

## Changes to the IRB Manual

Last updated: 4/28/08

*Notable changes are highlighted in yellow.*

Deletion of Study Budget section in table of contents since there was no corresponding section within the Manual.

Deletion of references to documents in the appendices since this information is either not applicable due to the eIRB system or in the eIRB system.

Change all references to Institutional Review Boards to a singular “IRB”, all reference from hospital/entity IRBs to IRB and remove references from entity designated IRB to “IRB”.

- Chapter 2 c
- Chapter 3
- Chapter 4
- Chapter 4 a, b, c, d
- Chapter 5 a, b, d, e, f, g, h, l, m
- Chapter 6 a, b, c, d, e, f, g, h
- Chapter 7 a, d, e
- Chapter 8 a, e, f, g, i, k
- Chapter 9 a, c, e, f, g, h, i, k, m, o
- Chapter 10 a, g, i, j, k, l, m, m, o, p, q, t, u, v
- Chapter 12 f, g, i, j, o
- Chapter 13 a, c, d, f
- Chapter 14 a, c, d, e
- Chapter 15 a, b, c, d, e, f
- Chapter 16 b, c, i
- Chapter 17

Define engagement. THR is engaged in the research study when: a) an entity of Texas Health Resources has contracted with a sponsor to conduct a clinical trial; or b) THR’s employees or agents provide administrative support, research coordination or hospital services to investigators in the conduct of a clinical trial; or c) an investigator recruits from the hospital grounds for the research study to include both study subject recruitment and study advertisements.

- Chapter 3 f

Add: “in which THR is defined as engaged” to all areas in which the IRB is required to review a protocol or governs the research study.

- Chapter 2 c
- Chapter 3 e
- Chapter 4 c
- Chapter 5 h
- Chapter 8 g, p
- Chapter 9
- Chapter 10 s

## Changes to the IRB Manual

Last updated: 4/28/08

- Chapter 12 d, g

Change: The THR Board of Trustees and not the CEO or his/her designee, SVP or COO shall designate a THR officer to serve as the THR Institutional Official for research activities.

- Chapter 4 a

Change references to THR System Compliance officer to THR Chief Compliance Officer.

- Chapter 4 a, d
- Chapter 5 b, f, l
- Chapter 8 b
- Chapter 9 p
- Chapter 11 g
- Chapter 12 o
- Chapter 16 i

Add: Each entity's Board will formalize the IRB.

- 4 b

Add: If the research study is not approved by the IRB, the investigator may not use their hospital affiliation in any portion of the research publications related to it.

- Chapter 4 c

Add: Reporting guidelines for Protocol Violations and repercussions for recurring and/or significant violations

- Chapter 4c

Add definition of protocol deviation/violations

PROTOCOL DEVIATION: Any alteration/modification to the IRB-approved protocol. The protocol includes the detailed protocol, protocol summary, consent form, recruitment materials, questionnaires, and any other information relating to the research study.

PROTOCOL VIOLATION: Any protocol deviation that is not approved by the IRB prior to its initiation or implementation.

- Chapter 4 c
- Chapter 9 i
- Glossary

Changed the adverse event reporting procedure.

- Chapter 4 c
- Chapter 5 c

## **Changes to the IRB Manual**

**Last updated: 4/28/08**

- Chapter 7 d
- Chapter 8 g, m
- Chapter 9 c, i, j, k
- Chapter 12 f, g
- Chapter 17

(Background) per the OHRP guidelines:

Upon becoming aware of an internal adverse event, the investigator should assess whether the adverse event represents an unanticipated problem following the OHRP guidelines. If the Investigator determines that the adverse event represents an unanticipated problem, the investigator must report it promptly to the IRB. If the Investigator determines that an adverse event is not an unanticipated problem, but the monitoring entity subsequently determines that the adverse event does in fact represent an unanticipated problem (for example, due to an unexpectedly higher frequency of the event), the monitoring entity should report this determination to the Investigator, and such reports must be promptly submitted by the Investigator to the IRB. When an unanticipated problem is submitted to the IRB the following information should be included in the report:

1. appropriate identifying information for the research protocol;
2. a detailed description of the adverse event;
3. an explanation of the basis for determining that the adverse event represents an unanticipated problem; and
4. a description of any changes to the protocol or other corrective actions that have been taken or are proposed in response to the unanticipated problem.

It is not necessary for reports of external adverse events of individual adverse events occurring in subjects enrolled in multi-center studies to be distributed to the IRB. External adverse event reports should only be reported to the IRB when a determination has been made that the particular adverse event or series of adverse events meet the criteria for an unanticipated problem. This report should include a clear explanation of why the adverse event or series of adverse events has been determined to be an unanticipated problem; and a description of any proposed protocol changes or other corrective action to be taken by the Investigators in response to the unanticipated problem.

