

19-114 Institutional Review Board (IRB) Process

We have completed our audit of the IRB process. This audit was performed at the request of the UTHealth Audit Committee and was conducted in accordance with the *International Standards for the Professional Practice of Internal Auditing*.

BACKGROUND

The Committee for the Protection of Human Subjects (CPHS) is the IRB for UTHealth. The CPHS is responsible for reviewing proposed research involving human subjects to determine whether adequate measures are in place to protect autonomy, safety, privacy, and well-being of those asked to participate in research. Research involving human subjects that is conducted, supported, or otherwise subject to regulation by any federal department or agency is governed by the Code of Federal Regulations (CFR) – 45 CFR § 46 and 21 CFR § 56.

The CPHS is composed of four IRB review panels and each panel meets monthly. A fully convened meeting of the IRB review panel is required to review and approve human subjects research that does not qualify for exempt or expedited review. Applications for review and approval are submitted in iRIS, the electronic IRB system. In 2018, CPHS reviewed and processed 13,564 submissions. Of which 1,127 are initial submissions.

The Clinical Trials Resource Center (CTRC) provides administrative support to clinical researchers and research staff. The CTRC is responsible for coordinating educational programs that provide researchers and research staff with tools to facilitate ethical conduct and management of research activities in accordance with good clinical practice guidelines. The CTRC staff provide regulatory assistance and help investigators navigate the U.S. Food and Drug Administration's approval process related to investigational new drug/investigational device exemption and clinical trials.gov compliance. The CTRC is also responsible for conducting routine post approval monitoring visits to promote compliance with good clinical practice guidelines.

The CPHS underwent an accreditation review by the Association for the Accreditation of Human Research Protection Programs (AAHRPP) in March 2017 and received "full reaccreditation" status. The AAHRPP accreditation process evaluates the quality and level of protection an organization provides to research participants.

OBJECTIVES

The objective of this audit was to determine whether controls around IRB processes are adequate and in accordance with federal guidelines.

SCOPE PERIOD

The scope period was September 1, 2018 – March 31, 2019, unless otherwise noted.

METHODOLOGY

The following procedures were performed:

- Reviewed CPHS policies and procedures related to the roles and responsibilities, IRB membership, review and approval process, education and training, record keeping requirements, reporting obligations, and informed consent. A suggestion was made to ensure the *Emergency Research and Exception from Informed Consent* policy included the requirement from 21 CFR § 56.109(g) related to providing the sponsor with a copy of the information that has been publicly disclosed under 21 CFR § 50.24(a)(7)(ii) and (a)(7)(iii). IRB Management has implemented corrective action and updated the policy.
- Reviewed the monitoring processes performed by the CTRC staff for appropriateness.
- Reviewed the controls over user access in iRIS for appropriateness.
- Selected a sample of studies (25) during the period from September 1, 2018 through March 31, 2019 and reviewed for:
 - Compliance with record keeping requirements
 - Processes around full board review and approval
 - Processes around expedited review and approval
 - Processes around exempt review and approval
 - Processes around reciprocity/cooperative review approval
 - Processes around verifying training as required by departmental policy and procedures. A suggestion was made to ensure there are notifications in iRIS related to training that has expired or not posted for members of the study team.
- Selected a sample of noncompliance occurrences (10) during the period from September 1, 2017 through March 31, 2019 and reviewed for compliance with the reporting obligations. Noncompliance occurrences refers to Protocol Deviation, Unanticipated Problem Report, and Internal Adverse Event that should be reported to the IRB.
- Selected a sample of consent forms (5, if available) from studies where consent forms were applicable (11) and reviewed for compliance with the general informed consent requirements, existence of basic and additional elements of informed consent, and when appropriate, additional element of informed consent for clinical trials.
- Selected a sample of meeting minutes and reviewed for sufficiency in details to ensure compliance with the federal guidelines.

