

The logo features the word "HONORHEALTH" in a bold, white, sans-serif font. The letters are set against a dark purple background that is composed of two overlapping horizontal bars. The top bar is on the left and the bottom bar is on the right, creating a stepped effect behind the text. A small "TM" trademark symbol is positioned to the right of the final letter "H".

**HONORHEALTH™**

**HonorHealth Research Institute**

Investigator Manual

July 27, 2017

Version 3.0

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## Scope

Throughout this document, “the Institute” refers to HonorHealth Research Institute.

## Version History

Version	Date	Change
1.0	January 26, 2017	Edited the statement (Page 20): <i>If your research involves investigational drugs, biologics, or devices, you must follow Investigational Pharmacy Procedures – please contact Karen Ansaldo, PharmD, <a href="mailto:Karen.Ansaldo@honorhealth.com">Karen.Ansaldo@honorhealth.com</a> for more information</i>
2.0	May 5, 2017	Added Section: Monitoring versus Auditin,g Added Section: What if the FDA wants to inspect my research?
2.1	May 19, 2017	Edited statement (Page 20); <i>If your research involves investigational drugs or biologics, you must follow Investigational Pharmacy Procedures – please contact Karen Ansaldo, PharmD, <a href="mailto:Karen.Ansaldo@honorhealth.com">Karen.Ansaldo@honorhealth.com</a> for more information.</i> (Deleted “devices”)
3.0	July 27, 2017	Removed Jonathan Wallach, JD as contact for Corporate Compliance. Replace with Jim Passey (Page 10). Research Integrity Office is no housed within Research Quality & Regulatory Compliance (Page 11)

## What is the purpose of this manual?

This document “INVESTIGATOR MANUAL” is designed to guide you through policies, procedures and resources related to the conduct of Human Research that are specific to HonorHealth Network. All human research related activities must be in full compliance with current HonorHealth Network and Institutional Review Board (IRB) policies and procedures while maintaining compliance with Federal regulations and assuring the protection of human research participants.

This document discusses the mechanics of working with the IRB and is intended as supplementary information to required training.

General information regarding Human Research protections and relevant federal regulations and guidance is incorporated into the required human research protections training. For additional information see “What training do my staff and I need to conduct Human Subject Research?”

## Abbreviations

ACOS/R&D	Associate Chiefs of Staff for Research & Development
AE	Adverse Events
COIC	Conflict of Interest Committee
CRADA	Cooperative Research and Development Agreement
CRADO	Chief Research and Development Officer
DHHS	Department of Health and Human Services
DoD	Department of Defense
FDA	Food and Drug Administration
IIS	Investigator-Initiated Study
IND	Investigational New Drug
IDE	Investigational Device Exception
IRB	Institutional Review Board
LAR	Legally Authorized Representative
OHRP	Office of Human Research Protections
ORD	Office of Research & Development
ORO	Operations Research Organization
PHI	Protected Health Information
PO	Program Office
R&D	Research & Development
VHA	Veterans Health Administration
WIRB	Western Institutional Review Board

## When am I engaged in research?

You are considered “engaged” in human participants’ research when you:

- 1) Obtain data through intervention or interaction with living individuals for research purposes, or
- 2) Obtain individually identifiable private information for research purposes. Further, a site is considered to be “engaged” in human participants’ research when it receives a direct Federal award to support the research.
- 3) Obtain the informed consent of a human subject.
- 4) Further, a site is considered to be “engaged” in human participant’s research when it receives a direct Federal award to support non-exempt human subjects research.

## Definition of Terms

“*Research*” is a systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge (45§46.102(d)). Examples of systematic investigations include:

- Clinical trials of drugs or devices
- Medical outcomes study comparing approved drugs or devices

- Surveys and questionnaires
- Interviews and focus groups
- Analyses of existing data or biological specimens
- Epidemiological studies
- Evaluations of social or educational programs
- Cognitive and perceptual experiments
- Medical chart review studies

“*Human subject*” means a living individual 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 (45§46.102(f)). This may be an individual who is or becomes a participant in research, either as a recipient of the test article or as a control. A subject may be either a healthy human or a patient (21§50.3(g)).