Unanticipated problems that are serious adverse events should be reported to the IRB within 1 week of the Investigator becoming aware of the event. Any other unanticipated problem should be reported to the IRB within 2 weeks of the investigator becoming aware of the problem. All unanticipated problems will be reported to appropriate institutional officials (as required by an institutions written reporting procedures), the supporting agency head (or designee), and OHRP within 1 month of the IRB's receipt of the report of the problem from the Investigator.

## Changes to the IRB Manual

Last updated: 4/28/08

### Add for IRB fee:

All submissions to the IRB will be paid according to the following fee unless exempt:

- Initial Submission - \$1,500
- Renewal - \$500
- Modification (if full board review required) - \$250

Fees are due at time of protocol submission. Investigator will not receive notification of the IRB's review action and stamped consent form of the submitted protocol until the appropriate IRB fee has been paid in addition to stipulations and requirements set forth by THR and the IRB.

### The following may be exempt from IRB submissions fees:

- NIH Funded study
- NIH-like funded study, if overhead is included and to be distributed to THR entity to cover IRB fee
- Unfunded studies of THR employees in a degree program (i.e. nursing students, medical students, residents)
- Studies that are requested by and which solely benefit a THR hospital (Hospital Initiated study)
- Unfunded Data/Record review study in which there is no financial benefit to the Physician Investigator
- Unfunded Investigator initiated study, with approval by THR legal counsel

All exemptions must be approved by the Institutional Signatory Official.

- Chapter 5 b

Addition: If a continuation is not submitted by its deadline the study will be suspended. Investigators may not recruit any subjects while a protocol is suspended.

- Chapter 5 d

Addition: Time frame of 180 days within which the investigator has to respond to a notice of disapproval and approval stipulations or the study will be closed. If a study is closed a new application will be required to be submitted.

- Chapter 5 e

Change to: The IRB **will not** accept responsibility for review and oversight of non-THR research without the written agreement of the THR Signatory Official, and in accordance with applicable regulatory requirements.

- Chapter 5 h

Add: "or the Investigator's Agreement" to also account for the document that is the equivalent to the FDA Form 1572 when conducting device studies.

- Chapter 5 k

Add: When discussing the Institutional Officials oversight in regards to

## Changes to the IRB Manual

Last updated: 4/28/08

protections for human subject, it was added that this would be done in coordination with the THR Compliance Officer and THR legal counsel.

- 5 l

Deletion: The reference to the Investigator Manual since it will be merge with the IRB Manual.

- 5 l

Deletion: The reference to THR entity was taken out as it is not longer applicable to the system set up.

- 5 l

Change from “The IRB is structured as a committee of the THR hospital system” to “The IRB is structured as a committee of THR”. Deletion of: The IRB may be structured as an administrative committee, a medical staff committee or as a joint committee. As such, the IRB is ultimately accountable to the Entity Board of Trustees, as well as to the THR Board of Trustees.

- 6 a

Add: IRB members that are non-THR employees may be financially compensated for their time to review protocols and attend IRB meetings.

- Chapter 6 a

Deletion: Community members of the IRB will be approved through the THR Hospital Staff

- Chapter 6 b

Addition: Information regarding the IRB member secondary reviewer duties

- Chapter 6 b and 9 d, h

Change from the IRB non-scientific member having an “expertise” in human rights issues...to the respective member(s) having training in human rights issues...

- Chapter 6 b

Delete the requirement that the IRB Chairperson will be a THR staff member.

- Chapter 6 c

Change: Appoint a Vice-Chairperson following consultation and agreement by other members of the IRB to When applicable, appoint a Vice Chairperson, with approval of the THR Signatory Official, and seek consultation and/or agreement by other members of the IRB.

- Chapter 6 c

## **Changes to the IRB Manual**

**Last updated: 4/28/08**

Change from the IRB Members will nominate their alternate to they may nominate their alternate.

- Chapter 6 d

Changed that IRB members will disclose conflict of interest to THR officials to the IRB.

- Chapter 6 i

Deletion: Revoking of entity authorization that does not provide sufficient resources to the IRB.

- Chapter 7 a

Change from the IRB staff taking direction of entity to just IRB Chairperson and Institutional Official.

- Chapter 7 b

Deletion: Drafting reports that go to Federal officials will only be done by the Institutional Official or the IRB Chairperson and not the entities.

- Chapter 7 d

Add Amendments, non-compliance issues and unanticipated problems/deviations to the list of IRB records.

- Chapter 8c

Add “protocol deviations/violations” to the list of applications regarding protocol amendments or modifications. Deleted the proposed change “(including relevant protocol deviations/violations)”.

- Chapter 8 g

Add DHHS and FDA citations 45 CFR 46.110 and 21 CFR 56.110, respectively.