AUDIT RESULTS

A&AS identified areas of improvement:

- Consent forms were not consistently signed by the applicable subject or the subject's legally authorized representative. In addition, consent forms for clinical trials did not consistently include the statement required by the federal guideline.
- The process for granting, terminating, and monitoring user access to iRIS had not been formalized. In addition, periodic user access review was not performed.
- The IRB chairperson had not designated reviewers for human subjects research that qualify for expedited review.

NUMBER OF PRIORITY & HIGH FINDINGS REPORTED TO UT SYSTEM

None

19-114 IRB Process

We would like to thank the staff and management within the CPHS, CTCR, and various members of the study team who assisted us during our review.



Daniel G. Sherman, MBA, CPA, CIA
Assistant Vice President

MAPPING TO FY 2019 RISK ASSESSMENT

Risk (Rating)	Data is shared without proper IRB approval. (High)
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DATA ANALYTICS UTILIZED

Data Analytic #1	None
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AUDITING & ADVISORY SERVICES ENGAGEMENT TEAM

Assistant Vice President	Daniel G. Sherman, MBA, CPA, CIA
Audit Manager	Nathaniel Gruesen, MBA, CIA, CISA, CFE
Auditor Assigned	Kathy Tran, CIA, CFE
End of Fieldwork Date	June 21, 2019
Issue Date	August 21, 2019

Copies to:

- Audit Committee
- Dr. Michael Blackburn
- Dr. Anne Dougherty
- Dr. Sujatha Sridhar
- Cynthia Edmonds
- Barbara Legate

Issue #1	<p>A&AS selected a sample of 25 studies for review. Of the 25 studies, 11 were applicable for review of the consent forms. For each of the 11 studies, a sample of five consent forms was selected for review for a total of 55, with the following exceptions:</p> <ul style="list-style-type: none"> • One study had a total of four subjects enrolled. • One study had both verbal and written consent forms approved by the IRB. For this study, of the five selected, one was written and four verbal. 45 CFR § 46.116(f)(3)(i) and 21 CFR § 56.109(c)(1) gives the IRB the authority to waive the requirement of written consent form if the IRB finds that the research presents no more than minimal risk of harm to subjects. Per information in iRIS, the IRB’s reviewer for this study indicated the study was minimal risk. <p><u>Signature on Consent Forms</u></p> <p>45 CFR § 46.117(a) and 21 CFR § 50.27(a) requires, unless the requirement is waived, informed consent is to be documented using a written informed consent form approved by the IRB and signed (including in an electronic format) by the subject or the subject’s legally authorized representative.</p> <p>Furthermore, the Director of CPHS confirmed no one other than the subject or the subject’s legally authorized representative should sign the consent form. When it is expected that a legally authorized representative may have to sign the consent form, the IRB will approve the form with language that indicates as such. For example, the consent form will have a signature line that states, “Name of Parent” or “Name of Legally Authorized Representative.”</p> <p>Of the 50 consent forms reviewed, the following was noted:</p> <ul style="list-style-type: none"> • One consent form showed a nurse signed on the “Signature of Subject” line with a note “signed by nurse because patient’s injuries prevented him from signing for himself.” Signatures from the person obtaining the informed consent and the translator were also on the form. The consent form for this study was one that anticipated a signature from a legally authorized representative on behalf of the subject; however, the legally authorized representative did not sign the form. • Two consent forms showed someone signed on the “Signature of Subject” line; however, the consent form for these two studies was not one that anticipated a signature from a legally authorized representative or anyone else other than the subject. <p><u>Clinical Trial Consent Form</u></p> <p>21 CFR § 50.25(c) requires the following statement be provided to each clinical trial subject in the informed consent documents, “A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. Law. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time.”</p>
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19-114 IRB Process

	Of the 50 consent forms reviewed, five consent forms for one study showed the required statement for clinical trial study was not included in the written consent form. According to the study application submitted by the Principal Investigator, this was a clinical trial study.
Recommendation #1	We recommend CPHS and CTRC Management develop and implement procedures to ensure: <ol style="list-style-type: none"> a) Consent forms are signed by the subject or the subject’s legally authorized representative, when appropriate. b) Consent forms for clinical trials include the statement required by the federal guideline.
Rating	Medium