- “*Intervention*” includes both physical procedures by which data are gathered (for example, venipuncture) and manipulations of the subject or the subject’s environment that are performed for research purposes (45§46.102(f)).
- “*Interaction*” includes communication or interpersonal contact between investigator and subject (45§46.102(f)).
- “*Private information*” includes information about behavior that occurs in a context in which an individual can reasonably expect that no observation or recording is taking place, and information which has been provided for specific purposes by an individual and which the individual can reasonably expect will not be made public (for example, a medical record). Private information must be individually identifiable (i.e., the identity of the subject is or may readily be ascertained by the investigator or associated with the information) in order for obtaining the information to constitute research involving human subjects (45§46.102(f)).
- “*Test article*” means any drug (including a biological product for human use), medical device for human use, human food additive, color additive, electronic product or any other article subject to regulation from the Public Health Service Act (21§50.3(j)).

Research results do not have to be published or presented at a professional meeting to be defined as human subject research. The intent to contribute to “generalizable (scholarly) knowledge” makes an activity research, regardless of publication. Research that never is published is still research.

All human subject research activities in which the Institute is engaged, regardless of sponsorship and overall intent, must be submitted to the IRB through the the IRBNet portal ([www.irbnet.org](http://www.irbnet.org)). The human subject research activities may not be initiated until approval is issued by the HonorHealth Research institute and appropriate IRBs.

“*Investigator*” means an individual who actually conducts a clinical investigation (i.e., under whose immediate direction the drug is administered or dispensed to a subject). In the event an investigation is conducted by a team of individuals, the investigator is the responsible leader of

the team. “Sub-investigator” includes any other individual member of that team. In conducting clinical investigations of drugs, including biological products, under 21 CFR part 312 and of medical devices under 21 CFR part 812, the investigator is responsible for:

- Ensuring that a clinical investigation is conducted according to the signed investigator statement for clinical investigations of drugs, including biological products, or agreement for clinical investigations of medical devices, the investigational plan, and applicable regulations
- Protecting the rights, safety, and welfare of subjects under the investigator’s care
- Controlling drugs, biological products, and devices under investigation (21 CFR 312.60, 21 CFR 812.100)

For more information please see [FDA Guidance Investigator Responsibilities](#)

“*Minimal Risk*” means the probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves that those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests (45 CFR 46.102(i)).

“*Sponsor*” means a person who takes responsibility for and initiates a clinical investigation. The sponsor may be an individual or pharmaceutical company, governmental agency, academic institution, private organization, or other organization. The sponsor does not actually conduct the investigation unless the sponsor is a sponsor-investigator. A person other than an individual that uses one or more of its own employees to conduct an investigation that it has initiated is a sponsor, not a sponsor-investigator, and the employees are investigators.

“*Sponsor-Investigator*” means an individual who both initiates and conducts an investigation, and under whose immediate direction the investigational drug is administered or dispensed. The term does not include any person other than an individual. The requirements applicable to a sponsor-investigator under this part include both those applicable to an investigator and a sponsor.

## Federalwide Assurance (FWA)

The HonorHealth maintains a current Federalwide Assurance (FWA 00001751) (HonorHealth signed Assurance Document) which obligates the Institution to uphold ethical principles and is applicable whenever research is conducted or supported by any U.S. federal department or agency that has adopted the U.S. Federal policy for the Protection of Human Subjects (also known as the Common Rule 45 CFR Part 46), unless exempt.

## Research Roles and Responsibilities

Human subject protection is a shared responsibility of all individuals and organizations involved in research. These entities include the federal agencies that enforce the human subject



research regulations, the institutions engaged in human subject research, the IRBs reviewing the human subject research and the investigators conducting the human subject research. The roles and responsibilities of these different entities are defined in federal and state laws and regulations pertaining to human subject research.

