the project will be scheduled for review at the board that the prisoner reviewer is a primary member. Depending on the funding source and type of research proposed, the Office for Human Research Protection (OHRP) may need notification, review, and approval before prisoner research can begin.

2. Devices - If the project includes the use of an experimental device, a copy of the application, the protocol and the device information will be sent to the designated device consultant prior to review by the full board (per 45 CFR 46.107(f)). The device review and recommendation will be sent to the assigned reviewer as part of the review packet and is required prior to IRB approval being granted.

3. Radiation or Biosafety - If the project includes radiation safety or biosafety, a copy of the application, consent, and the protocol will be sent to the radiation or biosafety office prior to review by the full board. The review and recommendation will be sent to the assigned reviewer as part of the review packet and is required prior to IRB approval being granted. Depending on the level of research, it is possible that radiation safety or biosafety may require additional reviews by their respective boards. If further review is needed, IRB approval may be delayed until approval from radiation or biosafety is received.

4. Investigational Drug Services (IDS) – If the project includes the use of medication(s), the IRB office will forward a report to the Investigational Drug Pharmacist. Trials involving the dispensing of investigational medications must be reviewed and approved by the IDS before they may be granted IRB approval. All trials must receive IRB approval prior to Pharmacy's dispensing any medications pursuant to that protocol. Pharmacy (IDS) controls the storage, dispensing, labeling, and distribution of investigational medications.

5. Accounting – If the project plans to provide compensation to subjects, it must receive receive approval from accounting prior to IRB approval being granted.

6. Conflict of Interest – If a conflict of interest is identified with the investigator and/or study staff and the proposed research, review by the Conflict of Interest (COI) committee is required. The investigator will be notified, as well as, the Office of Research about the possible conflict.
The investigator may be required to submit additional paperwork for review by the COI committee. Depending on the level of conflict and the degree to which it impacts the proposed study, IRB approval may be delayed until a resolution or management of the conflict has been developed.

7. *Veterans* – If the proposed research plans to recruit veterans and/or use VA resources and/or staff, review by the VA Research and Development Committee is required. VA R&D approval is not required prior to IRB approval. However, it will be required prior to conducting any portion of the proposed research at the VA Hospital.

**Project Approvals**

Prior to final approval being granted on any project, the IRB office will determine that the Principal Investigator and all key personnel have completed the required educational and/or HIPAA training. If the requirement has not been met, the Principal Investigator will be notified of the requirement and the process to meet the requirement. IRB approval will be held until the required training has been completed for all key personnel.

The Principal Investigator will be notified in writing of the approval of the project, the risk level assigned, the consent requirements, and the continuing review interval. Included with the final approval letter will be the approved consent and any other approved documents (such as recruitment materials, questionnaires, etc.). A copy of the approval letter and attached documents will be kept with the file in the IRB administrative office as proof of approval.
Purpose

To aid in assuring knowledge and compliance of all persons involved in any aspect of human subject research by documenting the policy for Investigator education.

Scope

The SOP applies to all human subject research falling under the purview of the Health Sciences Institutional Review Board.

Definitions

None

Policy/Procedure

The Health Sciences Institutional Review Board (“HS IRB”) is established pursuant to and in accordance with the regulations of the Department of Health and Human Services (45 CFR46.101); the Food and Drug Administration (21 CFR 56.101); the Belmont Report; and the FederalWide Assurance (FWA00002876) of the University of Missouri-Columbia. The HS IRB is an appropriately constituted administrative body established to protect the rights and welfare of human subjects that are recruited to participate in research activities conducted under the auspices of the University of Missouri-Columbia.
The Investigator shall:

1. Possess the professional qualifications and experience to adequately meet the degree of protocol complexity and risk to human subjects.
2. Complete the HS IRB Education and Training requirement prior to initiating any research project.
3. The HS IRB Education and Training requirement includes:
   a. Attending an HS IRB Education and Training Seminar; or
   b. Completing a web-based training module such as the NIH or OHRP training modules.
4. Assure continuing educational opportunities are obtained to maintain the professional qualifications and experience necessary to adequately meet the degree of protocol complexity and to assure adequate protection of human subjects involved in the investigator’s research project.

Prior to final approval being granted on any project, it must be determined that the Principal Investigator has completed the educational training requirement. If the requirement has been met, the project will proceed with notification of the action taken. If the requirement has not been met, the Principal Investigator will be notified of the requirement and means to meet the requirement. The project will not proceed be decided upon until training has been completed.
IRB Fees

Effective Date: July 1, 2003
Original Approval Date: July 1, 2003
Revised Date: August 1, 2004
August 4, 2004

Approved By: Niels Beck, PhD
Chair, Health Sciences IRB

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Purpose
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1.0 Purpose

To aid in assuring knowledge and compliance of all persons involved in any aspect of human subject research by documenting the requirements for collection of IRB fees.

2.0 Scope

The SOP applies to all human subject research falling under the purview of the Health Sciences Institutional Review Board.

3.0 Definitions

None

4.0 Policy/Procedure

The following describes the policy and procedure for the collection of IRB fees and is currently in effect.
The IRB charges for reviews of protocols that are industry sponsored or sponsored by other for profit entities. Fees are not charged for studies sponsored by NIH, non-profit foundations, state or federal government, or are internally funded.

Effective July 1, 2003 IRB fees are as follows:

Full Board initial review---------$1,500

Exempt, Expedited and Continuing reviews---$750.00

The IRB fee is for review not approval of the protocol. Therefore, the fee applies regardless of whether the study is approved or whether the study is ever initiated.

Sponsored programs office bills for the IRB fees.

IRB fees may be part of the project budget or not (department option, but needs to be documented whether in or out, documentation will minimally take the form of a separate budget line if included in the budget). ***Important- If not accounted for in the internal budget IRB fees need to be stated in the award document.

IRB fees are not included in the F&A base

Sponsored programs office determines the need for an invoice. The award document is checked to see what it states concerning IRB fees. Payment of the continuing review fee will be expected on the IRB approval anniversary date for any open project

If IRB fees are addressed in the award document they will be billed accordingly.

If IRB fees are not covered in the award document or the internal budget then the project is charged directly.

Any outstanding unpaid IRB fees will be charged against remaining balances for any project to be closed to a fixed price closeout Chartfield.

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Meeting Schedule

Effective Date: January 22, 2001
Original Approval Date: January 22, 2001
Revised Date: April 10, 2002
Review Date: October, 2005

Approved By: Niels Beck, PhD
Chair, Health Sciences IRB

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Purpose
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1.0 Purpose
To aid in assuring knowledge and compliance of all persons involved in any aspect of human subject research by documenting the policy for Board education.

2.0 Scope
The SOP applies to all human subject research falling under the purview of the Health Sciences Institutional Review Board.

3.0 Definitions
None

4.0 Policy/Procedure
HS IRB members will convene regularly to fulfill the mandate to oversee research involving human subjects at the University of Missouri Health Sciences Center and its affiliates.

The Board is divided into two subcommittees, each subcommittee meets one Wednesday each month (either mid-month or end-month). Meetings are convened at 2:00 pm and are scheduled to end by 5:30 pm; however, members are requested to stay and the meeting
business is continued after that time until complete, as long as the meeting room is available and quorum is maintained.

Submission of proposals is accepted at the IRB administrative office at any time. The administrative working deadline for submission of proposals for review at a specific meeting is the 20th of the previous month for review at the mid-month meeting and the 5th of the current month for review at the end of the month meeting. If a deadline falls on a weekend, then the next business day will be used for the submission deadline.
1.0 Purpose
To aid in assuring knowledge and compliance of all persons involved in any aspect of human subject research by documenting IRB meeting procedures

2.0 Scope
The SOP applies to all human subject research falling under the purview of the Health Sciences Institutional Review Board.

3.0 Definitions
None

4.0 Policy/Procedure
As meetings are convened for the dispensation of IRB business, certain procedures will apply. The HS IRB meeting procedures are as follows:

1. The IRB shall assure valid quorum is present before a meeting can be convened.
2. The IRB shall assure the attendance of at least one nonscientific member before convening the meeting.

3. The IRB shall assure a valid quorum is maintained throughout the meeting. If the quorum fails at any time during a convened meeting, the meeting is terminated from further action until a valid quorum can be restored.

4. The IRB shall record the names of every member present at each convened meeting in the minutes as evidence of a valid quorum.

5. The IRB Chair shall call the meeting to order.

6. Announcements shall be made and Chair comments will be delivered.

7. The meeting Chair shall initiate and proceed with the items of business as documented on the Agenda.

8. The Chair will identify the protocol immediately subject to review and the assigned Primary Reviewer, excusing any member with a conflict of interest with the protocol before presentation of the project occurs.

9. The Primary Reviewer will give an overview of the protocol, including but not limited to, the relevant requirements set forth by 45 CFR 46, the informed consent document, any supplemental materials, recommendations and rationale for proposed actions. The Primary Reviewer must also determine if the Board has sufficient information to take action on the proposal, and if not, must provide the board with the reason(s) for such a determination. The Primary Reviewer will end the overview by entering a motion of the recommended action.

10. Once the motion has been seconded, the nonscientific reviewer will present their concerns and comments and the motion will be opened to the floor for discussion.

11. The Chair will greet and escort out of the room any Principal Investigator, Consultant, or guest who has been requested to appear before the Board to answer questions pertaining to the project.

12. The Chair will call for a vote on the motion on the floor and will assure the votes are recorded in accordance with 45 CFR 46.115(a)(2) which specifies the recording the total vote count and the delineation of votes FOR, AGAINST, and ABSTAINING.

13. The Chair shall announce the results of the vote to the Board.

14. The Chair will proceed through the agenda to each item.

15. The IRB shall assure that the minutes record specific findings including specific information justifying those findings, the risk and approval period, the type of consent/assent and justification, which protocols require continuing review more
often than annually, in accordance with the federal regulations, FWA and HS IRB policies.

16. The IRB shall retain these records for at least three (3) years, and records relating to research that is conducted shall be retained for at least three (3) years after completion of the research.

17. At the conclusion of all business, closing announcements will be made.

18. The Chair will adjourn the meeting.
IRB Membership

Effective Date: September 1, 2004
Original Approval Date: September 1, 2004
Revised:
November 11, 2005
December 13, 2005

Approved By: Niels Beck, PhD
Chair, Health Sciences IRB

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1.0 Purpose

To aid in assuring knowledge and compliance of all persons involved in any aspect of human subject research by documenting IRB membership requirements.

2.0 Scope

The SOP applies to all human subject research falling under the purview of the Health Sciences Institutional Review Board.
3.0 Definitions

NA

4.0 Policy/Procedure

The Health Sciences IRB (HS IRB) is duly constituted in light of the anticipated scope of the institution's research activities and the types of subject populations likely to be involved, the appropriateness of the proposed initial and continuing review procedures in light of the probable risks, and the size and complexity of the institution. The HS IRB is composed of at least five (5) regular voting members as mandated by the federal regulations (45 CFR 46.107(a)). The membership is sufficiently qualified through the experience and expertise of its members, and the diversity of the members, including consideration of race, gender, and cultural backgrounds and sensitivity to such issues as community attitudes, to promote respect for its advice and counsel in safeguarding the rights and welfare of human subjects. Additionally, the HS IRB is able to ascertian the acceptability of proposed research in terms of institutional commitments and regulations, applicable law, and standards of professional conduct and practice.

The HS IRB is comprised of two subcommittees under the leadership of a single IRB Chair and with assistance of a central IRB administrative office. Each subcommittee is comprised of no fewer than 10 general and lay members representing the health service professions (medicine, nursing, and health professions), consumers, and members of the non-scientific community (lawyers, clergy, ethicists, educators, etc.).

Potential new members are identified by recommendation from deans and department heads in answer to solicitations for new members. The Vice Provost for Research appoints new members. Routinely, appointments and reappointments of the voting members of the Board will become effective at the beginning of the academic year (September 1). At times it is necessary to fill a void in IRB membership during the year. If the situation arises, a member will be solicited and appointed as soon as reasonably possible.

Board members

A general Board member will be a respected, active member of the faculty or staff who is a qualified scientific member of the IRB, is concerned about human rights and ethical issues and stays well informed in the changing regulations relevant to the use of human subjects in research. The member is appointed by the Vice Provost for Research to a three-year term, which is renewed yearly and may be reappointed at the discretion of the Vice-Provost of the Office of Research.

Responsibilities of the general Board member include, but are not limited to:
- Attend board meetings
- Review meeting material prior to Board meetings
- Serve as primary reviewer on assigned submitted proposals and prepare overview to present to Board and recommendation of action to be taken
• Determine whether proposal information is sufficient to allow knowledgeable vote (if not, determine if necessary to contact investigator or request review by outside consultant)
• Apply regulatory criteria for approval and vote on recommended action to proposal
• Evaluate submitted consent for appropriateness
• Assist in maintaining quorum, leaving only for emergencies
• Maintain confidentiality of Board discussions and all materials submitted for review
• Conduct review and act on any expeditable project sent for review in a timely manner
• Review and act on requests for amendments, adverse event and deviation reports
• Review and act on compliance issues that require board action
• Remain well informed on the changing regulations relevant to the use of human subjects in research.
• Fulfill all training requirements

**Lay Members**

A lay Board member will be a respected, active member of the community who is concerned about human rights and ethical issues and stays well informed in the changing regulations relevant to the use of human subjects in research. The member is appointed by the Vice Provost for Research to a one-year term, which can be renewed indefinitely. The terms of lay members may continue without limit as long as the member continues to possess the desired qualifications.

The lay member is generally not affiliated with the institution but may be affiliated in a non-scientific capacity. At least one lay member of each Board will be a non-institutional affiliated member and must be present at the meeting for quorum.

Responsibilities of the lay Board member include, but are not limited to:
• Attend board meetings
• Review meeting packet prior to Board meeting
• Serve as primary consent reviewer on assigned submitted proposals and prepare list of any consent concerns to discuss at the Board meeting
• Determine if informed consent is adequate to allow knowledgeable vote (if not, determine if necessary to contact investigator or request review by outside consultant)
• Apply regulatory criteria for approval and vote on recommended action to proposal
• Assist in maintaining quorum, leaving only for emergencies
• Maintain confidentiality of Board discussions and all materials submitted for review
• Remains well informed on the changing regulations relevant to the use of human subjects in research.
• Fulfill all training requirements

Non-scientific lay members will be appointed to serve a one-year term and may be reappointed at the discretion of the Vice-Provost. The terms of lay members may continue without limit as long as the member continues to possess the desired qualifications.
**Chair**

The Chair of the IRB has overall responsibility for both IRB boards (middle and end of month boards) and oversight of the IRB Administrative Office.

Qualifications for the IRB Chair are:
- The Chair will be a respected, active member of the faculty from one of the schools
- Is a qualified member of the IRB or has prior experience in research
- Is concerned about human rights and ethical issues and stays well informed in the changing regulations relevant to the use of human subjects in research.
- Fulfills all training requirements (see SOP 1.8.1.2)

The Chair is appointed by the Vice Provost for Research to a three-year term, which can be renewed and may be reappointed at the discretion of the Vice-Provost of the Office of Research.

Responsibilities of the Chair include, but are not limited to:
- Approve Board policies and procedures
- Resolve controversial substantive or procedural matters
- Keep current with regulations
- Assist in the education of investigators and board members
- Review and act on requests for emergency use of a test article/compassionate use
- Signatory for all approval letters, termination letters and other Board correspondence
- Reviews and acts on all exemption requests and annual reports in the absence of the Compliance Officer
- Oversight of the Board and IRB Administrative Office activities

**Vice-Chair**

The Vice-Chair of the IRB has responsibility for the IRB Board (either the mid-month or end-month) for which he/she serves as Vice-Chair.

Qualifications for the IRB Vice-Chair are:
- The Vice-Chair will be a respected, active member of the faculty from one of the schools
- Is concerned about human rights and ethical issues and stays well informed in the changing regulations relevant to the use of human subjects in research.
- Fulfills all training requirements

The Vice-Chair is appointed by the Vice Provost for Research to a three-year term, which can be renewed and may be reappointed at the discretion of the Vice-Provost of the Office of Research.