- Chapter 8 l

Add FDA citation 21 CFR 56.109 to the existing DHHS citation regarding justification of waiving documentation of informed consent.

- Chapter 8 s

Changed to all research must be prospectively reviewed by the IRB and not by the Institutional Official.

- Chapter 9

Added “industry sponsored contracts” to the list of existing documents the IRB will review upon a submission of a study.

- Chapter 9 b

Change from continuing review submissions will be conducted by the IRB if not expedited eligible for an expedited process to continuing review submissions will

## Changes to the IRB Manual

Last updated: 4/28/08

be reviewed by a convened meeting of the IRB if not eligible for an expedited process.

- Chapter 9 c

Add verbiage that continuing review documentation will include a status review of the grant or fully executed contract documentation.

- Chapter 9 d

Deletion: The verbiage regarding IRB “operated by THR” was deleted.

- Chapter 9 e

Add “not unexpected” to the list of items the IRB Chairperson or designee may disagree with the investigator about as this relates to the reporting of unanticipated problems or serious adverse events.

- Chapter 9 i

Deletion: The paragraph regarding The Notice of Intent to Modify Given to Other THR IRBs Monitoring Same Protocol was deleted.

- Chapter 9 i

Addition: IRB actions can also include approved contingent upon receipt of any ancillary information or documents requested by the IRB.

- Chapter 9 m

Change to: The subject must sign the informed consent document prior to initiation of any clinical screening procedures that are performed solely for the purposes of determining eligibility for research. If the subject is determined eligible for the study during the pre-screening process and the subject has had all his/her questions answered about the study that are not regarding clinical issues and/or medical treatment, non-investigational clinical screening procedures for the study, e.g. blood work, may be performed after the subject signs the research consent form and before signature by the physician investigator (See Chapter 10, section f,/ items 1 and 2 for additional details on the consenting process).

- Chapter 10 e

Add: 1) Studies that involve the practice of medicine, e.g. clinical testing, treatments, study device use or drug administration

In Texas, the duty of obtaining informed consent for medical treatment (the practice of medicine) is imposed solely upon the treating physician. Accordingly, it is a physician investigator’s non-delegable duty to obtain a subject’s consent for studies involving medical or surgical risks. However, upon the physician investigator’s request, a research coordinator for the study may review, with the proposed subject, the study process and the research consent form. The study subject will be given the opportunity to ask questions regarding the

## **Changes to the IRB Manual**

**Last updated: 4/28/08**

study process including the alternatives, risks, and benefits of taking part in the study.

- a) If the subject has questions concerning clinical issues and/or medical treatment (the practice of medicine), the process will stop and the subject will be given the opportunity to meet with the physician investigator prior to the start of any study procedures including any screening.
  - i. The physician investigator will then discuss the study with the subject and address any of the subject's questions and document the discussion with the subject in the clinical record. The physician investigator will obtain the study subject's signature on the research consent form. He/She will also sign the research consent form himself/herself, attesting to the fact that the physician investigator reviewed the study's purpose, its experimental and non-experimental procedures and interventions, the possible risks and benefits, the standard and research aspects of the study, the alternatives to participation, the voluntary nature of participation, the HIPAA Privacy Rule, the source of funding for the research, conflict of interest on the part of the research staff, if any and answered all of his/her questions.
- b) If the subject has no questions pertaining to clinical issues and/or issues related to medical treatment (the practice of medicine), the research coordinator may obtain the subject's signature on the research consent form, and the research coordinator will sign as having reviewed the research consent form with the subject and having witnessed his/her signature.
  - i. The study subject may then begin screening procedures.
  - ii. Prior to the subject participating in any investigational procedures involving medical treatment, the physician investigator will ask the subject whether he/she has any questions regarding the study and document the discussion in the clinical record. The physician investigator will sign the research consent form attesting to the fact that the physician investigator reviewed the study's purpose, its experimental and non-experimental procedures and interventions, the possible risks and benefits, the standard and research aspects of the study, the alternatives to participation, the voluntary nature of participation, the HIPAA Privacy Rule, the source of funding for the research, conflict of

## Changes to the IRB Manual

Last updated: 4/28/08

interest on the part of the research staff, if any and answered all of his/her questions.

- 2) Studies that do not involve medical treatment (the practice of medicine).

A non-physician Investigator may discuss the study procedures, alternatives, risks and benefits with the study subject, answer the questions of the study subject, obtain the signature of the study subject on the Informed Consent document and sign the document himself attesting to the fact that he has completed the informed consent process. The investigator will document the process in the clinical record.

- 3) The IRB may determine that additional informed consent precautions must be taken

- Chapter 10 f

Clarification regarding the investigator retaining and filing the original signed informed consent document unless otherwise instructed by the respective entity (i.e., keeping original in the medical record)

- Chapter 10 f and 11 k

Add: The consent form will be stamped with the date of the meeting in which the protocol was approved (approved or approved with changes).