### HonorHealth Research Institute

- The Institute bears responsibility for compliance with the DHHS and FDA regulations for the performance of all human subject research activities in which it is engaged.
- The Institute has responsibility for educating researchers on issues of research ethics and scientific integrity.
- The Institute has a mandated responsibility to investigate alleged cases of scientific misconduct. In addition, the Institute has a responsibility to have and enforce a policy on conflict of interest.
- The Institute has responsibility for establishing and maintaining procedures to ensure appropriate ethical review of research proposals by the IRB, administrative review of research protocols, contracts and grants, and scientific peer review as needed.

### Institutional Review Board

Ensures compliance with the Institute's policies and procedures, federal regulations, and state and local laws relative to the review of human subject research studies.

- Reviews all research activities involving human subjects and documents the findings regarding ethical considerations, scientific merit, and adherence to federal regulations and IRB policies and procedures.
- Reviews research activities to ensure that:
  - Risks to subjects are minimized by using procedures that are consistent with sound research design and that do not unnecessarily expose subjects to risk, and whenever appropriate, by using procedures already being performed on the subjects for diagnostic or treatment purposes.
  - Risks to subjects are reasonable in relation to anticipated benefits, if any, and to the importance of the expected knowledge. In evaluating risks and benefits, the IRB considers only those risks and benefits that may result directly from the research (as distinguished from risks and benefits that people would have even if not participating in the research); and
  - Selection of subjects is equitable. In making this assessment, the IRB takes into account the purpose(s) of the research and the setting in which the research will be conducted;
  - Informed consent is obtained from the subject or the subject's legally authorized representative and appropriately documented, unless waived in accordance with applicable federal regulations;
  - Where appropriate, the research plan makes provisions for monitoring the data collected to ensure the safety of subjects; and

- Where appropriate, there are provisions to protect the privacy of participants and to maintain the confidentiality of data.
- Where appropriate, additional safeguards are included in the study to protect the rights and welfare of subjects when some or all of them are likely to be vulnerable to coercion or undue influence (the Institute's employees, prisoners, pregnant women, handicapped, mentally disabled persons, or economically or educationally disadvantaged persons).
- Reviews research protocols and is authorized to approve, require modifications to secure approval, disapprove, and terminate or suspend.
- Conducts continuing reviews of approved research. Reviews proposed amendments, adverse events, protocol deviations and matters of noncompliance.
- Has the authority to:
  - Approve, require modifications to or disapprove human subjects research activities
  - Approve HIPAA Authorizations or Waivers for research
  - Require research progress reports;
  - Audit and/or monitor the research and researchers for adherence to the federal regulations, the Institute's policies and IRB policies and procedures; and
  - Report suspensions, terminations, and noncompliance to IRB officials, the Institute's officials, research administrative (RA) officials, and the federal government.
- Completes all training requirements and stay informed of current research related and regulatory developments.

### Corporate Compliance

Oversees all required Health Insurance Portability and Accountability Act (HIPAA) training and Conflicts of Interest Management

Contact: Jim Passey (480) 882-4298, [Jim.Passey@honorhealth.com](mailto:Jim.Passey@honorhealth.com)

### Research Quality, & Regulatory Compliance

- With the IRB, responsible for maintaining the Institute's FWA and for ensuring compliance with its terms.
- Responsible for compliance with the Institute's policies and procedures, federal regulations, and state and local laws relative to the conduct of human subjects research studies.
- Provides guidance regarding the interpretation of regulations, laws, and policies to the organization's researchers, staff and administrators.
- Develops and implements the Institute's human subject protection policies and procedures.
- Tracks and maintains records of all required human subject protection training requirements to ensure that investigators and key study personnel are in compliance with training requirements.