Responsibilities of the Vice-Chair include, but are not limited to:
- Review Board policies and procedures
- Resolve controversial substantive or procedural matters
- Conduct Board meetings
- Keep current with regulations
• Assist in the education of investigators and board members
• Review and act on project amendment requests
• Review and act on requests for emergency use of a test article/compassionate use in the absence of the Chair
• Review and acts on all exemption requests and annual reports in the absence of the Compliance Officer and/or Chair

Additional Consultants
The HS IRB uses consultants who are not regular voting members of the Board to review proposals in their areas of expertise, such as a device specialist or statistical consultant. If a situation arises where a proposal falls outside the expertise of the board members, an individual with expertise in the necessary area will be identified and asked to serve in the capacity of non-voting member consultant in that discipline.

Additional Members
In order to better meet the needs of some of the affiliated institutions as required each subcommittee will include an individual associated with:

1) Harry S Truman Memorial Veterans Hospital (two individuals per each HS IRB committee as required by VA regulations)
2) One member of the HS IRB is a designated prisoner consultant who has the appropriate background and experience to serve in that capacity.

The Office for Human Research Protection is updated annually of membership changes to the fully registered HS IRB.
Institutional Review Board
Health Sciences Section
University of Missouri-Columbia

Standard Operating Procedure

Minutes

Effective Date:
Original Approval Date: January 22, 2001
Revision Date: December 9, 2005

Approved By: Niels Beck, PhD
Chair, Health Sciences IRB

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1.0 Purpose
To aid in assuring knowledge and compliance of all persons involved in any aspect of human subject research by documenting the requirements for IRB minutes.

2.0 Scope
The SOP applies to all human subject research falling under the purview of the Health Sciences Institutional Review Board.

3.0 Definitions
NA
4.0 Policy/Procedure

The minutes of each HS IRB convened meeting will include the necessary documentation to enable reconstruction of the events and discussion of the meeting. The minutes will be recorded in sufficient detail to document the events of the meeting.

The compliance specialist will document the minutes in sufficient detail to include the following information:
1. Attendance - The names of every member present and their designation, if other than general member. Additionally, any guests, non-voting members, and IRB office staff will also be listed.
2. Announcements, information and/or education by the chair, vice-chair or compliance officer.
3. Review and approval of last month’s minutes or any necessary changes.
4. A summary of all materials included in the packet for review.
5. The IRB number, name, and investigator for each protocol that is acted upon.
6. A written summary of the discussion of the issues and documentation each study was reviewed in detail to make the required determinations as set forth in 45 CFR 46.111.
7. A summary of the resolutions to any issues including if the requested revisions will be reviewed administratively, by the primary reviewer or returned to the board.
8. The actions taken by the IRB, including the basis for requiring changes in or disapproving research.
9. The board’s findings for justifications for any waiver or alteration in informed consent or HIPPA.
10. The board’s assessment of the risk and period for review.
11. The board’s assessment of the risks and benefits of studies involving minors to determine the research category in accordance with 45 CFR 46.404 -.407.
12. The board’s determination of a child’s right to provide assent in accordance with 45 CFR 46.408
13. Documentation of discussion regarding justification of any safeguards have been included to protect the rights and welfare of vulnerable or special populations such as pregnant women, fetuses, veterans, neonates and/or prisoners.
14. The specific details for recording the number of votes for all IRB actions in accordance with 45 CFR 46.115(a)(2) detailing:
   a. The total votes
   b. The total votes FOR the action
   c. The total votes AGAINST the action
   d. The total votes ABSTAINING from voting
   e. The total votes absent from the room

The HS IRB does not regularly record the names of individual member votes in the minutes so as to protect the confidentiality of all members.

15. If there is a conflict of interest between a board member and a research project, the member will be excused from the room during discussion and vote (see conflict of interest policy for more information). This will be documented in the minutes.

16. The time the meeting was adjourned.
1.0 Purpose
The Central Institutional Review Board (CIRB) Initiative is a pilot project sponsored by the National Cancer Institute (NCI) in collaboration with the DHHS Office of Human Subjects Protection (OHRP) to develop an innovative approach to human subjects protection for national multi-center trials in cancer.

The CIRB’s primary function is initial and continuing review of protocols and the local institution’s primary function is consideration of local context and oversight of local performance for these protocols. The local institution, through its own local IRB, will decide on a protocol-by-protocol basis whether to accept the review of the CIRB or to conduct its own review of the protocol.

2.0 Scope
The SOP applies to all human subject research falling under the purview of the Health Sciences Institutional Review Board.
3.0 Definitions
None

4.0 Policy/Procedure

1) New projects

a. Investigators and study staff who wish to open a particular NCI CIRB-approved protocol have to download the protocol, informed consent and the CIRB application, from www.ncicirb.org and submit two copies of ALL other CIRB documents from the Members’ Area of the CIRB website to the University of Missouri-Columbia Health Sciences Institutional Review Board (HS IRB). A cover letter must be submitted with the application which includes:

- A timeline describing study status and events
- A list of personnel to be involved in the study locally
- Identification of the primary investigator and primary contact
- The number of subjects expected to be enrolled at this institution
- Whether the study involves any radiation or biosafety

The HS IRB will not require that a HS IRB project application be completed for CIRB studies, but instead the HS IRB office will manually create an IRB number for all CIRB studies.

b. The CIRB-approved consent form must be submitted with the local contact information filled out and include local liability and/or confidentiality language. Local investigators and HS IRB may tune up language, make the consent comply with state and local laws and requirements, or add things such as clarifications, safety visits, etc. These changes do not have to be submitted to CIRB. No sections can be taken out of the CIRB-approved consent and no changes can be made which would alter the meaning of any content. If such revisions and substantive changes are required by the HS IRB, then the HS IRB should communicate not to accept the NCI CIRB approval.

2) Review

a. HS IRB will designate a two-person committee (one of the IRB chairs and one IRB physician, preferably with some experience in hematology/oncology) to conduct the "facilitated review" of the study. The role of the reviewers is to determine whether there are any local concerns that need to be addressed and whether to accept the CIRB review. The HS IRB needs to comply with OHRP guidance that, "...an institution relying upon another institution's IRB has a responsibility to ensure that the particular characteristics of its local research context are considered through subsequent review by appropriate designated institutional officials, such as the Chairperson and/or other members of its local IRB."

b. HS IRB reviewers will be given two weeks to review the project, make the decision whether to accept or not the NCI CIRB approval, and to let the HS IRB office know about their decision.

c. HS IRB designated reviewers will have more than an "accept or reject" authority and will be able to propose and approve additions to the protocol and/or word substitutions in the informed consent. Potential suggestions regarding changes will be given to the HS IRB office and
subsequently communicated to the PI who will need to comply before the NCI CIRB approval is accepted.

d. As part of the local "facilitated review", the HS IRB may add stipulations or local requirements to protocols, particularly to increase subjects' safety, to clarify procedures, etc., but may not delete or contradict any protocol contents. The HS IRB reviewers also need to consider additions or deletions to the informed consent, dealing with state and local law, institutional requirements, or IRB policies. Minor word substitutions or additions in the informed consent document, particularly to facilitate better comprehension by the local population, are allowed as long as the proposed changes do not alter the meaning of the CIRB approved contents. These additional requirements (regarding protocol and/or consent form) would constitute requests placed only on the local investigators and would not become a formal part of the protocol.

e. Per current OHRP/NCI guidance, any deletion or substantive modification of information concerning risks or alternative procedures contained in the sample informed consent document must be justified in the IRB minutes and sent by the investigators to the Cooperative Group administering a particular protocol. Since local revisions to the NCI CIRB-approved consent form will be only minor and since the local “facilitated review” will take place outside the IRB convened meetings, information about local revisions will not be placed in the IRB minutes.

f. The designated reviewers will receive all submitted materials as well as any documents available on the restricted NCI CIRB web site, so they can decide whether a particular protocol and informed consent documents are acceptable and whether they are appropriate in their local context. Access to the NCI CIRB restricted web site requires a user ID and the password and is only available to IRB administrators, IRB chairs and/or IRB members. To facilitate the review process additional materials (such as minutes and CIRB reviewer comments) will be downloaded from the NCI IRB restricted site by the HS IRB office and forwarded to HS IRB reviewers along with other documents.

g. Reviewers will make the recommendation to the HS IRB chair and HS IRB office whether to accept CIRB approval as is; accept it with minor modifications, or not to accept it.

h. If the CIRB approval is not accepted, and if the PI still wants to conduct the trial, then a HS IRB application will need to be completed per standard IRB policies regarding submission of new studies.

i. If the CIRB approval is accepted, HS IRB will notify the PI and CIRB Administrative Office about the acceptance decision. The HS IRB must notify the Central IRB Administrative Office each time it accepts the CIRB review and approval of a protocol. The CIRB, HS IRB and the PI will keep appropriate records of that decision on file.

j. The decision to accept CIRB approval will be conveyed to IRBs as a line item on agenda attachments.

Note: Projects, for which the HS IRB accepts NCI CIRB approval, may need to be submitted and reviewed by the Radiation Safety Committee (RSC) and Institutional Biosafety Committee (IBC). No project-related activities may take place before appropriate RSC and/or IBC approvals are obtained. If review and approval are need from RSC and/or IBC, the project information will be forwarded to RSC and/or IBC as per our current process. NCI CIRB review and approval will be formally accepted only when RSC and/or IBC approvals are on file with the HS IRB office.
3) Amendments

a. CIRB-approved amendments will be forwarded to investigators by the Group and subsequently submitted to the HS IRB by the PI.

b. Two copies of all amendment materials (summary of changes, revised protocol, revised consent, and approval letter from CIRB) should be submitted. This information must be downloaded from the CIRB website. Submission of an HS IRB amendment form will not be required, but instead the HS IRB office will administratively enter the review into the eIRB system.

c. The consent form should be on the CIRB template and include the most up-to-date protocol version. The consent should include local contact information, confidentiality and liability information.

d. HS IRB will review the amendment per HS IRB office policies for review of amendments (whether it is minor/administrative changes or significant changes). If the amendment is significant, the HS IRB will forward all the submitted materials and any applicable materials from the NCI CIRB restricted site to the HS IRB physician who has been initially designated as part of the two-person committee. The reviewer will make recommendation to the IRB Chair whether to accept CIRB approval as is; accept it with minor modifications or not to accept it.

e. If the HS IRB requires substantive changes to the amendment, which would preclude acceptance of the NCI CIRB approval of such amendment, the HS IRB office will communicate with the PI and the NCI CIRB office to discuss the situation and seek resolution. However, if after all efforts the CIRB approval of an amendment is not accepted, then the HS IRB has to back out of the original approval of the project and the original study would have to be brought back to the full board for review and approval. This would cause delays and possibly pose patient safety issues, however, the understanding is that once the HS IRB has accepted the initial NCI CIRB review and approval of a protocol, the HS IRB has given NCI CIRB the authority to do the subsequent reviews.

The NCI CIRB does not have to be notified if the HS IRB accepts CIRB approval of an amendment. The HS IRB will notify the PI about the acceptance decision and both the HS IRB and investigators will keep appropriate records of that decision on file.

f. The HS IRB will stamp the CIRB approval letter which was submitted with the amendment with the ‘approval’ stamp and signature. This will be the only notification of approval of the amendment by the HS IRB, which will be returned to the investigator for their files.

g. Decision to accept CIRB approval of a particular amendment will be conveyed to IRBs as a line item on agenda attachments.

4) Adverse Events (AEs)

a. On-site serious AEs must be submitted by the PI to the HS IRB and to the Group per HS IRB policy. All off-site AEs will be submitted to the CIRB. These off-site AEs need to be submitted to the HS IRB during annual review (per IRB office policy regarding off-site AEs). If there are
any issues and/or problems connected with off-site AEs, the Group will notify investigators and CIRB Administrative Office will notify the HS IRB.

5) **Continuing Review Reports (CRRs)**

a. PIs must submit a brief report on the progress of a project to the HS IRB in the form of a letter. This letter must address:

- Study status (i.e. active, open to enrollment; closed, long term f/u; closed to enrollment, active treatment or f/u continues, etc)
- current on-site enrollment
- any on-site AEs
- local staff changes
- A timeline of amendments over the past year

The letter must also be accompanied by **two** copies of CIRB materials for the particular CRR (such as CIRB approval, revised consent, new protocol, etc). The HS IRB will electronically generate a CRR report to assist in triggering the submission of the CRR, however the form does not need to be filled out. Instead, the HS IRB will administratively enter the review into the eIRB system. This report, regardless of the nature of the study, would be reviewed by expedited procedures.

b. CRRs will be reviewed per HS IRB office polices for review of CRRs (whether reviewed through full board or expedited procedures). If the CRR needs review by the full board, all the submitted materials will be forwarded to the designated physician reviewer (as described above).

c. Information about the CIRB approval of a CRR for a particular project will be conveyed to IRBs as a line item on agenda attachments

6) **Transferring of old studies to CIRB**

a. Studies which were previously approved by the HS IRB and wish to be transferred to the CIRB can do so at one of two time points:

- If the HS IRB expiration date comes first, then a HS IRB CRR form must be submitted. On the CRR form (under the ‘progress’ section) please state that this study will be transferred to the CIRB. Revised consents in the CIRB format must be included (if the study is still open to enrollment), a copy of the latest approved CIRB protocol, and any other relevant documentation. Please also state when the study will expire according to CIRB.
- If the CIRB expiration date comes first, please submit a CRR for the CIRB study (as described above) with a note on the cover letter stating the desire to transfer this to CIRB.

b. Studies which request to be transferred to the CIRB will be reviewed per HS IRB office policies regarding review of CRRs (whether reviewed through full board or expedited). If the studies are deemed to need full board review, they will be sent to the designated primary reviewer (as described above).

c. If the CIRB approval is accepted, HS IRB will notify the PI and CIRB Administrative Office about the acceptance decision. **The HS IRB must notify the Central IRB Administrative**
Office each time it accepts the CIRB review and approval of a protocol. The CIRB, HS IRB and the PI will keep appropriate records of that decision on file.
Non-compliance

Effective Date: December 12, 2005
Original Approval Date: December 12, 2005

Approved By: Niels Beck, PhD
Chair, Health Sciences IRB

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Purpose
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Noncompliance that may be reviewed by the Chair
Noncompliance that may be reviewed by the Board

1.0 Purpose

To aid in assuring knowledge and compliance of all persons involved in any aspect of human subject research by documenting noncompliance.

2.0 Scope

The SOP applies to all human subject research falling under the purview of the Health Sciences Institutional Review Board.

3.0 Definitions

*research noncompliance*—research that deviates from institutional policies, procedures, stipulations, decisions, state or federal law.

*Serious non-compliance*—All non-compliance substantially affecting participants’ rights and/or welfare, or impacting upon the risks or benefits is serious non-compliance.

*Continuing non-compliance*—the systematic and habitual disregard of restrictions, procedures, stipulations, or decisions of the IRB.
research (scientific) misconduct - fabrication, falsification, plagiarism or other practices that seriously deviate from those that are commonly accepted within the academic community for proposing, performing, or reviewing research, or reporting research results. Misconduct does not include honest error or honest differences in interpretations or judgments of data.

Collected Rules - 420.010 Research Dishonesty
http://www.umsystem.edu/ums/departments/gc/rules/research/420/010.shtml

Suspension - a temporary withdrawal of approval of some or all research, or a permanent withdrawal of approval of some research activities.

Termination - a permanent withdrawal of approval of all research activities

4.0 Policy/Procedure

In order to demonstrate appropriate oversight of research activities and to comply with federal and state statutes, regulations, policies and guidelines; and applicable University policies and procedures, all incidences and allegations of research non compliance will be investigated and resolved. When allegations of non compliance cannot be resolved informally, the chair and the Board have the authority to investigate and take appropriate action to ensure compliance or to terminate the research.