Management Response #1a	Existing Controls: <ol style="list-style-type: none"> 1. Informed consent training is available online and is required for coordinators and research nurses who consent participants at Memorial Hermann Hospital. 2. Research staff orientation addresses the appropriate method for consent documentation. 3. CPHS and CTRC policies address consent documentation. 4. Research compliance staff conduct study audits and educate research staff when errors in consent documentation are found. 5. Routine monitoring visits performed by the Research Compliance staff includes an audit of the consent documentation that verifies consent forms are signed by the subject or the subject’s legally authorized representative. <p>Additional controls:</p> <ol style="list-style-type: none"> 1. Weekly update and coordinator newsletter to research staff will include education on consent documentation at least once every quarter. Additional training will be done if monitoring shows an increase in trend of consent documentation errors.
Responsible Party	Cynthia Edmonds, Director of the Office of Research Support Committees Sujatha Sridhar, Executive Director Research Compliance, Education, and Support Services
Implementation Date	February 28, 2020

Management Response #1b	Existing controls: <ol style="list-style-type: none"> 1. The CPHS consent template includes the language “A description of this clinical trial will be available on http://www.clinicaltrials.gov, as required by U.S. Law. This will not include information that can identify you. After the study has ended, website will include a summary of the results. You can search this website at any time.”
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19-114 IRB Process

	<p>2. There is a process to identify trials that require registration. IRB coordinators review consent forms to ensure the required language is in the consent forms for trials that require registration.</p> <p>Additional controls:</p> <ol style="list-style-type: none">1. IRB coordinators were reminded to ensure that the required language is present in consent forms for applicable trials at their staff meeting.2. For the next 6 months, Research Compliance staff will conduct targeted audit of random consent forms to ensure the required language is present. After 6 months, this will be included in routine audits.
Responsible Party	Cynthia Edmonds, Director of the Office of Research Support Committees Sujatha Sridhar, Executive Director Research Compliance, Education, and Support Services
Implementation Date	February 28, 2020

<p>Issue #2</p>	<p>CPHS used iRIS for the submission, review, approval, and management of human subject protocols. The system contains human subjects' protocol information, not human subject data. Although there is no HIPAA data stored in iRIS, the research data is considered "intellectual property" per HOOP 201 <i>Intellectual Property</i>. As a result, the system is ranked as "high risk application" by the IT Risk and Compliance Manager in Information Technology due to the loss of reputation in an event the data is lost or breached.</p> <p>A&AS reviewed the requirements for user access controls and noted the following:</p> <ul style="list-style-type: none"> • Control AC-1 of the Control Standards Catalog (a supplement to Texas Administrative Code 202) requires the creation, distribution, and implementation of an account management policy, which defines the rules for establishing user identity, administering user accounts, and establishing and monitoring user access to information resources. • ITPOL-004 <i>Access Control Policy</i>, Section 6.2.6 states, "Owners or their designees must review access at least quarterly to ensure access privileges, including administrative and special access accounts, are appropriate. A user's access authorization shall be appropriately modified or removed when the user's employment or job responsibilities within the agency change." • ITPOL-004 <i>Access Control Policy</i>, Section 6.2.14 states, "All OEM (original equipment manufacturer) or vendor default passwords must be changed from their default values and meet university standards before the system is deployed. This includes systems deployed to test, development or production environments." <p>At the time of review, A&AS noted the following:</p> <ul style="list-style-type: none"> • CPHS has a process for granting, terminating, and monitoring user access to iRIS; however, the process is not formally documented. All UTHealth employees have basic access to iRIS to submit and view their own study. Special access to iRIS (e.g. able to search and view all research protocols) is approved by the Director of CPHS and granted by the Senior Business Systems Analyst. • There is not a set schedule for reviewing employee access. Appropriate actions are taken whenever inappropriate access is identified. Guest accounts are reviewed annually and can be renewed at the discretion of the IRB of CPHS. Upon A&AS inquiry, the Director of CPHS and the Senior Business Systems Analyst performed an access review of all users with special access in iRIS in April 2019. • A default "Administrator" account exists in iRIS since the system was first implemented in 2005. The Senior Business Systems Analyst (administrator for iRIS) does not use the account. Users are required to have an active UTHealth LDAP account in order to log into iRIS. Upon A&AS inquiry, the account was removed from the list of accounts with special access in iRIS as of April 23, 2019. • There were five iMedRIS employees, the vendor for iRIS system, with special access to iRIS. A Business Associate Agreement is not on file with
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19-114 IRB Process