- Responsible for providing opportunities for human subject protection training to investigators, key study personnel, the Signatory Official, and all the Institute's staff who participate in the human subject protection program.
- Performs quality assurance monitoring of research protocols and investigates matters of noncompliance. Makes recommendations to implement corrective action as needed in accordance with the Institute's policies and IRB policies and procedures.
- Monitors federal regulatory Web sites and other research-related resources to stay current with regulatory changes in human subject protection guidelines and policies. Communicates pertinent information to staff in a timely manner.
- Conducts audits as requested by IRB, the principal investigator or for cause.
- Houses the Research Integrity Office which oversees scientific and research misconduct.

**Contact:** Dr. Aurea M. Flores (480) 323-4196, [Aurea.Flores@honorhealth.com](mailto:Aurea.Flores@honorhealth.com)

#### IRB Administration Staff

- Coordinates the activities of the HonorHealth Institutional Review Board (IRB).
- Maintains all study-related documentation in accordance with the Institute's policies, IRB policies and federal regulations.
- Pre-reviews all items submitted to IRB.
- Assists PI and research staff to ensure completeness of submitted materials.
- Makes recommendations to correct documents, in order for items to be ready for IRB review.
- Serves as an experienced IRB member.
- Maintains a comprehensive knowledge of all aspects of the institution's system of protections for human subjects.
- Is knowledgeable of all federal regulations for human subjects research in order to clarify and provide information to the IRB regarding this areas.
- Reviews minor IRB revisions, staff changes, and other items at the discretion of the IRB Chair.
- Reviews Conflicts of Interest forms and refers to the Compliance Administrator for resolution as needed.
- Updates IRB policies, procedures and forms.
- Serves as the Human Protections Administrator on the FWA, is familiar with the Institution's commitments under FWA, and plays a key role in ensuring that the institution fulfills its responsibilities under FWA.
- Manages [IRBNet](#) – document repository for HonorHealth IRB.

**Contact:** Julie Washington, CIP (480) 323-3071, [Julie.Washington@honorhealth.com](mailto:Julie.Washington@honorhealth.com)

#### Principal Investigator (PI)

- Oversees and conducts the research process and is responsible for the conduct of the investigators and research staff at all study sites for which he/she is listed as the Principal Investigator.

- Ensures all research activities are conducted in compliance with research protocols, and applicable federal, state, and local laws and regulations, the Institute's policies, and IRB policies and procedures.
- Responsible for the safety and welfare of subjects.
- Ensures compliance with the protocol's data and safety monitoring plan, and reports adverse events to the IRB, study sponsor and appropriate federal agencies.
- Ensures that informed consent is appropriately obtained from all subjects and that subjects are treated with respect and dignity.
- Completes all required human subjects protection and HIPAA training, and ensures that investigators and key study personnel complete required training.
- Reviews all IRB policies and procedures as part of the required initial training for conducting human subject research. Routinely reviews the IRB policy website for new or revised IRB policies and procedures.
- Reviews scientific literature to ensure that protocol interventions are consistent with current research data and do not place subjects at unnecessary risk.
- Submits modifications in accordance with IRB regulations when new information merits changes to the study protocols and design.
- Is responsible for the suitability of all submissions to the IRB including protocol applications, amendments and adverse event reports.
- Ensures the timely continuing review of protocols and the submission of all re-approval applications before the protocol's expiration date.
- Submits proposed changes to the research in the form of protocol amendments to the IRB before the changes are implemented, except when such changes must be implemented immediately to ensure the health and well-being of research subjects.
- Responsible for the protection of subjects' privacy and confidentiality according to applicable HIPAA policies, the Institute's policies, and IRB policies and procedures.
- Maintains all study-related documentation in accordance with the Institute's policies, IRB policies and federal regulations.