IRB Procedures

Administrative Review

The Administrative review is designed to determine whether the allegations of research noncompliance can be substantiated and whether it requires further review by the chair or Board. An Administrative review is initiated when an allegation is received from an individual; it is deemed by the Office of Research or the chair of the IRB that a review is necessary, or when informal or formal monitoring activities reveal potential research noncompliance.

Administrative Reviews are conducted by the IRB Compliance Officer. An Administrative Review may include: review of files, literature, and documents from the Investigator and others, which could serve to validate or dismiss the allegation.

When an Administrative Review reveals information that appears to substantiate an allegation of noncompliance with policies or regulations, the chair of the IRB is consulted for further action. All efforts will be made to resolve the matter informally.

Possible outcomes of an Administrative Review are:
- Dismiss the allegation,
- Achieve compliance with the cooperation of the Investigator (and report to the IRB and/or federal Agency when required),
- Recommend review by the IRB,
- Recommend reclassification as possible scientific misconduct (and refer to the Office of Research)
The results of an Administrative Review will be communicated by the IRB staff in writing to the Investigator (with a copy to the IRB chair) within 30 days of the conclusion of the review. This communication will either: notify the Investigator that the allegation was dismissed, confirm that compliance was achieved, inform the Investigator that Board Review was recommended, or apprise the Investigator that the incident may be investigated as a matter of scientific misconduct.

In cases where the result of an Administrative Review suggests that an Investigator has demonstrated an apparent pattern of disregard for research regulations, policies, or procedures, an IRB review may be recommended even when the specific finding of noncompliance is resolved informally.

**Board Review**

IRB Review is initiated after a completed Administrative Review suggests that an incident of noncompliance appears to have occurred and when informal resolution was not achieved or when informal resolution is achieved but the Investigator has been determined to have engaged in a pattern of disregard for research regulations, policies or procedures. IRB review may be conducted by full committees or by subcommittees charged by the committee chairs. Whenever possible, the result of an IRB Review will be informal resolution. Such reviews may include: review of files, literature, and other documents; requests for additional information from and/or interviews with the Investigator, complainant or others, and review of other documents which could serve to validate or dismiss the allegation.

Possible outcomes of an IRB Review are:
- dismiss the allegation,
- achieve compliance with the cooperation of the Investigator (and report to the appropriate federal Agency when required),
- impose sanctions to achieve compliance (and report to the appropriate federal Agency when required), or
- Recommend reclassification as possible scientific misconduct (and report to the Office of Research).

The results of an IRB Review will be communicated by the committee chair in writing to the Investigator (with a copy to the appropriate protocol file) within 60 days of the conclusion of the review. This communication will either: notify the Investigator that the allegation was dismissed, confirm that compliance was achieved, inform the Investigator of recommended sanctions, or apprise the Investigator that the incident may be investigated as a matter of scientific misconduct.

If sanctions are recommended or if a report to an external agency is required, a copy of the results of the review will also be sent to the Vice Provost for Research, the Department Chair, and the Dean of the school within which the research activity took place.
Sanctions for Research Noncompliance

Whenever possible, IRB staff will be available to assist Investigators with resolving noncompliance issues. In cases where cooperation does not occur or when it is determined that subjects or the institution has been placed at risk, sanctions may be imposed by Institutional Review Boards. Possible sanctions include:
  • requiring more frequent review of an investigator's research activities;
  • suspending research activities until compliance is achieved; or
  • terminating committee approval for research activities.

Other Sanctions by the Vice Provost for Research

In addition, the IRB may recommend additional sanctions to the Vice Provost for Research. Possible sanction recommendations include:
  • research privilege probation,
  • suspension of research privileges,
  • termination of research privileges, or
  • embargo of publications.

The Vice Chancellor's decision will be communicated in writing to the Investigator (with a copy to the IRB chair, the department chair, the dean of the school within which the research activity took place, the Provost).

Reporting to Federal Oversight Agencies

OHRP (in accordance with the terms of the University of Missouri FWA) and the FDA (for studies subject to 21 CFR Parts 50 and 56) are notified in a timely manner of: (1) serious or continuing noncompliance; (2) unanticipated problems involving risks to participants or others; or (3) suspension or termination of IRB approval for a study.
Non-English Speaking – Study Requirements

Effective Date: July 1, 2004
Original Approval Date: July 1, 2004
Revision Date: June 9, 2004

Approved By: Niels Beck, PhD
Chair, Health Sciences IRB

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1.0 Purpose
To aid in assuring knowledge and compliance of all persons involved in any aspect of human subject research by documenting the processes for the review and implementation of studies that include participants who primarily speak a language other than English. This is to ensure that non-English speaking subjects are properly consented per 45 CFR 46.116 and 21 CFR 50.20.

2.0 Scope
The SOP applies to all human subject research falling under the purview of the Health Sciences Institutional Review Board.

3.0 Definitions

*Non-English Speaking Subject:* A person whose primary language is other than English. This includes persons who have a limited ability to read English and/or understand spoken English.
4.0 Policy/Procedure

Requirements of study staff

If a study specifically includes a non-English speaking population, it is the role of the study staff to obtain translated versions of all documentation that would be disseminated to this population. Such documents include, but are not limited to, consent forms, advertisements, and questionnaires.

These documents, with their English equivalents, must be submitted to the IRB as part of the application (or amendment) review process.

If the use of a translator is required, such as for reading survey questions and recording answers, this translator must be added to the application and receive appropriate training as part of the study staff before approval can be granted. Study staff must not rely upon the subject’s family or friends as the translator.

A translator must be available to non-English speaking subjects when the subjects may have questions or concerns. This availability must coincide with the availability of the counterpart English-speaking study staff. This availability of the translator must be described in the application. For example, this includes how the translator will be present at multiple study visits, or if a non-English speaking subject calls the study staff with questions.

The translator’s qualifications must be forwarded to the HS IRB office as documentation of ability. This must be done prior to granting IRB approval.

When consenting a non-English speaking subject with a written consent form, a copy of the non-English consent must be given to each subject per 45 CFR 46.117 and 21 CFR 50.27.

It may be helpful for a translator to be present in order to facilitate conversation during consenting, even if the consent is presented in the subject’s primary language.

The Principal Investigator (or other study staff as appropriate) is responsible for ensuring each non-English speaking subject clearly understands the information presented.

Requirements of the HS IRB

The HSIRB must have all final versions of all non-English documents (consent, flyers, questionnaires, etc.), and their English equivalents, at the time of review for any study targeting non-English speaking subjects.

If the study is targeting only non-English speaking participants, an English equivalent must still be submitted.

If the Principal Investigator decides to include non-English speaking populations after original study approval, non-English and English versions of appropriate documents must be submitted for amendment review.
The board has the authority to require an uninvolved third party to perform back-translation of the non-English version if there are concerns of translation validity.

The HS IRB may require a translator be present during the consenting process.

Unexpected Encounter with non-English speaking subject

On occasion, a subject may come forward who speaks a language other than the targeted populations, and so no translated consent may presently exist for the subject. In this event that study documents were written in a language other than the language used by the new potential subject, a translator may be used on rare occasions using the English version of the consent (or other documents). If this should occur, the primary investigator should document in the research record the event.

Studies should consider all populations that may be targeted so that unexpected encounters are minimized.

If additional subjects may be encountered who use this non-English language, the Principal Investigator should proceed to create documents in the new language through an amendment.

Translation sources

Various language departments exist throughout the University of Missouri-Columbia campus that can aid in translation. Below are possible sources for translation.

- Romance Languages & Literature: Spanish, Italian, French
- Classical Studies: Greek, Latin
- German & Russian Studies: German, Russian, Chinese, Japanese, Hebrew, Korean
- Black Studies: African Languages
- The International Center may also be of assistance.

None of these services at UMC are certified translators.

Many departments will refer requests to graduate students, whose availability may be limited. Fees may be charged for these translations.

Another source is an on-site interpreter from University Health Care’s Approved Interpreter list.

- Go to the Docushare website at https://docs.hsc.missouri.edu/
- Click on University of Missouri Health Care
- Click on University of Missouri Health Care Policies & Procedures
- Select the Foreign Language Interpreter List
- This list provides a directory of people fluent in various languages.
Participant Complaints

Effective Date: August 23, 2002
Reviewed: October, 2005
Approved By: Niels Beck, PhD
Chair, Health Sciences IRB

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1.0 Purpose
To aid in assuring knowledge and compliance of all persons involved in any aspect of human subject research by documenting the procedure for handling a research participant complaint.

2.0 Scope
The SOP applies to all human subject research falling under the purview of the Health Sciences Institutional Review Board.

3.0 Definitions
None

4.0 Policy/Procedure

All participant complaints referred to the HS IRB office will be investigated and a solution satisfactory to all involved parties will be sought. Complaints may be received directly from a study participant or through an entity such as Guest Services or Risk Management departments of University of Missouri HealthCare.

When a complaint is received about the conduct of a study or participation in said study, all information received from the participant will be documented. Once all information on the complaint has been received from the participant, the IRB office will notify the
Chair of the IRB of the complaint. The HS IRB office staff and the IRB Chair will then review the study information on the IRB database and contact the Principal Investigator and/or Site Study Coordinator to verify the participation of the complainant. Once participation is verified, the IRB will document all information received from the study staff pertaining to the participant and said complaint.

After reviewing the information provided by all parties concerned, the IRB may seek the advice of legal counsel to help determine the appropriate action. The IRB will notify the Vice-Provost in the Office of Research of the complaint and investigation and recommended solutions.

The IRB will convey the findings of the investigation, the solution, and actions to be undertaken to both the investigators involved in the study and the participant lodging the complaint.

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# Primary Investigator - Designation

**Effective Date:** October 1, 2004  
**Original Approval Date:** October 1, 2004  
**Revision Date:** N/A  

Approved By: Niels Beck, PhD  
Chair, Health Sciences IRB

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- Purpose
- Scope
- Definitions
- Policy/Procedure

## 1.0 Purpose

To aid in assuring knowledge and compliance of all persons involved in any aspect of human subject research by documenting the requirements for designating a principal investigator.

## 2.0 Scope

The SOP applies to all human subject research falling under the purview of the Health Sciences Institutional Review Board.

## 3.0 Definitions

*Principal Investigator* - The principal investigator is ultimately responsible for assuring compliance of the study with University policies and procedures including Hospital and IRB policies, DHHS General Policy and regulations, FDA regulations, and for the oversight of the conduct of the study.

## 4.0 Policy/Procedure

Any faculty, staff, or student of the University of Missouri may be a principal investigator (PI) on an
IRB study. Some limitations apply for students or investigators from outside the institution (see related SOPs). Below are the IRBs requirements for who may be designated as PI.

1) Any faculty or staff member of the University of Missouri-Columbia may be a PI. Any investigator and/or staff member listed on any application must adhere to all responsibilities of the PI as outlined in the SOP on PI Responsibilities. Additionally, the HS IRB educational training, and if appropriate, the HS IRB HIPAA training module must be completed prior to a final approval being granted.

2) Students, residents and fellows who are listed as Principal Investigators (PI) on research projects must have a faculty member listed as an advisor. See related SOP on “Requirements for research by students.”

3) Investigators not associated with the University of Missouri-Columbia (UMC) and/or its affiliated sites, who would like to conduct research projects at UMC and/or its affiliated sites, must have a faculty member listed as a Principal Investigator. Preferably the faculty PI should be designated from the department which will be involved in a particular research project.

However, investigators not associated with UMC and/or its affiliated sites, can sign an Unaffiliated Investigator’s Agreement (UIA) (attached). By signing the UIA, the investigator may conduct research at UMC without a faculty member listed as an investigator on the project. The UIA gives the UMC and the HS IRB authority to inspect, copy, and have general oversight over any and all research records and conduct related to the study.

5.0 Related SOPs

Requirements for research by students
PI Responsibilities
APPENDIX 1

Unaffiliated Investigator(s) Agreement

Name of Institution with the Federalwide Assurance (FWA): University of Missouri - Columbia

Applicable FWA #: 00002876

Unaffiliated Principal Investigator’s Name:

Unaffiliated Co-Investigators’ Names:

Research Covered by This Agreement: IRB #, IRB title

(1) The above-named Unaffiliated Principal Investigator and the above-named Co-Investigators have reviewed: 1) The Belmont Report: Ethical Principles and Guidelines for the Protection of Human Subjects of Research; 2) the U.S. Department of Health and Human Services (DHHS) regulations for the protection of human subjects at 45 CFR 46; 3) the Federalwide Assurance (FWA) referenced above; and 4) the University of Missouri-Columbia web-based Human Subjects Research training (MU Health Sciences Center IRB module).

(2) The Principal Investigator and Co-Investigators understand and hereby accept the responsibility to comply with the standards and requirements stipulated in the above documents and to protect the rights and welfare of human subjects involved in research conducted under this Agreement.

(3) The Principal Investigator and Co-Investigators will comply with all other national, state, or local laws or regulations that may provide additional protection for human subjects.

(4) The Principal Investigator and Co-Investigators will abide by all determinations of the University of Missouri-Columbia Health Science IRB (HS IRB) designated under the above Assurance and will accept the final authority and decisions of the HS IRB including but not limited to directives to terminate participation in designated research activities.

(5) The Principal Investigator and Co-Investigators will complete any educational training required by the University of Missouri-Columbia prior to initiating research covered under this Agreement.

(6) The Principal Investigator and Co-Investigators will report promptly to the HS IRB any proposed changes in the research conducted under this Agreement. The investigator will not initiate changes in the research without prior HS IRB review and approval, except where necessary to eliminate apparent immediate hazards to subjects.

(7) The Principal Investigator and Co-Investigators will report immediately to the HS IRB any unanticipated problems involving risks to subjects or others in research covered under this Agreement.
(8) The Principal Investigator and Co-Investigators will obtain, document, and maintain records of informed consent from each subject or the subject’s legally authorized representative as required under DHHS and FDA regulations and stipulated by the HS IRB.

(9) The Principal Investigator and Co-Investigators acknowledge and agree to cooperate in the HS IRB’s responsibility for initial and continuing review, record keeping, reporting, and certification. The Principal Investigator and Co-Investigators will provide all information requested by the HS IRB in a timely fashion.

(10) In conducting research involving FDA-regulated products, the Principal Investigator and Co-Investigators will comply with all applicable FDA regulations and fulfill all investigator responsibilities (or investigator-sponsor responsibilities, where appropriate), including those described at 21 CFR 312 and 812.

(11) The Principal Investigator and Co-Investigators acknowledge that the HS IRB will have the oversight authority over the entire research project referenced above, regardless of the performance site of the project-related activities.

(12) If in the course of carrying its duties, the HS IRB needs to audit study records, the Principal Investigator and Co-Investigators will make all the study records available to the HS IRB for review.

(13) Emergency medical care may be delivered without the HS IRB review and approval to the extent permitted under applicable federal regulations and state law. However, data and information obtained as a result of emergency medical care may not be included as part of federally-supported or – conducted research.

(14) This Agreement does not preclude the Principal Investigator and Co-Investigators from taking part in research not covered by the Agreement.

(15) The Principal Investigator and Co-Investigators acknowledge that they are primarily responsible for safeguarding the rights and welfare of each research subject, and that the subject’s rights and welfare must take precedence over the goals and requirements of the research.

Principal Investigator Signature: ____________________________ Date _______________

Name: _______________________________ Degree(s): ____________________________

Address: _______________________________

Phone #: _______________________________
Co-Investigator Signature: _________________________________ Date ________________

Name: _________________________________ Degree(s): _________________________________

FWA Institutional Official (or Designee): _________________________________ Date ________________

Name: _________________________________ Institutional Title: Vice Provost for Research

Address: University of Missouri – Columbia, 205 Jesse Hall, Columbia, MO, 65211

Phone #: 573-882-9500
Principal Investigator - Responsibilities

Effective Date:   October 1, 2004
Original Approval Date:  October 1, 2004
Revision Date:   N/A

Approved By:    Niels Beck, PhD
Chair, Health Sciences IRB

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Purpose
Scope
Definitions
Policy/Procedure

1.0 Purpose

To assure knowledge and compliance by documenting the responsibilities of principal investigator for the Health Sciences IRB.