- Chapter 10 f

### Add: **Recruiting Advertisements**

Direct advertising for research study subjects (i.e. advertising that is intended to be seen or heard by prospective subjects to solicit their participation in a study) shall be reviewed by the IRB. Direct advertising includes, but is not necessarily limited to: newspaper, radio, TV, bulletin boards, posters, flyers, e-mail blasts and THR digital screens.

IRB review and approval of listings of clinical studies on the THR internet/intranet is not required. The internet/intranet listings will limit the information provided to basic study information, such as: The title; purpose of the study; protocol summary; basic eligibility criteria; study site location(s); and how to contact the study site for further information. All study advertisements to be placed on the THR digital screens and those to be disseminated to THR employees via e-mail blasts must be submitted to TREI (The Research and Education Institute for Texas Health Resources) for placement onto the screen and e-mail dissemination.

- Chapter 10 m

Change from "OHRP" recommends to "THR" recommends regarding advisement on subjects who are prisoners.

- Chapter 10 o

## Changes to the IRB Manual

Last updated: 4/28/08

Add: If THR entity has not received study payment from Principal Investigator or Study Sponsor within 6 months from time of study subject receiving hospital treatment, the study will be placed on hold to new enrollment and the Chief Compliance Officer and the Entity President will be notified.

- Chapter 10 w

Change from billing inquires being directed to the Chief Compliance Officer to the billing office.

- Chapter 11 g

Add paragraph to state that the involvement/participation of a THR employee as a subject in a research study is voluntary and has the right to refuse to take part, right to drop out without any penalty or loss of benefits.

- Chapter 11 h

Add: In Texas, the duty of informed consent for studies involving medical or surgical risks is imposed solely upon the treating physician: it is the physician's non-delegable duty.

- Chapter 11 j

Add "after appropriate IRB review and approval" when referencing a non-significant risk device study beginning immediately since the study does not need FDA review.

- Chapter 12 d

Change adverse event to unanticipated adverse device effect

- Chapter 12 g

Add a reference to 21 CFR 312.2(b)(1) that provides the six conditions that indicate whether it is required to submit an IND for a off-label use of a product.

- Chapter 12 h

Add Parallel track citation of [57 FR 13250].

- Chapter 12 i

Add regulatory citations for Emergency Use of Devices [21 CFR 812.35(a)] and [50 FR 42866].

- Chapter 12 k

Change to only the Institutional Official and not the Compliance Officer in addition be notified by the IRB Chairperson when emergency research is approved by the IRB.

- Chapter 12 o

Deletion of Chapter 16 and reference to the Conflict of Interest Policy.

## Changes to the IRB Manual

Last updated: 4/28/08

- Chapter 16

Changes to IRB forms to reflect addition of the eIRB.

- Chapter 17

### Added definitions to glossary:

Possibly related: There is a reasonable possibility that the incident, experience, or outcome may have been caused by the procedures involved in the research.

Internal (on-site) Adverse Events: AEs that occur in study participants for which THR is the IRB of record.

External (off-site) Adverse Events: AEs that occur in study participants for which THR is not the IRB of record.

Unexpected - an unanticipated event is any adverse experience where the nature, severity or frequency is not identified in the informed consent form, investigator brochure (or similar document), described in the protocol and other relevant sources of information, such as product labeling and package inserts or the expected natural progression of any underlying disease, disorder, or condition of the subject(s) experiencing the adverse event and the subject's predisposing risk factor profile for the adverse event.

A serious adverse event is described as any adverse event that:

- (1) results in death;
  - (2) is life-threatening (places the subject at immediate risk of death from the event as it occurred);
  - (3) results in inpatient hospitalization or prolongation of existing hospitalization;
  - (4) results in a persistent or significant disability/incapacity;
  - (5) results in a congenital anomaly/birth defect; or
- based upon appropriate medical judgment, may jeopardize the subject's health and may require medical or surgical intervention to prevent one of the other outcomes listed in this definition (examples of such events include allergic bronchospasm requiring intensive treatment in the emergency room or at home, blood dyscrasias or convulsions that do not result in inpatient hospitalization, or the development of drug dependency or drug abuse).

NCI's (National Cancer Institute) definition for an Adverse event – an unexpected medical problem that happens during treatment with a drug or other therapy. Adverse events do not have to be caused by the drug or therapy, and they may be mild, moderate, or severe.

- Definitions in eIRB

**Changes to the IRB Manual**

**Last updated: 4/28/08**

Change “Institutional Signatory Official” to “Institutional Official”

Change all reference to “informed consent form” to “informed consent document”.

Delete HR agent and replace “agent” with “affiliate”.

Replace “patient” with “study subject” throughout manual.

Corrected misspellings and made minor clarifications.