#### Co-investigator (or Sub-investigator)

- Records and maintains accurate documentation of all activities in compliance with federal, institutional and sponsor requirements, including collecting data using case report forms and maintaining appropriate source documents.
- Recruits and screens research subjects according to the inclusion/exclusion criteria.
- When requested, obtains appropriate informed consent from all subjects and in doing so treats subjects with respect and dignity.
- Where applicable, ensures proper use of randomization schedules.
- Carries out the protocol-specified procedures and adheres to the protocol-defined timelines.
- Secures and controls the use of the investigational agent(s) or device(s).

- Reports all adverse events and unanticipated problems according to the requirements of federal regulatory agencies, the IRB and the study protocol.
- Tracks financials and ensures payments are made to suppliers and providers of services for the research.
- Complies with the IRB-approved research protocols, applicable federal, state and local laws and regulations, the Institute's policies, and IRB policies and procedures (this includes ensuring all appropriate approvals are obtained prior to initiation of the research).
- Protects subjects' privacy and confidentiality according to applicable HIPAA policies, the Institute's policies, and IRB policies and procedures.
- Fulfills commitments made to the sponsor and/or to the FDA (e.g., form 1572 or the Investigative Agreement).
- Completes all required human subject protection training, and, if applicable, HIPAA training.

#### Biostatistician

- Serves as a resource for the development of design, measurement and analysis strategies.
- Provides statistical analyses and interpretation of study results.
- Reviews methodological and statistical review for manuscripts, grants, and other investigator-led studies.
- Assists with data visualization to generate graphics and pictorial representations for reporting and dissemination.
- Conducts and reviews prospective power analyses to determine sample size requirements according to design and investigator-defined parameters (i.e., alpha, power, and effect size).
- Assists with database creation, management, and cleaning of data for statistical analysis.
- Where applicable, assists with the design and validation of data collection systems and instruments.

**Contact:** Kevin Gosselin, Ph.D., [Kevin.Gosselin@honorhealth.com](mailto:Kevin.Gosselin@honorhealth.com)

#### Study Coordinator/Research Nurse\*

- Maintains data pertaining to research projects and completes source documents.
- Assists with patient recruitment and enrollment.
- Attends study meetings.
- Reviews medical records and/or conducts screenings for recruitment of study participants, performs interviews and conducts questionnaires. Gathers, coordinates and processes pertinent data specific to each research project.
- Collects study specimens according to protocol.

- Assists with literature search and protocol development.
- Coordinates services, schedules procedures, creates and maintains case packages, and monitors charges.
- Assists with quality assurance.
- Assists in documentation of adverse events/serious adverse events.
- Orders and maintains equipment and supplies.
- Participates in on-call schedule as needed.
- Completes all required human subject protection training, and, if applicable, HIPAA training.

#### Data Manager\*

- Completes case report forms and performs data entry.
- Interfaces with study monitor visits.
- Resolves study data queries.
- Attends study meetings.
- Assists with quality assurance.
- Completes all required human subject protection training(CITI), and, if applicable, HIPAA training.

#### Regulatory Affairs Coordinator\*

- Completes new study and amendment applications to IRB.
- Completes IND submissions and annual reports to FDA.
- Assists in submissions and reporting to ClinicalTrials.gov
- Tracks regulatory submissions.
- Reports Serious Adverse Events (SAE).
- Reports major study violations.
- Completes continuing reports for IRB submission.
- Attends study meetings.
- Assists with quality assurance.
- Completes all required human subject protection training (CITI), and HIPAA training, if applicable.

#### Project Manager\*

- Responsible for overall project and financial management.
- Responsible for contract and budget development.
- Responsible for negotiations for clinical trials and grants.
- Leads and coordinates all activities required for study start-up, and feasibility.
- Assists with quality assurance.
- Completes all required human subject protection training (CITI), and HIPAA training, if applicable.

**Research Laboratory Technician\***

- Orders and maintains laboratory supplies.
- Responsible for specimen processing, storage and shipping.
- Attends study meetings.
- Assists with quality assurance.
- Completes all required human subject protection training (CITI), and HIPAA training, if applicable.