2.0 Scope

The SOP applies to all human subject research falling under the purview of the Health Sciences Institutional Review Board.

3.0 Definitions

Principal Investigator - The principal investigator is ultimately responsible for assuring compliance of the study with University policies and procedures including Hospital and IRB policies, DHHS General Policy and regulations, FDA regulations, and for the oversight of the conduct of the study with regards to specific responsibilities.

4.0 Policy/Procedure
The principal investigator (PI) is responsible for ensuring the risks to research subjects are minimized by using procedures that are consistent with sound research design and do not expose subjects to unnecessary harm, and which include the appropriate safeguards. The PI is expected to be knowledgeable and involved in all aspects of the conduct of the study. Even though the PI may delegate some responsibilities to others on the study staff, the PI is still the ultimate point of responsibility and must oversee the delegation to ensure compliance. The investigator must be qualified by training and experience in the area in which the research will be conducted.

The general responsibilities of the principal investigator are:

- Ensuring the selection of subjects is appropriate for the research
- Ensuring that risks are reasonable relative to anticipated benefits (if any) to the participant and the projected gain of knowledge to society
- Ensuring participants are adequately educated on all requirements of the informed consent and that the consent is obtained in accordance with HS IRB policy, federal regulations and if appropriate University Hospital policies.
- Ensuring that subjects are monitored throughout the study for safety
- Conducting the study in strict accordance to the approved protocol except when immediately hazardous to participants. All changes to and deviations from the protocol must be reported to the HSIRB
- Reporting all serious adverse events or adverse events which occur in accordance with the HS IRB adverse event policy
- Ensuring that in the event of an adverse event, all reasonable efforts are made to provide research subjects with adequate care
- Ensuring all other investigative personnel are listed on the application, are appropriately trained and are familiar with conducting the research in accordance to the protocol and the regulations
- Maintaining adequate, accurate, and current records of research data, outcomes, and adverse events to allow for an ongoing assessment of the risk to benefit ratio of study participation
- Ensuring subjects are kept informed of any new information which may affect their willingness to participate
- Ensuring the subjects privacy and the confidentiality of the data that are maintained
- Ensuring approval for the study does not expire by completing a continuing review report form at least thirty days prior to expiration
- Complying with the conflict of interest policy

5.0 Related SOP

Informed consent
Adverse event
Conflict of Interest

6.0 Review Panel
1.0 Purpose

To aid in assuring knowledge and compliance of all persons involved in any aspect of human subject research by documenting the requirements for the definitions of the ‘project status’ and ‘item status’ for the Health Sciences IRB.

2.0 Scope

The SOP applies to all human subject research falling under the purview of the Health Sciences Institutional Review Board.

3.0 Definitions

Item: Any submission to an approved IRB project. Items include but are not limited to all amendments, continuing reviews, revised investigator brochures, adverse events, and/or deviations.

Item Status: The status of each individual item within a project.

Project Status: The status of the project as a whole.

Project activities: Including, but is not limited to: screening, recruitment, records review, administering study related procedures/treatments, data analysis, long-term follow-up.
4.0 Policy/Procedure

Project Status Definitions – Projects as a whole have an individual approval status determined by the IRB during initial and continuing review. A single project can have multiple project statuses throughout the course of the study.

- Active-Open to Enrollment – Study is approved by the IRB and can actively enroll subjects.

- Closed to Enrollment: Treatment and/or Active Follow-Up – Study is approved by the IRB, closed to the enrollment of subjects, but some/all subjects are still actively receiving study treatment/intervention.

- Closed to Enrollment: Long-Term Follow-Up Only – Study is approved by the IRB, closed to enrollment of subjects, and all subjects have completed all study related treatment/intervention, but are being followed per study protocol to monitor study related outcomes.

- Closed to Enrollment: Data Analysis Only – Study is approved by the IRB, closed to enrollment of subjects, and all subjects have completed all study related treatment/interventions, including long-term follow-up. The data is currently being analyzed.

- Completed – All study related activities, including data analysis, are finished. Study records have been shipped to the sponsor (if a sponsored study) and this site has been closed out (if multi-site study). If there is a need to reevaluate the data at any point the study is not considered completed, but instead is closed to enrollment, data analysis only (see above definition).

- Expired – Approval period for the study has passed and the study was not renewed through the appropriate Continuing Review paperwork.

- Never Activated – Study was approved by the IRB but was never initiated by the researcher and/or sponsor at this site (if multiple site study).

- On-Hold – A study may be placed on-hold for many reasons, including a request by the sponsor, regulatory agency (FDA), or for noncompliance. No subjects may be enrolled during the on-hold period and no study activities may take place, excluding treatment/interventions for currently enrolled subjects for which stopping the treatment/intervention may cause undue harm to the subject.

- Temporarily Closed – Usually a study is temporarily closed to enrollment of subjects during a planned interim analysis or occasionally for review of adverse events by a data safety monitoring board. The study is still approved by the IRB, however no new subjects are enrolled during the closure. Subjects currently enrolled in the study may still receive treatment/intervention.

- Terminated – Study was terminated by investigator

- Terminated for Non-Compliance – Study was terminated by IRB for cause
• Other – For use when none of the above categories apply.

• Transferred to Campus IRB – Studies which are better suited for review by the Campus IRB due to the nature of the study and/or the expertise of the Campus IRB, or for an investigator which is under the purview of the Campus IRB but accidentally submitted an application to the HS IRB.

Item Status Definitions: Each individual item within a particular project has an individual approval status as determined by the IRB. The approval of an individual item does not dictate the overall project approval, as they are independent from each other. An individual item may, however, dictate the overall project status be changed. For example, an amendment may be submitted which states the project is now closed to enrollment. This item, the amendment, will be acknowledged (as defined below) and the overall project status will be changed to “closed to enrollment” to reflect the new status.

• New – An item has been started by an investigator on the eIRB, but it has not been submitted.

• Pending – An item has been submitted through the eIRB, but it has not been reviewed by the IRB. Once a form has been submitted and is listed as pending, the investigator may not edit or change the form unless it is returned to them (see definition of returned).

• Returned – An item that has been submitted through the eIRB but for some reason (such as to necessitate revisions) the form has been returned to the investigator for editing.

• Supporting Documents Needed – An item has been submitted through the eIRB, but the supporting materials (such as the required signature page, revised forms, or supplemental materials) have not been received by the IRB office. The item will not be reviewed until the supplemental materials have been received.

• Under Review – The item is currently being reviewed by the IRB.

• To Reviewer – The item has been sent for review to a designated board member.

• Signature Pending – The item is pending a signature from one of the board chairs.

• Deferred – The item was deferred at a board meeting pending clarification.

• Postponed – The item was unable to be reviewed at the scheduled board meeting due to a lack of a reviewer or other circumstances (such as loss of quorum) and will be held over until the next available meeting.

• Approved – The item was approved by the IRB.

• Disapproved – The item was disapproved by the IRB.

• Acknowledged – The item was acknowledged by the IRB. Acknowledgement signifies the IRB’s receipt and acceptance of the materials. Items that are acknowledged generally include but are not limited to removal of study staff, completion forms, notices of closure to
enrollment, revised investigator brochures or drug inserts, and adverse events.

- Withdrawn – The item was withdrawn from review prior to IRB approval. Items may be withdrawn from review for multiple reasons, such as a duplicate entry or the investigator does not wish to continue with pursuing the item.
Project Reviews and Assessments

Effective Date: December 12, 2005
Original Approval Date: December 12, 2005
Revision Date:

Approved By: Niels Beck, PhD
Chair, Health Sciences IRB

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1.0 Purpose
To assure that all research and sponsored projects involving human subjects are conducted in an ethical manner and comply with regulatory standards for research involving human subjects.

2.0 Scope
The SOP applies to all human subject research falling under the purview of the Health Sciences Institutional Review Board.

3.0 Definitions
None

4.0 Policy/Procedure

Study Identification
Studies will be identified for review either randomly or for cause. Coordination will be attempted to work with VA auditing on studies utilizing approved at MU and the VA and with billing.
compliance audits. Every effort will be made to avoid duplication of effort and burden on the investigator.

Notification
A written review notification will be sent to the principal investigator by the IRB Office. The Investigator will then be contacted to arrange a time for the review. At the beginning of the review, an initial meeting will take place with the PI and study coordinator to review the review schedule.

Audit Review
The project review will consist of review of all documentation pertinent to the study. This includes but is not limited to:

- Informed consents
- Selection of subject records
- Study documents and correspondence
- Interviews with study staff

At the conclusion of the review, a closeout meeting will take place to discuss review findings and answer any questions. A project review report containing findings and recommendations will then be prepared by the Compliance Officer and sent to the Principal Investigator and the IRB Chair.

Report of Findings
All efforts will be made to resolve issues found informally with the Investigator and study staff. If serious violations are found procedures will be followed per the HS IRB Noncompliance policy.
Quorum Requirements for Board Meetings

Effective Date: February 16, 2001
Original Approval Date: February 16, 2001
Revised Date: May 5, 2003
Reviewed: October, 2005

Approved By: Niels Beck, PhD
Chair, Health Sciences IRB

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1.0 Purpose
To aid in assuring knowledge and compliance of all persons involved in any aspect of human subject research by documenting quorum requirements.

2.0 Scope
The SOP applies to all human subject research falling under the purview of the Health Sciences Institutional Review Board.

3.0 Definitions
None

4.0 Policy/Procedure

The HS IRB defines quorum as a simple majority (or 51%) of the Board membership. As long as a quorum is present, a simple majority of voting members present is necessary for a motion to pass.

The HS IRB requirements for quorum for a meeting are:
1. The IRB shall assure valid quorum is present before a meeting can be convened.

2. The IRB shall include at least one nonscientific member in a valid quorum.

3. The IRB shall assure a valid quorum is present before review and action on any items before the board.

4. If the quorum fails at any time during a convened meeting, the meeting is terminated from further action until the quorum can be restored.

5. Any actions taken in the absence of a valid quorum is ineffective and lacks IRB authority.

6. The IRB shall record the names of every member present at each convened meeting in the minutes as evidence of a valid quorum.

7. The IRB shall record the number of votes for all actions in accordance with 45 CFR 46.115(a)(2) which specifies the recording the total vote count and the delineation of votes FOR, AGAINST, ABSTAINING, and ABSENT.

8. The IRB shall retain these records for at least three (3) years, and records relating to research that is conducted shall be retained for at least three (3) years after completion of the research.

If the issue of quorum is in question for a particular subcommittee Board meeting, a member of the other subcommittee Board will be asked to attend the alternate meeting and will be counted as part of the quorum for that meeting since the individual is a documented Board member.

If a conflict of interest arises with one of the Board members, a valid quorum must be present or the meeting must be terminated from further action until a valid quorum is obtained.

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Radiation Safety

Effective Date: June 1, 2004
Original Approval Date: October 1, 2002
Revision Date: May 1, 2004
May 17, 2004

Approved By: Niels Beck, PhD
Chair, Health Sciences IRB

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- Purpose
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- Policy/Procedure
- Administrative
- Procedure

1.0 Purpose

To aid in assuring knowledge and compliance of all persons involved in any aspect of human subject research by documenting the requirements for Radiation Safety review.

2.0 Scope

The SOP applies to all human subject research falling under the purview of the Health Sciences Institutional Review Board.

3.0 Definitions

Radiation: Ionizing radiation that includes the use of, but not limited to, x-rays, CTs, nuclear medicine treatments, radiation therapy, or radioactive materials administration.
4.0 Policy/Procedure

Administrative

The Radiation Safety Committee (RSC) is a separate University entity, under the auspices of Environmental Health & Safety, empowered with the “review and approval of all new requests for authorization and requests for significant changes in existing authorizations” (Radiation Safety Manual) as described in the University’s licenses granted by the Nuclear Regulatory Commission.

Review and approval by the RSC is REQUIRED for any IRB study or amendment which involves the use of ionizing radiation (e.g. x-ray studies, CT’s, nuclear medicine studies or treatments, radiation therapy, or radioactive materials administrations) REQUIRED for the protocol, even if it is not part of the research question. This requirement comes directly from the RSC and the regulations which it must follow. The IRB only serves as a flow-through of information.

The review of radiation related issues is beyond the expertise of the Board; and therefore, the IRB will defer its opinion on radiation safety issues to the Radiation Safety Committee per 45 CFR 46.107(f). The IRB will hold its final approval until approval from the RSC has been received in the IRB office.

Procedure

1) If the question on the IRB application which asks, “Is ionizing radiation required for this project even if it is not part of the research questions?” is marked “Yes,” the HS IRB office will forward to the RSC a copy of the project application, consent form, and protocol (information which was provided to the IRB as part of the required number of copies). The HS IRB office staff will also provide RSC information to which IRB meeting a particular project was assigned and when the IRB packets are delivered to board members.

2) The RSC office will directly contact the investigator if there are any radiation-related questions and issues, as well as requests for additional information and/or materials.

3) The RSC will make every effort to provide to the HS IRB its administrative and scientific review and approval in a timely fashion, preferably before the IRB meeting when a particular project will be discussed. Dr. Westgate, Chair of the Medical Quorum, RSC subcommittee, has already provided to the HS IRB office a letter documenting his conflict of interest status. Due to hematology/oncology department policies, Dr. Westgate is listed as a co-investigator on all hematology/oncology protocols. Dr. Westgate will not provide reviews and/or advise HS IRB on in-house or industry-sponsored projects on which he serves as a Principal Investigator. If there are any radiation questions/issues on those projects, RSC will need to secure an appropriate consultant.

4) The HS IRB will make its approval contingent upon receiving approvals from RSC, unless otherwise indicated by RSC for a specific project.

5) The following paragraph will be placed in the HS IRB “received application pending letter/e-mail”: 
Please note that it is the researcher responsibility to make sure that all protocols needing Radiation Safety Committee (RSC) and Institutional Biosafety Committee (IBC) approvals receive such approvals prior to protocol initiation. The HS IRB will not issue the final project approval if RSC and/or IBC approval is not on file in the HS IRB office. To assist in the review process, the IRB office will forward a copy of the relevant study materials to the RSC or IBC for review, when needed. The RSC or IBC will directly contact the investigator with any questions or request for follow-up. Please contact the Radiation Safety Office at 573-882-7221 for more information on RSC requirements or the Institutional Biosafety Committee office at 882-7018 for more information on IBC requirements.
1.0 Purpose

To aid in assuring knowledge and compliance of all persons involved in any aspect of human subject research by documenting the requirements for record keeping.

2.0 Scope

The SOP applies to all human subject research falling under the purview of the Health Sciences Institutional Review Board.
3.0 Definitions

*Research Data* - Recorded information regardless of the form or media on which it may be recorded. It may include laboratory workbooks, notes, technical data, questionnaires, case histories, synthetic compounds, cell lines, mapping information, plant, animal, chemical compounds or any other materials and/or information required to replicate or verify the results of an experiment or other scholarly exercise (per Records Management Policy, see [http://www.umsystem.edu/ums/departments/fa/management/records/](http://www.umsystem.edu/ums/departments/fa/management/records/)).

*University Record* - Any papers, E-mail, electronic record, electronic image, maps, photographs, original microfilm, or other documentary materials regardless of physical form or characteristics, made, produced, executed or received by any academic or administrative staff member in connection with the transaction of University business (per Records Management Policy, see [http://www.umsystem.edu/ums/departments/fa/management/records/](http://www.umsystem.edu/ums/departments/fa/management/records/)).

*Electronic Record* - University information created, retained or maintained in any digitized configuration on a mainframe, PC, hard disk, tape, cassette, floppy or any other magnetic storage format, electronic image (optical disk, CD-ROM) or other optical technology, and any other type of electronic technology, may be an electronic record that must be retained to meet administrative, fiscal, legal, research and historical requirements of the University (per Records Management Policy, see [http://www.umsystem.edu/ums/departments/fa/management/records/](http://www.umsystem.edu/ums/departments/fa/management/records/)).