	<p>Procurement Services or the Office of Legal Affairs for iMedRIS since protected health information (PHI) is not stored in iRIS. It should be noted that for individuals who do not have an active UTHHealth LDAP account, a guest account can be created. When requesting access, guests are required to sign <i>the Information Resources User Acknowledgement Form</i> which includes the statement, "All confidential information, including research data, SSNs, and information protected by HIPAA and FERPA, must be protected in accordance with UTHHealth policies, UT System Policy 165 and state and federal laws."</p>
Recommendation #2	<p>We recommend CPHS Management work with the administrator for iRIS at UTHHealth to develop and implement formalized procedures for granting, terminating, and monitoring user access to iRIS to ensure compliance with TAC 202 and ITPOL-004. Evidence of the periodic user access review performed should be documented and retained.</p>
Rating	<p>Medium</p>
Management Response	<p>Existing controls:</p> <ol style="list-style-type: none"> 1. iRIS System is secured through the LDAP directory with individually assigned userids. Termination of an individual's relationship with the University automatically terminates their access to iRIS. 2. Non-UTHHealth faculty, staff or students who request for access to iRIS need to obtain a UT Houston guest account. Guest accounts are reviewed and renewed annually. 3. IRB members have special access. Each September at the start of a new term, access for the members who are no longer on the IRB is reverted back to their default access. <p>Additional controls:</p> <ol style="list-style-type: none"> 1. Staff in certain positions have special access (e.g. Sponsored Projects, Research Compliance, IRB office, MHH research office etc.). A new process has been established to conduct a quarterly review of everyone who has special access to identify any individuals whose job requirements might have changed. If these individuals are no longer in a position that requires special access, their access will be reverted back to default. This review will be documented.
Responsible Party	<p>Cynthia Edmonds, Director of the Office of Research Support Committees Barbara Legate, Senior Business Systems Analyst</p>
Implementation Date	<p>September 30, 2019</p>

19-114 IRB Process

Issue #3	<p>21 CFR § 56.110(b) and 45 CFR § 46.110(b)(2) states, “Under an expedited review procedure, the review may be carried out by the IRB chairperson or by one or more experienced reviewers designated by the IRB chairperson from among the members of the IRB.”</p> <p>CPHS Policy on <i>Expedited Review</i> states, "An expedited review procedure consists of a review of research involving human subjects by the IRB chair or by one or more reviewers designated by the chair from among the IRB membership who have received training relative to the expedited review categories."</p> <p>At the time of review, A&AS noted the IRB chairperson has not formally designated a list of reviewers for expedited studies. The IRB staff is responsible for assigning a research proposal to a reviewer in iRIS based on the IRB staff’s assessment of the reviewer’s level of expertise, tenure as an IRB member, and prior experience, if any, as an expedite reviewer.</p>
Recommendation #3	We recommend CPHS Management develop and implement procedures for expedited review in accordance with the federal guidelines.
Rating	Medium
Management Response	CPHS policy on expedited review has been amended to include the statement “Members who have at least one-year experience as an IRB member are considered automatically designated by the IRB chair as members who may be assigned as expedited reviewers.”
Responsible Party	Cynthia Edmonds, Director of the Office of Research Support Committees
Implementation Date	August 19, 2019 (to be verified by A&AS)