**Investigational Pharmacist**

- Maintains perpetual inventory of investigational drugs.
- Order investigational supplies.
- Assist in the review of physician orders for therapeutic clinical studies.
- Responsible for storage, dispensing, destruction of investigational drug supplies.
- Assists with quality assurance.
- Completes all required human subject protection training (CITI), and HIPAA training, if applicable.

\*The tasks above may be combined into one or more positions depending on the structure of the particular program. These tasks must be assigned to personnel that is qualified by education, training and experience to assume responsibility for completing this tasks in compliance with applicable regulations.

**Who is eligible to be a Principal Investigator?**

The Institution's Full members and Affiliate members as well as Faculty participant (U of A, ASU, Mayo, TGen) may serve as the principal investigator on a research project involving human subjects. In certain situations, students/fellows may also assume roles as principal investigators but must have a HonorHealth Full Member Senior Faculty Sponsor to assume responsibility over the project and student/fellow regarding all clinical research activities.

**May a student or medical resident be a Principal Investigator?**

This Institution allows students or medical residents to act as Principal Investigators in human subject research. They must have a HonorHealth Full Member Senior Faculty Sponsor to oversee, guide, and sign off on their research. The Faculty Sponsor is required to be listed as part of the research personnel (staff) of the study and to complete a human subject research online training course (CITI). For more information see What Training do my staff and I need to conduct human subject research?

Non-HonorHealth employed students (e.g., nursing students) may be serve as principal investigators under the oversight of an HonorHealth Full Member Senior Advisor but cannot be involved or perform direct patient care.

## May researchers, who are not faculty, students, or employees of HonorHealth Network, conduct human subject research at HonorHealth Network?

If you are **not** a faculty member, student, or employee of HonorHealth Network and wish to conduct human subject research at any HonorHealth Facilities or with HonorHealth Network faculty, students, or employees, you must contact the Director of Research Administration, HonorHealth Research Institute in writing via e-mail ([Maribeth.Schade@honorhealth.com](mailto:Maribeth.Schade@honorhealth.com)) before engaging in any research activities.

## May research personnel, who are not faculty, students, or employees of HonorHealth Network, conduct human subject research at HonorHealth Network?

These are sub-contractors to perform specific functions within the research project. Investigators and researchers who wish to include research personnel who are **NOT** a faculty member, student, or employee of HonorHealth Network must contact the Director of Research Administration, HonorHealth Research Institute in writing via e-mail ([Maribeth.Schade@honorhealth.com](mailto:Maribeth.Schade@honorhealth.com)) before allowing the research personnel to engage in human subject research activities.

## What training do my staff and I need to conduct Human Research?

This section describes the training requirements imposed by HonorHealth IRB and the Institute. You may have additional training imposed by other federal, or state policies. Any additional requirements will be directed by the funding agency, Sponsored Programs, Legal Affairs, Compliance, Contracts, your department, and/or the IRB Administration. Investigators and staff conducting research involving more than minimal risk to subjects must complete the Collaborative Institutional Training Initiative (CITI) human subjects online training program.

Investigators and staff conducting clinical trials are required to take Human Subject Research training, GCP training, and Responsible Conduct of Research through CITI.

If you have completed Human Subject Research training through CITI as part of another organization/institution, some or all modules may apply for HonorHealth requirements. Each organization chooses CITI modules depending on their scope of research practices. Therefore, it is important that you add HonorHealth to your affiliations in your CITI user profile, if you have one. You may add any number of affiliations to your CITI user profile, in case you conduct clinical research at multiple organizations/institutions that require CITI training. CITI will automatically populate your CITI HonorHealth profile with those modules you may have completed. You will need to complete any HonorHealth-required modules that you have not completed.