4.0 Policy/Procedure

**IRB Records**

*General information* - The HS IRB will prepare and maintain adequate documentation of IRB activities per 45CFR46.115 and 21CFR56.115, including the following:

1. **Protocols**: All available documents related to submission of a research protocol including, but not limited to, the IRB application, protocol, scientific evaluations, grant (if applicable), Investigator’s Brochure (if applicable), consent form(s), progress reports submitted by the Principal Investigator (PI), recruitment and advertisement materials, and reports of injuries to subjects.

2. **Minutes**: Minutes of the committee meetings that document the:
   - Attendance at meetings
   - Actions taken by the Committee
   - Vote on these actions (including the number of members voting to approve, disapprove, and abstaining).
   - Basis for requiring modifications or disapproving the research, and a summary of controverted issues and their resolution.

3. **Continuing Review**: Records of Continuing Review activities including, all supporting documentation. See CRR SOP for detailed information.

4. **Correspondence**: Copies of all correspondence between the IRB and PIs will be filed in the relevant protocol file.

5. **Membership Lists**: A list of committee members identified by:
   - Name
   - Earned degrees
   - Representative capacity
• Indications of experience such as board certifications, licenses, etc. sufficient to describe each member’s chief anticipated contributions to IRB deliberations.
• Any employment or other relationship between each member and the IRB (e.g. full-time employee, part-time employee, member of governing panel or board, stockholder, paid or unpaid consultant).

Changes in IRB membership shall be reported to OHRP in accordance with 45CFR46.103(a).

The HS IRB office routinely sends IRB records to Records Management in accordance with University policy regarding retention of records. Records relating to research which are completed, terminated, withdrawn, or otherwise closed are maintained in the IRB office for a period of one year. After one year, the IRB office transfers all study records to Records Management to be stored until policy dictates they be destroyed and/or archived.

**Investigator Records**
Investigator records are considered the official research file. The IRB office only maintains copies of documents sent to the investigator. It is the investigator’s responsibility to maintain adequate documentation of research procedures/process. In case of a request to review the file all information must be readily available to be reviewed by the appropriate individuals in a reasonable and a reasonable manner.

Research records must be retained for at least three years after completion of the research, similar to requirements for IRBs. However, the University of Missouri policy regarding the retention of research data states the data must be retained “for seven (7) years after the final report on the research project has been submitted” (from [http://www.umsystem.edu/ums/departments/fa/management(records/guide/academic/01801.shtm](http://www.umsystem.edu/ums/departments/fa/management/records/guide/academic/01801.shtm)).

Additional requirements for records retention may apply depending on the language in the contract or the type or sponsor of the research (see section on “special circumstances” below). For studies that are sponsored, it is common that after data collection is completed at this site the records are shipped off to the sponsor for records storage and data analysis. The sponsor, then, is required to adhere to all regulations regarding records storage. The university maintains policies regarding the storage of research records (see Records Management for more information: [http://www.umsystem.edu/ums/departments/fa/management/records/](http://www.umsystem.edu/ums/departments/fa/management/records/)).

**Ownership**
Any record that is determined to be a University Record (see definitions above) is property of the University of Missouri. This includes research records created, developed, or otherwise maintained or created under the auspices of employment, contract, or grant with the University. Original research records must remain at the University even if the researcher has left the institution. The researcher’s department must provide a means of securing and storing the research records in connection with all applicable rules relating to this and Records Management policies. A researcher may, however, make copies of the original research records to take with them if they leave the institution for continued analysis and future research.

**Special Circumstances**
Additional requirements for records retention may apply depending on the type and/or sponsor of the research. Below are some possible additional requirements to consider when determining whether records may be removed or destroyed.
VA Research Records
Records retention by investigators either using or who are part of the Truman VA Memorial Hospital may have additional records retention requirements other than stated in the above policy. All records pertaining to the VA must also comply with any VA policies.

FDA Regulated Research
Records retention by investigators for FDA regulated trials may have additional requirements regarding maintaining records. All records pertaining to FDA regulated trials must also comply with any FDA records retention policies.

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Recruitment of Special Populations

Effective Date:  February 16, 2001
Reviewed Date:  October 2005
Approved By:  Niels Beck, PhD
Chair, Health Sciences IRB

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1.0 Purpose
To assure knowledge and compliance by documenting the regulations pertaining to recruitment of subjects in human research.

2.0 Scope
The SOP applies to all human subject research being conducted which falls under the purview of the Health Sciences Institutional Review Board.
3.0 **Definition**

1. **Assent**: A child’s affirmative agreement to participate in research. Mere failure to object should not be construed as assent.

2. **Assurance**: a formal binding document submitted by an institution to a federal agency within the Department of Health and Human Services, that assures institutional commitment to and compliance with the requirements of the federal regulations governing the protection of human subjects involved in research.


4. **Benefit**: A valued or desired outcome; an advantage.

5. **Children**: Persons who have not attained the legal age for consent to treatment or procedures involved in the research, as determined under the applicable law of the jurisdiction in which the research will be conducted.

6. **Cognitively Impaired**: Having either a psychiatric disorder, an organic impairment that affects cognitive or emotional functions to the extent that capacity for judgment and reasoning is significantly diminished. Persons under the influence of or dependent upon alcohol or drugs, suffering from degenerative diseases affecting the brain, terminally ill patients, and persons with severely disabling physical handicaps, may be compromised in their ability to make decisions in their best interests.

7. **Competence**: A legal term used to denote the capacity to act on one’s own behalf; the ability to understand information presented, to appreciate the consequences of acting or not acting on that information, and to make a choice.

8. **Dead fetus**: An expelled or delivered fetus that exhibits no heartbeat, spontaneous respiratory activity, spontaneous movement of voluntary muscles, or pulsation of the umbilical cord.

9. **Emancipated minor**: A legal status conferred upon persons who have not yet attained the age of legal competency as defined by state law, but who are entitled to treatment as if they had by virtue of assuming adult responsibilities, such as self-support, marriage or procreation.

10. **Fetus**: The product of conception from the time of implantation until delivery. If delivered or expelled fetus is viable, it is designated an infant. Generally
“fetus” refers to later phases of development, and “embryo” refers to earlier phases of development.

11. **Guardian**: An individual who is authorized under applicable state or local law to give permission on behalf of a child to general medical care.

12. **Human In Vitro Fertilization**: Any fertilization involving human sperm and ova that occurs outside the human body.

13. **Incapacity**: An individual’s mental status and means inability to understand information presented, to appreciate the consequences of acting or not acting on that information, and to make a choice.

14. **Institutional Review Board**: A specially constituted review body established or designated by an entity to protect the welfare of human subjects recruited to participate in biomedical or behavioral research.

15. **Minimal Risk**: Where the probability and magnitude of harm or discomfort anticipated in the proposed research are not greater, in and of themselves, than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests.

16. **Recruitment**: To solicit, communicate, question a potential subject with the intention of enrolling them into a research project under the jurisdiction of the University of Missouri-Columbia.

17. **Research**: A systematic investigation, including research development, testing and evaluation, or gathering and analysis of information, designed to develop or contribute to generalizable knowledge. Activities that meet this definition constitute research whether or not they are conducted or supported under a program, which is considered research for other purposes. For example, some demonstrations and service programs may constitute research activities.

18. **Subjects**: Individuals whose physiologic or behavioral characteristics and responses are the object of study in a research project. Under the federal regulations, human subjects are defined as a living individual(s) about whom an investigator (whether professional or student) conducting research obtains: (1) data through intervention or interaction with the individual; or (2) identifiable private information.

19. **Jurisdiction**: the power to rule, exercise control, and authority over a matter.

20. **Protocol**: The written design or plan of an experiment, research activity, survey, observation proposal submitted to an IRB for review and to an agency for research support. It should include a description of the research design or
methodology to be employed, the eligibility requirements for prospective subjects and controls, the treatment regimen(s), the proposed methods of analysis, and relevant federal requirements codified in 45 CFR 46, that will be performed on the collected data.

4.0 Policy/Procedure

The HS IRB recognizes the importance of its role in ensuring the equitable selection of research subjects. In fulfilling this responsibility, the HS IRB shall review the methods that investigators use to recruit Subjects and subscribe to the following guidelines:

1. RECRUITMENT OF SPECIAL SUBJECT POPULATIONS
Federal Regulations require that the HS IRB gives special consideration to protecting the welfare of particularly vulnerable subjects, such as children, prisoners, pregnant women, mentally disabled persons, or economically or educationally disadvantaged persons. Investigations involving these subjects require the HS IRB to take additional steps to assure their safety and welfare.

NOTE: Exempt Review Inapplicable
The exemptions of 45 CFR 46.101(b) does not apply to research involving prisoners, fetuses, pregnant women, or human in vitro fertilization.

The exemption of 45 CFR 46.101(b)(2), for research involving survey or interview procedures, or observation of public behavior, does not apply to research involving children, except for research involving observations of public behavior when the investigator does not participate in the activities being observed.

a. Women of Childbearing Potential
Research involving women who are or may become pregnant receives special attention from the HS IRB because of the additional health concerns during pregnancy and because of the need to avoid unnecessary risk to the fetus. Therefore, the women of childbearing potential will receive the same review considerations from the Campus IRB as followed for Pregnant Women in Research. Please refer to item (3) for further discussion.

b. Use of Pregnant Women in Research
Research involving women who are or may become pregnant receives special attention from the HS IRB because of the additional health concerns during pregnancy and because of the need to avoid unnecessary risk to the fetus. The IRB must determine when the informed consent of
the father to the research is required. The IRB must take additional measures to assure the protection of this subject category by:

a. assessing whether the research is directed toward the mother’s health or toward the fetus; and
b. the risks to the woman and to the fetus or infant are minimal
c. assessing the exclusion of women from research to assure the reason is an equitable one that doesn’t deprive women from the possibility of benefiting from the study. However, women of childbearing potential may be excluded because of the concern for the welfare of the fetus, possible legal liability, and harm to mother.
d. Informed consent must be in writing. Oral consent is prohibited. The written consent should be obtained from both the father and the pregnant woman, unless:
   i. the purpose of the research is to meet the health needs of the mother;
   ii. the father’s identity or whereabouts cannot reasonably be ascertained;
   iii. he is not reasonably available’ or
   iv. the pregnancy resulted from rape.

No monetary incentives may be offered to induce a woman to terminate her pregnancy.

c. Fetuses and Human In Vitro Fertilization
   The HS IRB recognizes that research involving the human fetus raises special concerns due to the unique and inextricable relationship to the mother, in that the fetus and human in vitro cannot consent to being a research subject.

d. Use of Children and Minors in Research
   The HS IRB recognizes the special vulnerability of children and takes special ethical and regulatory considerations when reviewing research projects involving this category of subjects. The IRB shall consider the benefits, risks, and discomforts inherent in the proposed research and assess their justification in light of the expected benefits to the child-subject or to society as a whole.

The IRB should calculate the Degree of Risk in relation to the Benefit derived from participating in the research. The federal regulations require the IRB to classify research involving children into one of the four categories and to document their discussions of the risks and benefits of the research study. The four categories of research involving children based upon the degree of risk and benefit to the subjects is:
Research Categories:

a. **LEVEL I** Research not involving greater than minimal risk.[45 CFR 46.404].

b. **LEVEL II** Research involving greater than minimal risk, but presenting the prospect of direct benefit to an individual subject. Research in this category is approvable provided:
   i. the risk is justified by the anticipated benefit to the subject; and
   ii. the relationship of risk to benefit is at least as favorable as any available alternative approach [45 CFR 46.405].

c. **LEVEL III**: Research involving greater than minimal risk with no prospect of direct benefit to individual subjects, but likely to yield generalizable knowledge about the subject’s disorder or condition. Research in this category is approvable provided:
   i. the risk represents a minor increase over minimal risk;
   ii. the intervention or procedure presents experiences to subjects that are reasonably commensurate with those inherent in their actual or expected medical, dental, psychological, social, or educational settings; and
   iii. the intervention or procedure is likely to yield generalizable knowledge about the subject’s disorder or condition that is of vital importance of the understanding or amelioration of the subject’s disorder or condition [45 CFR 46.406].

d. **LEVEL IV**: Research that is not otherwise approvable, but which presents an opportunity to understand, prevent, or alleviate a serious problem affecting the health or welfare of children. Research that is not approvable under 45 CFR 46.404, 46.405, or 46.406 may be conducted or funded by DHHS provided that the IRB and the Secretary, after consultation with a panel of experts, finds that the research presents a reasonable opportunity to further the understanding, prevention, or alleviation of a significant problem affecting the health and welfare of children. The panel of experts must also find that the research will be conducted in accordance with sound ethical principles [45 CFR 46.407].

Consent Procedures

When children or minors are involved in research, the investigator must obtain the ASSENT of the child or minor and the PERMISSION of the parent(s) or legal representative, in place of the consent of the subjects. The IRB must:

a. Obtain the permission of both parents if possible, or determine the conditions under which one parent may be considered “not reasonably available.” [45 CFR 46.408]. This requirement may be waived by the IRB on a case-by-case basis.
   a. The IRB may consider alternative procedures for protecting the rights and interests of the child. (i.e. Court appointment of a special guardian).
b. If the parents' permission is insufficient, inappropriate, or in opposition to the best interests of the child, the IRB may consider asking for a court to review the parent’s decision.

c. The HS IRB shall be aware of the age of majority specific to state law and court decisions.

d. The HS IRB shall consider inviting a legal consultant to serve as a secondary reviewer on the proposal.

b. Recognize that a child may not have the legal capability of giving informed consent, but does possess the ability to assent or dissent to participation in research.

c. The HS IRB shall determine if child assent should be sought from given subjects on a case-by-case basis. Assent will be sought if the IRB determines that the child is capable of providing it. The IRB may waive this requirement at anytime.

research, but may overruled by the child’s parents at the discretion of the IRB. If the child is a mature adolescent and death is imminent, it is recommended that the child’s wishes should be respected.

d. The Assent document should include:

   a. an explanation of the proposed research procedures in a language specific, understandable, and appropriate for the age, experience, maturity, and condition of the child.
   b. an explanation of the benefits of the research.
   c. an explanation of the risks, discomforts, and inconveniences associated with the research;


e. Use of Prisoners in Research

The HS IRB recognizes that research involving prisoners raises the issue of whether the subjects’ situation prohibits the exercise of free choice to participate in research and whether or not the prisoners’ confidentiality will be adequately maintained.

When reviewing research involving prisoners, the IRB shall:

a. Invite a prison representative with the appropriate background, who is not a member of the board, to review the proposal and consult on behalf of the prisoner’s rights;

b. the research MUST fit into one of the four categories:

   a. Category I: Studies of the possible cause, effects, and processes of incarceration and criminal behavior, and involves no more than minimal risk;
   b. Category II: Studies of prisons as institutional structures or of prisoners as incarcerated persons, and involves no more than minimal risk;
   c. Category III: Studies on particular conditions affecting prisoners as a class; and
d. Category IV: Studies involving a therapy likely to benefit the prisoner subject

c. Consider the benefit in relation to the risk to the subject, including the potential for retaliation for receiving a research benefit.
d. Assess whether the risks involved in the research commensurate with risks that would be accepted by nonprisoner volunteers.
e. Selections of subjects are fair and immune from arbitrary intervention by prison authorities or prisoners.
f. Inform the prisoner that participation will not affect parole decisions, and assure that parole boards will not consider the research in making their decisions.
g. Obtain certification from the institution that all of the above responsibilities have been fulfilled.
h. Understand that the “risk” assessed in this category, is not the risks “normally encountered...by prisoners,” but rather with risks “normally encountered in the daily lives, or in the routine medical, dental or psychological examination of health persons.”
i. Review the institution’s permission letter sent to the investigator, which outlines the granting of permission, purpose of research, prison contact person;
j. Measures that provide the subject the opportunity to participate without coercion, undue influence, deprivation of privacy or confidentiality of responses during the subject’s completion of instruments, interviews, or designated research activity.

f. Use of Cognitively Impaired Persons:
The HS IRB appreciates the ethical concerns in research involving individuals that are cognitively impaired which may compromise their capacity to understand the information presented and their ability to make a reasoned decision about participating in research. The IRB suggests this category of research shall be conducted only where:

a. Confidentiality and protection of the subject’s privacy are maintained;
b. Subject comprises the only appropriate subject population;
c. Research focuses on an issue unique to the subject population;
d. Research involves no more than minimal risk, unless the purpose is therapeutic;
e. Special review considerations are required for institutionalized subjects and must be reviewed by the full board;
f. Assess the risk compared to the benefit of participation;
g. Require the investigator to specifically describe the psychological or medical screening criteria;
h. Assure that the investigator satisfies the Informed Consent criteria:
a. Presume the subject is competent to consent unless there is evidence of serious mental disability that would impair reasoning or judgment.

b. Obtain consent from the legally authorized individual who has been appointed to act on behalf of the subject, cautioning against the use of:
   i. institutional officials
   ii. family members;
   iii. financial administrators.
   i. Seek a legal consultant to determine the applicable laws of the state, if needed.
   j. Seek the subject’s assent where applicable, and determine whether the subject’s dissent shall override the legal representative’s consent on a case-by-case basis.

g. Use of Students and Employees
   The HS IRB recognizes the special concerns that may present when students participate in research projects. Since the federal regulations do not provide explicit protections for these subjects, the IRB shall take extra measures to ensure the safety and welfare for students. The IRB will:
   a. Pay special attention to protect against coercion and offense to the voluntary requirement for research involving humans:
   b. Add heightened scrutiny for projects requiring participation in the research project for course credit to assure the participants are not coerced to participate;
   c. In research projects that offer extra-credit for participation, the investigator must provide an comparable alternate method of credit for a student declining to participate:
      a. The paper may not be graded and receive the same amount of points as research participants do, however, the quality and quantity of time devoted to the paper should be worthy in comparison to the study participant’s investment of time;
      b. The student shall not lose the extra credit if they withdraw from the study;
   d. The investigator should consider recruiting subjects through general announcements or advertisements, rather than through individual solicitations or classroom solicitations.
   e. The study must be minimal risk

Employees Involved in Research
   The issues with respect to employees as research subjects are essentially identical to those involving students as research subjects, in that employee research programs may raise the possibility that the decision will affect performance evaluations or job advancement. It may also be difficult to maintain the confidentiality of personal
medical information or research data when the subjects are also employees.
Use of Low-Income Persons
The HS IRB realizes the importance of achieving an equitable representation of subjects involved in research, and may create special concerns during the review process. The IRB will assure that:
   a. Avoidance of coercion and undue influence upon subjects to participate;
   b. Assess the mechanism for offering incentives of value to the subjects:
   c. The subject’s privacy rights and confidentiality are addressed.
   d. Opportunity for reasonable alternatives are available.

h. Use of Minorities
The HS IRB is aware that members of racial and ethnic minority groups raises concerns about appropriate levels of inclusion and generalizability of study results, similar to the inclusion of women in studies. The involvement of minorities in research may raise concerns about the selection of subjects, the possibility of special vulnerability on the part of some prospective subjects, and about consent and the relative strengths and weaknesses of vulnerable groups in the consent process.

Investigators must provide:
   a. A clear compelling rationale for their exclusion or under representation of the subject.
   b. Select an equitable choice of a geographic area for recruitment must be representative of the racial and ethnic groups in study populations;
   c. Safeguard the consent process to ensure open and free communication:
      a. Written in a language specific to the population
      d. Consider cultural norms when instituting the consent policy.

i. Use of Elderly/Aged Persons
The HS IRB realizes that the participation of the Elderly and Aged subjects in research poses several issues for consideration, primarily whether the subject needs special protections. The IRB must balance the need to protect with the need to provide respect for persons. There is no age requirement at which time prospective subjects should become ineligible to participate in research, therefore the inclusion of elderly subjects in research is very important. The IRB shall:

   a. Take special consideration to closely monitor research conducted in nursing homes or other institutions, unless the involvement of the institutional population is necessary to the conduct of the research.
b. The IRB may consult with an expert on this subject prior to making a determination about the research.

j. International Research
All human subjects research in which American investigators are involved, and which would be subject to the federal regulations if it were conducted wholly within the United States, must comply with the federal regulations for the protection of human subjects in all material respects.
Reporting Structure of the IRB

Effective Date: February 16, 2001
Reviewed Date: October 2005

Approved By: Niels Beck, PhD
Chair, Health Sciences IRB

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1.0 Purpose

To assure knowledge and compliance by documenting the reporting responsibilities of the Health Sciences IRB

2.0 Scope

This SOP applies to all human subject research being conducted which falls under the purview of the Health Sciences Institutional Review Board

3.0 Policy/Procedure

The Health Sciences IRB (HS IRB) is established pursuant to and in accordance with the regulations of the Department of Health and Human Services (45 CFR 46.101); the Food and Drug Administration (21 CFR 56.101); the Belmont Report; and the Multiple Project Assurance (#M1502) of the University of Missouri-Columbia. The HS IRB is an appropriately constituted administrative body established to protect the rights and welfare of human subjects that are recruited to participate in research activities conducted under the auspices of the University of Missouri-Columbia.
The HS IRB shall ensure prompt reporting to:

*Vice Provost for Research – University of Missouri-Columbia:*

1. All initial review, continuing review, and amendments to research projects that are reviewed by the HS IRB on a regular basis.
2. All adverse events involving risks to subjects or others.
3. Any serious or continuing noncompliance issues in violation of 45 CFR part 46 and HS IRB Policies.
4. Any HS IRB suspension or termination of approved research.
5. All Principal Investigator invoked closure of a research project.
6. The HS IRB shall retain all research records for at least three (3) years after the completion of the research project, and assure that all research records shall be accessible at all times for inspection and copying by authorized representatives of the HS IRB.

*Federal Department Heads or Agency and OHRP:*

1. All adverse events involving risks to subjects or others
3. Any HS IRB suspension or termination of approved research.
4. The HS IRB shall retain all research records for at least three (3) years after the completion of the research project, and assure that all research records shall be accessible at all times for inspection and copying by authorized representatives of the Federal Department or Agency and OHRP.

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Requirements for research by students

Effective Date: July 1, 2004
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Revision Date: NA

Approved By: Niels Beck, PhD
Chair, Health Sciences IRB

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1.0 Purpose
To assure knowledge and compliance by documenting the necessary elements of the requirement for research by students.

2.0 Scope
The SOP applies to all human subject research falling under the purview of the Health Sciences Institutional Review Board.

3.0 Definitions
Oral History - Activities consisting of systematic investigations involving open-ended, qualitative interviews that are designed to develop or contribute to generalizable knowledge (that is, designed to draw conclusions, create policy or generalize findings), or create archives for purposes of providing a resource for others to do research.

Research - A systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge.
Student – Any person who is enrolled in, auditing, or otherwise taking classes at the University of Missouri-Columbia or any other educational institution. Postdoctoral students and medical residents are considered students. Employees of the University of Missouri-Columbia or any other educational institution may also be enrolled in, auditing, or otherwise taking classes at the respective educational institution. Research conducted under the auspices of their employment, and not for a class, does not constitute student research. However, if in their function as a student in a class they plan to conduct research, then this does constitute student research and the following SOP applies.

4.0 Policy/Procedure

General Information
Research conducted by students at any entity under the purview of the HS IRB (see policy on scope of IRB authority), are subject to the same policies and procedures as research conducted by faculty (see policy on PI responsibilities). The IRB, in line with the University’s mission for teaching and research, will assist student researchers as much as possible in conducting human subject research according to sound ethical principles.

Graduate theses and dissertations are clearly understood as research and fall within the IRB purview when human participants are involved. The IRB process should be initiated before a thesis or dissertation proposal is accepted. Changes required by the committee should be submitted to the IRB using the amendment form on the eIRB. Major changes may necessitate the submission of a new IRB protocol.

Any student who wishes to conduct research at the University of Missouri-Columbia must have an advisor, mentor, or other faculty member who is employed by the University of Missouri-Columbia oversee their research study. If a student from outside the institution wishes to conduct research at a facility owned and operated by the University of Missouri-Columbia, and his/her research falls under the purview of the HS IRB, then he/she must have an advisor, mentor or other contact person employed by the University of Missouri-Columbia listed on the application. Additionally, the advisor/mentor/teacher must be listed on the consent form under “who to contact if you have questions.”

Class Projects:
Undergraduate or graduate student research activities, which reach outside of the classroom, may fall under the federal definition of research depending upon the type of interaction with the research participant(s). Educational activities designed to train students in research methods in the normal classroom setting usually do not fall within the federal definition of research as described in 45 CFR 46.102(d). However, any research conducted with the intent to either contribute to generalizable knowledge or to construct knowledge related to a specific situation that will be published or presented within an academic discipline, even that originating from the classroom activity, falls within the requirement for human subjects review. Please note that survey research, all pilot studies, and oral history research do meet this definition and must be approved by the IRB before a student sends out questionnaires, interviews subjects, or otherwise have contact with potential subjects.

Oversight of oral histories is based on the prospective intent of the investigator and the definition of “research” in 45 CFR 46.102(d) as a “systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge.” In other words, oral history and similar open ended interview activities that only
document a specific historical event or the experiences of individuals, without an intent to draw conclusions or to generalize findings do not constitute “research” as defined in 45 CFR 46 and thus are not subject to IRB review.

Class projects which are one, singular project conducted by the entire class may be submitted to the IRB under one investigator, the teacher. All students, however must be listed on the application and complete the required training. Individual class projects must be submitted as individual applications for review and approval.

Student researchers:
- Must obtain the signature of his/her advisor/mentor on all eIRB forms and/or documents submitted to the IRB before it will be reviewed. This includes the initial application, amendments, adverse events, and continuing review reports.
- Are subject to all PI responsibilities outlined in the SOP on PI Responsibilities.
- Must complete the appropriate IRB educational and HIPAA training (if appropriate).
- Need to submit a protocol, such as a dissertation or thesis, to be reviewed and approved with the application.
- Need to submit the required paperwork before any research is conducted. The IRB has a high volume of studies and has set deadlines to review studies on a first-come, first-serve basis. If the research must be completed within a certain semester, the IRB strongly recommends that students submit the required paperwork as soon as possible, so as to allow enough time to conduct the research before the school session ends.

Advisor/Mentor or Faculty/Teacher responsibilities:
For in-class educational activities designed to train students in research methods, the faculty instructor has the responsibility of ensuring that the students are educated on the general principles of research ethics, human subject protection, and that the students receive human subjects training.

For all other student research, including dissertation/theses, the faculty/teacher or advisor/mentor holds an equal amount of responsibility for the conduct of the research as the student researcher. Since this is an institution of higher education, it is expected that faculty/teacher or advisor/mentor will oversee and mentor student researchers through the research process. It is their responsibility to ensure that student researchers conduct the research in accordance with all applicable laws and regulations.

If a student is unavailable or has left the institution, it is the responsibility of the faculty/teacher or advisor/mentor to complete the required paperwork, including any Continuing Review or Completion paperwork.
Requirements for Research Outside of the Institution

Effective Date: July 1, 2004
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Approved By: Niels Beck, PhD
Chair, Health Sciences IRB

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1.0 Purpose
2.0 Scope
3.0 Definitions

Purpose

To aid in assuring knowledge and compliance of all persons involved in any aspect of human subject research by documenting the requirements for research conducted away from the University of Missouri-Columbia or MU Health Care.

Scope

The SOP applies to all human subject research falling under the purview of the Health Sciences Institutional Review Board.

Definitions

Engaged in research - Collaborating institutions become "engaged" in human subject research whenever their employees or agents (i) intervene or interact with living individuals for research purposes; or (ii) obtain, release, or access individually identifiable private information for research purposes. Also, institutions are engaged in research whenever they receive a direct HHS award to support such research, even where all activities involving human subjects are carried out.

Institution - Any public or private entity or Agency (including Federal, State, and other agencies)

4.0 Policy/Procedure

In research that is conducted away from the University of Missouri campus and MU Health Care, researchers incur additional obligations: (a) obtaining the permission of institutions to conduct the research in their locations and with subjects for whom they have some responsibility, (b) obtaining assurances from those institutions that they will conform to Federal regulations and University policy regarding human subject research, and (c) assurance that all study staff/investigators are trained and added to the study.

The IRB requires that researchers provide documentation from the off-campus institution that the researcher has been given permission to conduct research at locations administered by the institution. The type of permission depends on the location and the nature of the research. However, the following guidelines apply.

1. IRB Review: When the off-campus institution has an Institutional Review Board (IRB), then the researcher must provide a letter from the off-campus IRB stating its approval for research to be conducted at that location. Examples of institutions with IRBs include another comprehensive university, a teaching hospital, or a state mental health institution.

Additionally, if the research is to be conducted under the name of the University of Missouri, connected in any way to the researcher’s employment at the University of Missouri, utilizes University of Missouri resources, and/or will be published under the name of the University of Missouri, then approval from the Health Sciences IRB must be obtained, regardless of whether the other institution has their own IRB. If the research will take place primarily at the different institution, then the HS IRB and investigator will work with the local IRB to develop a consent form and/or HIPAA authorization that meets the requirements of both institutions.

If the research is to be conducted independent of any affiliation with the University of Missouri, then HS IRB approval is not necessary; however, approval at the other institution may still be required.

If a University of Missouri-Columbia investigator is participating in a research project at another institution, but their involvement does not include dealing with human subjects in any way (including but not limited to recruitment, implementation of study procedures, and/or data analysis), then review by the HS IRB is not necessary. This type of involvement may include activities such as when acting as a consultant or serve in a similar advisory or administrative capacity. These roles must have no direct involvement with human subjects or their data and must not be engaged in research as defined above (see section 3.0).
2. **Letter of permission**: At times, the IRB may determine that the role of the off-campus institution is to provide space or some service, and that the other institution is in no way collaborating in the research. In such cases, the IRB may require a letter of permission from an official of the institution (IRB permission will always be required when the other institution has an IRB). For example, if a researcher recruits subjects during an activity sponsored by a church or social club, and it is explicit that the church or social club does not have any additional role in the research (such as obtaining informed consent), then the IRB will ask that the researcher provide the IRB with documentation that the church or club has given permission for the recruitment of subjects.

Research using the school districts occurs frequently, and as such, a letter of permission is required from the superintendent and possibly even each individual principal and/or teacher from the school/system. Research also occurs frequently at nursing homes and the appropriate permission must be obtained from the nursing home director prior to the research being conducted.

Special care should be taken to make sure that the off-campus institution is not engaged in research as defined by OHRP in their guidance issued January 26, 1999 entitled, Engagement of Institutions in Research (see definition above). If the off campus institution is engaged in research, then an FWA will be needed (see below).

3. **Independent/Unaffiliated investigator agreement (IIA)**: This agreement is for use by investigators outside of the University of Missouri-Columbia (MU) who are participating in an MU research project (regardless of funding source) when acting in their name independent of any hospital, clinic, or other facility (see appendix 1). These investigators may be local physicians or other private individuals not affiliated with the University of Missouri or any other institution. The IIA is a formal document that is available from the IRB office. The IIA states that the investigator will abide by the ethical guidelines, Federal regulations, and University policies regarding human subject research. The IIA also grants the IRB authority and oversight over the research project. The investigator must agree to allow the IRB to audit, view, or otherwise enter the private premise to review, when necessary, any study related files and/or procedures (such as the consent process) before the University will allow the research to take place. This agreement must be signed by the investigator. It is then sent through General Counsel’s office before it can be reviewed and signed by the Institutional Official (Vice Provost for Research). A copy of the agreement will be placed in the study file, the original will be returned to the investigator, and a copy will be kept on file in the Office of Research.

4. **Federal Wide Assurance (FWA)**: Each legally separate entity that engages in federally conducted or supported human subject research needs its own Assurance. FWAs are available from the Office of Human Subjects Protection (OHRP). Additionally, if the institution is not engaged in federally conducted or supported research, but still conducts research (not funded federally), then an FWA should be submitted. Institutions that have an FWA generally also have an IRB. In those circumstances where institutions do not have an IRB, then the MU HS IRB may be designated as the IRB of record for that institution on the FWA. If the MU HS IRB is designated as the IRB of record, then it also grants the IRB authority and oversight over the research project. The separate institution must agree to allow the IRB to audit, view, or otherwise enter the private premise to review, when necessary, any study related files and/or procedures (such as the consent process) before the University will allow the research to take place.
5. **Single Project Assurance (SPA):** A SPA may be used when the off-campus institution does not have an IRB, FWA, or does not plan to engage in any further research beyond the project in question. The SPA is grant/project specific and expires at the end of a particular grant/project. If the institution might engage in research beyond the single project, then an FWA should be submitted. SPAs are available from the Office of Human Subjects Protection (OHRP). An official of the off campus institution must sign the SPA with the researcher and the University of Missouri-Columbia. The SPA states that the institution will abide by the ethical guidelines, Federal regulations, and University policies regarding human subject research. The SPA also grants the IRB authority and oversight over the research project. The off-campus institution must agree to allow the IRB to audit, view, or otherwise enter the private premise to review, when necessary, any study related files and/or procedures (such as the consent process) before the University will allow the research to take place. The SPA is a formal document that is available from the IRB office. Examples of institutions that may require an SPA include small colleges or independent health care clinics.

6. **Additional Concerns:**

- Any person(s), regardless of location or affiliation, who is in direct contact with subjects or their individually identifiable private information, must be listed on the IRB application and complete both the MU IRB educational and HS IRB HIPAA training (if appropriate).
- Sometimes more than one item above may apply to a particular study. Investigators must keep in mind the time frame required to obtain the necessary permissions/approvals.
- The IRB will not allow research to be conducted at any outside institution until the appropriate approvals/permissions are in place.

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Subject Compensation

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Approved By: Niels Beck, PhD
Chair, Health Sciences IRB

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1.0 Purpose

To aid in assuring knowledge and compliance of all persons involved in any aspect of human subject research by documenting the requirements for subject compensation.

2.0 Scope

The SOP applies to all human subject research falling under the purview of the Health Sciences Institutional Review Board.

3.0 Definitions

Compensation – Any payment to a study participant which may be in the form of cash, credit, voucher, or gift. Alternative forms of compensation can include items such as free medical care, extra vacation time, and academic rewards (in the form of a grade or a letter of recommendation).
4.0 Policy/Procedure

General Information
It is not uncommon for subjects to be compensated for reimbursement for time and/or expenses incurred as part of the research study. In such cases, the IRB must review the amount of payment to assure that no undue coercion or influence is being placed on the subject. The IRB must take into account whether compensation given to subjects is reasonable, not coercive, and is reflective of the degree of risk, inconvenience, or discomfort associated with participation. Coercion or undue influence may occur if the entire payment was to be contingent upon completion of the study, or if the payment was unusually large. The IRB will determine on a case-by-case basis whether the amount of compensation is appropriate, and upon review may request changes in the amount or method of compensation.

Per the IRB policy on recruitment, specific monetary amounts provided as compensation for participation may not be stated in the recruitment materials. A statement that reimbursement/compensation is provided will be allowed but the specific dollar amount of said compensation is not allowed.

Accounting Approval
The method of payment must be reviewed the general accounting office in addition to IRB approval. See the Business Policy & Procedures Manual regarding the policy on participant compensation: http://www.missouri.edu/~muacct/BPPM Research Participant Compensation.htm. Studies involving compensation must have this approval prior to final IRB approval being given.

The IRB office will notify the investigator for any study which has compensation as part of the protocol of the requirement for accounting approval. The investigator will be responsible for communicating with the accounting office to obtain the necessary approval. Accounting will forward the IRB their approval of the method of compensation. Once the approval from accounting is received, the IRB will move forward with final approval. After a study is approved, the IRB will notify the accounting office of the approval so that funds may be released.

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SUBJECT RECRUITMENT

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Chair, Health Sciences IRB

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1.0 Purpose

To aid in assuring knowledge and compliance of all persons involved in any aspect of human subject research by documenting the necessary elements of the subject recruitment process for the Health Sciences IRB.

2.0 Scope

The SOP applies to all human subject research falling under the purview of the Health Sciences Institutional Review Board.
3.0 Definitions

Cold calling – potential participants identified through means other than personal contact are contacted by researchers unknown to them and with whom there has been no previous contact by someone involved in a treatment relationship with the individual. (see below)

Passive recruitment – assumption that absence of a definitive “no” to participation equates to an agreement to participation. (see below)

Recruitment – procedure by which potential participants to a study are identified and affirmative interest is obtained to gain participants for research studies.

Screening activities – activities (such as questions, tests or procedures) conducted to help determine eligibility for a study.

4.0 Policy/Procedure

Federal Regulations 45 CFR 46.111, 21 CFR 56.107(a) and 21 CFR 56.111 charge the IRB with ensuring that appropriate safeguards exist to protect human subjects when participating in research. Recruitment is an important tool in the conduct of a research study and is often considered the first step in the informed consent process. As such, it must be thought about in terms of the protection of the potential participant to the study.

As an important first step in the conduct of research projects, recruitment methods must comply with all applicable regulations relating to protection of the participant and proper conduct of the proposed research project. Recruitment procedures and materials must be disclosed to the HS IRB in adequate detail to allow the IRB to determine that adequate protection measures are in place as well as lack of coercion and equitable subject selection.

The optimum method of recruitment is one which allows the potential participant to contact the study personnel and indicate an interest in participating. The recruitment methods discussed within this SOP are some of the more commonly used methods but there are many other ways that studies may recruit participants. Each must be fully explained to facilitate adequate IRB review and action. Information that must be provided to the IRB includes, but is not limited to:

- What is the recruitment method?
- Who will be doing the recruitment?
- Where will recruiting occur (including the location of posted flyers)?
- How and where is information gathered from a potential participant stored; who may access it?
- What happens to gathered information if the potential participant declines to participate?

As mandated by the Federal Regulations, the IRB must review and approve all study recruitment before identification and recruitment of potential participants is undertaken. Recruitment materials should be appropriate for the study and presented in a clear, straightforward manner. Recruitment materials must not be coercive and should not make any claim as to the safety or effectiveness of the research or superiority to current standard practices.
Local Recruitment Methods

The optimum method of recruiting and protection involves the placement of paper advertisements which allow interested parties to contact the study staff of their own accord. Persons involved in receiving these calls must be knowledgeable members of the study staff (knowledgeable in ethical conduct of research and familiar with the elements, purpose and procedure of the particular study) in order to answer any questions the caller may have prior to indicating interest in participation. At this initial contact, a time should be arranged to meet to begin the consent process. Care should be taken at this initial contact to avoid study screening activities. Screening activities may not occur until valid consent has been obtained from the participant. Some studies may want to apply for two consents, one for the screening process and one for the main study. Depending on the detail of the screening procedure, it may be possible to obtain screening information through the use of a waiver of documentation of consent rather than a written consent.

Another recruitment method widely used is the identification of potential participants through medical record information or referral from treating physicians. When participants are identified in this manner, except under exceptional circumstances, they may not be contacted directly by the study staff. Contact with these potential participants should be made by their treatment provider or someone known to them on the treatment provider’s staff. The treatment provider should indicate to the potential participant the existence of a study and contact information to obtain more information on the study and potential participation in the study.

With the emergence of the world wide web, another recruitment tool is recruitment databases. In these cases, the web sites contain advertisements for studies currently open to enrollment but also include a section where the potential participant may complete some basic information identifying any conditions/diseases which he/she may have and for which he/she may want to be involved in a research study. The information requested on the potential participant must be limited to:

- Name
- contact information
- disease/condition of research interest

The introduction to the database information must clearly state that providing this information is completely voluntary and also must state the method by which the participant may withdraw the provided information in the event he/she decides he/she would not want to participate in future research studies. Potential participants also must be informed regarding how long the information is kept, the protection of confidential information that is in place for the site and an indication of to whom the information may be provided.

Personal contact is sometimes used as a recruitment method. Study staff who approach potential participants about a research study should be mindful of the issues related to confidentiality and convenience to the potential participant. Examples of inappropriate personal contact recruitment would be to ask a patient in a crowded waiting room if he/she would be willing to complete a survey on sexual habits or approaching a potential participant about participating in a surgical study as he/she is in the pre-op room being prepped for surgery. See the “Other Recruitment Techniques” section of this SOP for more information on recruitment techniques that may be discouraged.
Radio/Television/National Media campaigns are usually cost prohibitive for locally initiated recruitment and are used more on a nationally sponsored level. However, if these types of recruitment procedures are initiated locally, the same issues must be addressed as for other types of recruitment.

**Forms of Recruitment**

Paper advertisement – includes items such as posters, flyers, newspaper and periodical advertisements.

Verbal advertisement – includes local radio and television advertisements or word-or-mouth recruitment.

Electronic advertisement – includes web pages and mass e-mails.

**Recruitment Materials**

For all types of recruitment, whether printed or verbal, there are certain elements that must be contained within the recruitment materials. These materials should be statements of study facts as documented in the protocol and the study consent form.

- Indication this is a research study
- Indication of the condition under study or purpose of research
- Brief, clear, concise statement of what is involved with participation including time commitment
- Statement of possible benefits
- Statement of possible risks
- Statement of main inclusion/exclusion criteria
- Statement of important deterrents to participation
- No coercive language
- A statement that reimbursement/compensation is provided is allowed, but the specific dollar amount of said compensation is not allowed
- Statement of how to contact the study personnel to indicate participation interest

The posted recruitment materials should not contain the IRB approval stamp or reference that the IRB has approved the study and recruitment materials. This may be perceived as an endorsement of the study by the HS IRB and that is not accurate or allowable.

**Other Recruitment Techniques**

“Passive recruitment” is discouraged as a recruitment method by the HS IRB. Passive recruitment methods include sending a recruitment postcard to potential participants and asking them to return the postcard if they are not interested in participating. This method assumes that if the postcard is not returned to deny participation, the potential participant is agreeing to be contacted about further participation. The HS IRB will consider requests to use passive
recruitment methods on a case by case basis and researchers wishing to use passive recruitment need to be prepared to justify use of these methods relative to the use of active recruitment and increased risks to subjects that may be associated with passive recruitment.

“Cold calling” is strongly discouraged as a recruitment method by the HS IRB since such unsolicited contact may be viewed as an invasion of privacy. In the vast majority of circumstances the participant should contact study personnel to indicate interest or potential subjects must be contacted about participation by someone who is known to them and/or involved in a treatment relationship with them. Treatment relationships include all health care professionals and are not just limited to physician/patient relationships. It is acceptable for participants to be contacted by a research member of a specific clinic even though the relationship may be with a non-research clinician. An example of this is that a patient of the cardiology clinic may be contacted by a cardiology researcher without a direct treatment relationship because they have a treatment relationship with the clinic, however an orthopaedic researcher could not contact a patient of the cardiology clinic.

Requests for recruitment methods which require “cold calling” of potential research subjects, especially if they are patients or ex-patients, will be carefully reviewed by the HS IRB on a case by case basis. Researchers wishing to utilize these methods will need to carefully justify the use by addressing their impact on the study’s risk/benefit ratio, as well as the use of less intrusive recruitment procedures.

Recruitment materials must not be coercive in nature. Use of boldface type, highlighting, and font size to highlight language in recruitment materials must be used carefully to avoid the perception of coercion. Additionally, words such as ‘free treatment’, ‘new breakthrough’, ‘exciting study’, etc. should not be used within recruitment materials.

Specific monetary amounts provided as compensation for participation may not be stated in the recruitment materials. A simple statement that compensation may be provided is acceptable.

Use of employees/students under the direct supervision of an investigator as participants in a research study is strongly discouraged because of the actual or implied perception of coercion or conflict of interest.

Individuals who decline to participate in a study should not be questioned about his/her refusal and should not be re-contacted at a later date to see if they may have changed their mind.

If information on individuals who decline to participate is a scientifically important and pertinent issue, this should be indicated to the HS IRB in the initial application with a justification of the need for the information and information on the consent, collection, retention, use, storage, and disposal of said information. The request to obtain information on a declining participant will be evaluated by the HS IRB on a case-by-case basis. An additional consent to obtain this information may be required.

**IRB Review**

The investigator must submit to the HS IRB in the initial application a detailed plan of the recruitment process including how potential participants will be identified and approached,
recruitment methods, and recruitment materials. Recruitment materials must include anything that will be seen or heard by the potential participant including, but not limited to:

- Flyers
- Print advertisements
- Recruitment speech
- Audio advertisements
- Video advertisements

The audio and video advertisements should be provided to the HS IRB in both text format and the final draft in the media form in which they will be used. The IRB will review the text of the advertisement to ensure that no inappropriate or coercive information is provided in the advertisement. The IRB will review the final drafts of the audio/video media to ensure that there are no inadvertent voice inflections, tones, or other language that may be coercive in nature.

The IRB should be informed as to placement of advertisements (e.g., local newspaper, local radio or television). An important point to remember when posting flyers is that permission may need to be obtained from the posting location prior to posting the flyer.

If the recruitment is to be through personal contact, the following information should be provided to the HS IRB:

- Who will approach the potential participant
- When will the potential participant be contacted
- Where will the potential participants be approached
- Amount of time the potential participant will be provided to consider participation

If the recruitment process or materials change during the conduct of the study, the HS IRB must be notified and all revised methods and materials must be submitted at that time. The revised process may not be implemented until review and approval by the HS IRB.

The HS IRB is charged with reviewing all proposed recruiting methods and materials to ensure adequate protection of all research participants. The HS IRB assures that the methods or materials are not coercive in any way, that the method or materials are applicable to the research study, that the recruitment method or materials accurately reflect the research purpose, and that all possible steps have been taken for subject protection.

Any questions that the IRB has on the recruitment process will be resolved through communication between the reviewer, the investigator and the HS IRB Administrative Office. If all issues can be satisfactorily resolved, the recruitment process will be approved.

The investigator will be notified in writing of the decision by the HS IRB on the proposed recruiting process.

**Study Recruitment Incentives**

It has become common practice for many sponsors to offer monetary or other types of incentives to a PI and/or study staff when set recruitment goals have been met. These incentives are above
and separate from the money awarded as payment for the conduct of the study. The HS IRB must be notified of the existence of these recruitment incentives.

The IRB does not allow the payment of “finders fees”. A PI may not pay someone outside the study to identify or recruit potential participants into a research study.

**Local vs. National Recruitment Processes**

Many sponsors provide national advertising campaigns as study recruitment tools. These national campaigns must be submitted to and reviewed by the HS IRB. The HS IRB realizes the extent of oversight may not reach to these national ad campaigns, however, if blatant errors are noticed in the national materials, the HS IRB may communicate with the sponsor through the PI to correct these errors. If satisfactory resolution cannot be obtained, the HS IRB has the authority to deny the conduct of the study at this location.

With the emergence of the worldwide web, many registries of currently available research trials have been established. Examples of these national registries are the NCI Cancer Clinical Trial Listing and AIDS Clinical Trials Information Services (ACTIS). The FDA has issued guidance that these listings are not felt to need IRB review as long as the listing is limited to:

- Study title
- Purpose of study
- Protocol summary
- Basic eligibility criteria
- Study site location(s)
- Information on how to contact site for further information

Sponsors may send recruitment information to the local PI and state that these materials do not need review by the local IRB because they meet the guidance issued by the FDA. Regardless of the sponsor’s request, the HS IRB must be notified that study information has been added to one of the national study registries. Additionally, as required by FDA, if the study is added to any registry that allows inclusion of more information than that which is stated above as permitted, the HS IRB must review and approve the materials prior to inclusion in the registry.

It is possible that a local study may wish to include information in a national research trial registry as well. Any information added to a national research trial registry by the local study, regardless of the limitations of the registry information, must be submitted to the HS IRB for review and approval before addition to the registry.

Sponsors may also employ national, non-involved, third-party call centers to be the first point of contact for a participant inquiry. If such a method is used, the receptionist script to be used by the call center must be submitted to the HS IRB. An explanation of the procedures used by the call center during the recruitment call must also be submitted to the HS IRB. Additional information that should be submitted to the HS IRB includes information on what the call center does with the collected information if the caller declines participation, ends the interview, or hangs up the telephone; whether information collected on a caller deemed ineligible for the particular study is destroyed or maintained and used as a future recruitment tool for another study; and what happens to the information collected by the call center after a caller has been referred to a specific study site.
Public Service Activities

Many times PIs are asked to provide local media outlets a synopsis of studies being conducted. This information may also be requested by conferences, workshops, or in-house publications. These synopses should be a simple statement of the purpose of the research and results to date. As such they are not considered recruiting tools and should not be used as such. The IRB should be notified of the activity prior to participation. If information other than purpose and results to date are to be provided, these public service activities are then considered to be recruiting tools and the HS IRB must be notified of that intent. Additionally, if these activities may include an open question/answer forum which might turn into questions about participation and recruitment, the HS IRB must be notified of the study staff intent to participate in such a venue. Any handouts, other than those already reviewed and approved by the HS IRB, which may be disseminated during these activities must be reviewed and approved by the HS IRB prior to their use at the event.

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Use of Human Biological Specimens

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1.0  Purpose

To aid in assuring knowledge and compliance of all persons involved in any aspect of human subject research by documenting the requirements for banking of human biological materials.

2.0  Scope

The SOP applies to all human subject research falling under the purview of the Health Sciences Institutional Review Board.

3.0  Definitions

Banking - Specimens are stored past termination of main study for future research. Banking can be included in addition to any other category of research. Banking also includes the collection, processing, and storage of specimens which are intended to be made available to other researchers.

Human biological materials – From subcellular structures (such as DNA), to cells, tissues (including blood, bone, muscle, connective tissue, and skin), organs, gametes (sperm and ova), embryos, fetal tissues, and waste (hair, nail clippings, urine, feces, and sweat).

Pharmacokinetics - Is the study of the way a drug is "processed" by the body, including its absorption from the stomach (or blood, or skin, etc.), where and how it travels in the tissues, how long it remains in the body, how it is changed by the liver, how it and/or its by-products are eliminated by the bowel and/or kidneys, etc.

Pharmacogenetics - Is the study of specific genes (DNA) that may influence the response to a drug as well as the genes and genetic products that cause, or are associated with certain inherited disorders or diseases (such as cystic fibrosis).

Pharmacogenomics - Focuses on the way an individual's genetic makeup may influence the way that person responds to a particular drug.

Prospective - The information (data, documents, specimens, etc.) does not exist at the time the IRB request is made.

Publicly available – Available to the general public, in the form of records, documents, files, etc.

Retrospective – The information (data, documents, specimens, etc.) already exists, has been collected and are “on the shelf” at the time the IRB request is made.

Secondary use – The information (human biological materials, data, documents, etc.) and the information derived from them are used or analyzed for purposes that extend beyond the purpose for which they were originally collected.
Specimen – Any human biological material (see human biological materials)

Third parties- Any person or entity other than the subject who is enrolled to participate in the study or about whom information is gathered.

4.0 Policy/Procedure

General Information
The use of human biological materials for research purposes is essential to the advancement of science and human health. It is crucial, therefore, to have clearly defined conditions under which these specimens can be used. Additionally, the people who provide the specimens should be protected and the conditions under which the specimens were collected and/or stored should be kept in mind.

Specific concerns to be addressed when conducting research using human biological materials are addressed below. Generally, however, the following items should be kept in mind when preparing protocols for using human biological materials:

- Under what conditions were/are the specimens collected (e.g. clinical versus research setting).
- Whether the specimens were already collected and stored, or are to be collected in the future
- Whether the specimen can be linked by anyone (or combination of people) to its source
- Whether the risks posed by the research affect individuals, communities, third parties, etc.
- The types of protections that might be employed to protect against harms, specifically to protect against invasion of privacy or discrimination.

Protocols involving human biological materials may be reviewed either as exempt, expedited, or full board. The determination of which level is appropriate depends on the type of research being conducted and level of identification of the specimens. Additionally, the type of consent required will depend on what type of research is being conducted and how were the samples initially collected. The HS IRB will review all proposed research to determine whether it involves human subjects and at which level of review is appropriate.

What type of research procedures will be used?
1. Specimens collected prospectively specifically for the purposes of research
Specimens which are collected prospectively and procedures performed specifically for research require either full board or expedited review (if the research meets the criteria for expedited review). Prospective collection does not meet the criteria for exempt review. In most cases, written consent is required for the prospective collection of any specimen, however, waiver of documentation of written consent may be requested if the elements of the waiver requirements are satisfied (45 CFR 46.117(c)).

2. Samples collected initially for clinical, diagnostic and/or assessment purposes
   a. Samples collected prospectively for the purposes of clinical diagnosis and/or assessment
Samples collected prospectively for the purposes of clinical diagnoses and/or assessment may be used for research purposes after the specimens have been used as needed for the clinical treatment of the patient, provided that the appropriate consent is obtained. These include samples such as tumor tissue taken after surgery, left over urine/blood after clinical tests have been performed, etc. In most cases, written consent is required for the prospective collection of any specimen, however, waiver of documentation of written consent may be requested if the elements of the waiver requirements are met (45 CFR 46.117(c)).

When conducting research using samples obtained for clinical purposes investigators must keep in mind that the research is not retrospective, even though the research performed on the sample will be done after the sample is removed. Per the definitions above, this process is still prospective collection.

**EXAMPLE**
A patient is prospectively enrolled in a study and consent is obtained to use tumor tissue removed from a surgery for research after it is used for clinical purposes. The tissue did not exist and it was not on the shelf at the time IRB approval was obtained to conduct the study, therefore this research is not a retrospective use of specimens, but rather prospective collection of specimens for research.

b. **Retrospective use of samples obtained for clinical diagnosis and/or assessment**
The retrospective use of samples initially obtained for clinical purposes may be used for research, again after all clinical diagnoses and/or assessments have been completed. The type of consent required depends on whether the research can be expedited (45 CFR 46.110(a)(5)) or whether it is exempt (45 CFR 46.101(b)(4)). In most cases either waiver of consent or waiver of documentation of written consent may be obtained. Research involving the retrospective use of samples must meet the definition of “retrospective.” (see section above on “Samples collected prospectively for the purposes of clinical diagnosis and/or assessment”)

3. **Samples which are publicly available**
In order for samples to be publicly available, they must be available to the general public in the form of records, documents, files, etc. Many organizations make data available to researchers at a reasonable cost. These materials generally are not available to the general public. If data is obtained from any of these sources the data cannot be assumed to be “publicly available.”

**What type of testing will be involved?**
The risks presented by research using human biological specimens generally are risks of social and psychological harm, more so than risks of physical injury. Additional unknown risks are also possible. Risks associated with research using specimens can include anxiety and confusion, damage familial relationships, and compromise subjects’ insurability and employment opportunities. Of particular concern to the HS IRB is whether subjects can be identified and that privacy and confidentiality are maintained so as to minimize any possible harm. Special considerations must be given to the information provided to subjects in the informed consent process. A separate consent form is many times required which addresses issues regarding privacy, confidentiality, commercialization, etc.
1. Genetic Research
   - Genetic testing - Genetic research involves the testing of human biological specimens for genetic characteristics, such as inherited traits, the typing of the genome, etc.
   
   - Pharmacogenetics studies - Is the study of specific genes (DNA) that may influence the response to a drug as well as the genes and genetic products that cause, or are associated with certain inherited disorders or diseases (such as cystic fibrosis).
   
   - Pharmacogenomics - Focuses on the way an individual's genetic makeup may influence the way that person responds to a particular drug.

2. Nongenetic testing - Pharmacokinetics
   Many clinical trials wish to collect specimens for the purposes of testing the level of a certain drug in a subject’s body throughout the course of a study. Pharmacokinetics (PK) is the study of the way a drug is "processed" by the body, including its absorption from the stomach (or blood, or skin, etc.), where and how it travels in the tissues, how long it remains in the body, how it is changed by the liver, how it and/or its by-products are eliminated by the bowel and/or kidneys, etc.

   These specimens are typically stored until the study is complete and then destroyed. Informed consent must be obtained to conduct this testing, however a separate consent is not necessary if the research is required as part of the protocol, meaning the subjects can not participate in the study if they do not also participate in this portion of the protocol. If the PK testing is in addition to the protocol, if additional research beyond what was described in the informed consent document is requested, and/or the specimens wish to be kept for additional unspecified future research, and additional consent must be obtained (see section below on unspecified future research).

3. Unspecified future research
   Sometimes specimens obtained for clinical and/or research purposes wish to be used for additional unspecified future research; and sometimes these specimens are stored indefinitely for future research, also known as “banking.” The secondary use of specimens (which are specimens obtained for one purpose but wish to be used for additional purposes in the future) must be given special consideration. The HS IRB will consider, on a case-by-case basis, whether unspecified future research is allowable. Care will be taken to consider the circumstances in which the sample was obtained initially, what (if any) consent was obtained from the subject regarding the use of the sample, and whether the sample is identifiable (see section below on “Are the samples identifiable”). In most cases, written consent will be required from the subject for the approval of the use of their specimen, unless the requirements for waiver of documentation of written consent or waiver of consent can be satisfied.

   A special note about banking: Banking can be included in addition to any of the above categories of research. Banking also includes the collection, processing, and storage of specimens which are intended to be made available to other researchers outside of the approved research study. When samples are intended to be distributed to other investigators, additional regulations regarding
tissue repositories apply. A separate written consent generally is required. More information regarding consent can be found in the section on consent.

Example One
An investigator requests the retrospective use of samples which were previously obtained for clinical purposes and remain and are stored in the pathology department. The investigator wishes to develop a series of assays using the samples. The samples have no personal identifiers linked with the samples and the identity of the subject is unknown.

In this scenario, the samples are being obtained for development of assays and will kept until the sample is all used. The exact length and type of testing is unknown. The samples contain no identifiers, however, and were initially collected for clinical purposes. Waiver of consent may be requested.

Example Two
A subject was prospectively enrolled in a study and had blood drawn to test for pharmacokinetic properties of the drug being tested. There was additional specimen remains after the testing. The sponsor is requesting to use the remaining sample to test for additional properties related to different drugs and to look at different diseases.

In this scenario, the sample would be used for additional research other than what the subject agreed to and that was described in the informed consent document. The subject, therefore, must provide their written consent for the additional use of their tissue unless the elements for waiver of documentation of informed consent are satisfied.

Example Three
A subject with breast cancer agrees to have their tissue, which was removed after surgery, to be used for genetic research testing involving breast cancer. There was additional specimen remains after the testing. The sponsor is requesting to use the remaining sample to test for different diseases other than breast cancer.

In this scenario, the sample would be used for additional research other than what the subject agreed to and that was described in the informed consent document. The subject, therefore, must provide their written consent for the additional use of their tissue unless the elements for waiver of documentation of informed consent are satisfied.

Are the samples identifiable?
The level of review (full board, expedited, or exempt) is determined partly by the level of identification of the specimens. Additionally, more identifiable specimens lead to greater concern for increased risk to the subject.

1. Identified – Samples/data labeled with personal identifiers such as name or social security number.

2. Coded – Samples/data labeled with a clinical trial or research number that can be traced or linked back to the subject only by the investigator. These samples do not carry any personal identifiers.
3. De-identified – Samples/data are double-coded and labeled with a unique second number. The link between the clinical trial or research number and the unique second number is maintained, but unknown to investigators and patients. Samples do not carry any personal identifiers.

4. Anonymized – Samples/data are double coded and labeled with a unique second number. The link between the clinical trial or research number and the unique second number is deleted. Samples do not carry any personal identifiers.

5. Anonymous – Samples/data are those that do not have any personal identifiers, and the identity of the subject is unknown. Anonymous samples may have population information (e.g. the samples may come from patients with diabetes) but no additional individual data is maintained.

Consent
Obtaining specimens from individuals who are fully informed about and have consented to the collection of their tissue and its use for research purposes is a best practice. The type of consent depends on the type of research wishing to be conducted using the specimens. The consent should address the basic elements of informed consent as stated in the regulations (45 CFR 46.116(a-b)). Additional information should be added to the consent which includes information on:

- how long the specimen will be stored
- who owns the materials and whether the subject will receive any compensation
- who will have access to the specimen
- whether the subject will be informed of the results of the research with their specimen
- whether the specimen will be identifiable
- how to withdraw the specimen

Specimens collected prospectively for the purposes of research require written consent. In certain circumstances, waiver of documentation of written informed consent may be granted.

Consent is also required for the prospective use of specimens that were collected initially for clinical purposes. Again, written consent is generally required unless the elements for the waiver of documentation of written consent are satisfied.

If the collection of the specimens is required as part of the protocol and subjects cannot participate in the study if they do not also consent to the use of their specimen as specified, then a separate consent is not needed. If additional research is proposed as optional beyond what the protocol specified, then a separate “banking” consent should be obtained in addition to the main consent. The following information may help to determine whether a banking or separate consent is needed:

- Is the collection/use/storage of specimens optional? Optional means that the subject can still participate in the study even if they do not agree to the use of their specimen.
- If the proposed research is optional, typically a separate consent addressing the relevant information should be used.
- If the proposed research is not optional and is in fact required, then a separate consent generally is not needed. However, it may be useful to have an additional section of the
consent or a different consent entirely to address the information for use of the specimen for research so as not to make the consent form extensively long.

Specimens used in retrospective research may have consent waived (per 45 CFR 46.116(d)) or may have the requirement for obtaining written informed consent waived (45 CFR 46.117(c)) if all the requirements are met.

**Commercialization**
The use of specimens often leads to commercial developments. However, the time frame in which any commercial product can be developed is often years away from the when the sample was initially collected. The informed consent must address whether subjects will retain any commercial or equity interests in their specimens once they are used for research purposes.

**Privacy**
Individuals who contribute specimens must have the right to withdraw their consent and have their specimen removed and/or destroyed. Many times, however, identifiers are stripped from the specimen after it leaves the primary investigator’s control and it is not possible to identify the specimen. Subjects should be informed of the method by which to remove their specimen, and at what point or time frame the specimens are no longer able to be removed. Additionally, the informed consent should address how the samples will be identified (see section above on identification of samples), what protections are in place to protect the identify of the specimens, and who will have access to the specimens and for what purposes.

**Third party interests**
At this time, there is no overarching rule stating that informed consent must be obtained from family members on whom medical history information is collected through someone else in their family who is a full participant in a research study. However, in January 2000, the Office for Human Research Protections (OHRP) (formerly Office of Protection from Research Risks) recommended that IRBs should consider the potential risk to family members in the study design when research involves data, specimens, or information from third parties (see the 1/12/00 Washington Post article by Jay Mathews entitled "Father's Complaints Shut Down Research, US Agencies Act on Privacy Concerns").

When considering whether consent should be obtained from third party subjects the IRB must:
- consider and determine the level of risk to the third party
- consider and determine whether the rights and welfare of the third party would not be adversely affected
- consider how the third party would be contacted and recruited
- consider whether there are any confidentiality issues involved (e.g. extended family members may not know an individual is sick or has a specific condition)

The IRB should determine whether the conditions for informed consent can be waived. If a waiver of informed consent is granted, the minutes of the IRB meeting should state that the potential social, psychological, and legal risks presented by research that involved the collection of detailed social and medical history information about relatives were considered, and that the decision to waive the requirement for informed consent was made after discussion.