## Procedure to complete CITI Certification

Go To <https://citiprogram.org>

Click on Register

Step 1: Choose participating institution – HonorHealth Research Institute. Click Next

Step 2: Enter first, last name and e-mail address. Click Next

Step 3: Create Username and Password. Click Next

Step 4: Complete Demographic Information. Click Next

Step 5: Continuing Education credit option. Click Next

Step 6: Complete. Click Next

Step 7: Complete. Click Next

Go to Main Menu – Top menu bar left

Click on HonorHealth Research Institute Courses

There are 4 Questions to answer which will determine which courses must be completed

- a. Question 1: **Human Subjects Research**
  - i. Biomedical Research Investigators – majority of clinical research staff falls in this category
  - ii. Social & Behavioral Research Investigators – for staff involved primary in human subject research within the Social and Behavioral Sciences
  - iii. Research with data or laboratory specimens ONLY – No direct contact with human subjects. For data managers, regulatory specialists, billing specialists, science laboratory staff
  - iv. IRB members – for IRB members
- b. Question 2: Institutional/Signatory Officials & IRB Chair – NOT APPLICABLE
  - i. Institutional/Signatory Officials
  - ii. IRB Chair
- c. Question 3 : **Good Clinical Practice (GCP)**
  - i. US FDA Focus – majority of clinical research staff falls in this category
  - ii. Medical Devices (International Focus) – intended for clinical research staff working with non-FDA sanctioned investigational medical devices
  - iii. Investigational Drugs (ICH/International Focus) – intended for clinical research staff working with non-FDA sanctioned investigational drugs
- d. Question 4: **Responsible Conduct of Research**
  - i. Biomedical Responsible Conduct of Research Course – majority of clinical research staff falls in this category

- ii. Social and Behavioral Responsible Conduct of Research Course – for staff involved primary in human subject research within the Social and Behavioral Sciences

Every research staff must complete one each of Questions 1, 3 and 4. Question 2 is only for the Institutional Official or the IRB chair.

Click on Submit. A window with the list of courses selected will appear

Click on a course

Click on Complete the Integrity Assurance Statement before beginning the course

Each course has modules

Complete each module and its associated quiz found at the bottom of the module

Once all modules are completed and passed, you will be able to view and print a copy of the certificate for uploading. If you add your CITI ID number to your IRBnet user profile, all completed courses will be automatically shared with HonorHealth and uploaded into your IRBnet profile.

Continue with the next course until all courses are completed.

For a detailed procedure with screen shots, please go to <https://support.citiprogram.org>

In case of questions regarding which modules to complete, please contact [irb@honorhealth.com](mailto:irb@honorhealth.com)

Training is valid for a four-year period, after which time the training must be repeated. All members of the research team involved in the research must complete training. Members of the research team who have not completed human subject research protection training may not take part in aspects of the research that involve human subjects.

### Linking IRBNet and CITI Program Accounts

All members of the research team involved in the research must link their CITI program accounts with IRBNet account.

#### Procedure:

Login to your [IRBNet](#) account

Click User Profile

In the External Accounts section (near the bottom of the page), click Add External Account

A pop-up window will appear with CITI Training Program as default

Please enter your CITI Member ID. It is found at the top of your [CITI Program](#) homepage upon login.

To verify ownership of the CITI account, you will receive a verification link to the institutional e-mail address associated with your CITI affiliation. If your institutional e-mail is blank, the verification link will be sent to your preferred e-mail address.

Once you receive your e-mail, click the verification link and your two accounts have been link. Your CITI coursework will be automatically pulled into IRBNet over the next 24 hours.

## HIPAA Training

Investigators and staff conducting clinical trials are required to complete HIPAA training, either through HonorHealth ([HealthStream](#)) or through an appropriate provider (e.g., DHHS).

## What are my obligations as a Principal Investigator when developing a research project?

- Make sure that you have the adequate resources to protect the rights, welfare and safety of human participants involved in the research, including:
  - Sufficient time to conduct, oversee and complete research
  - Adequate number of qualified staff
  - A process to ensure that all persons involved in the design, conduct and/or reporting of research are adequately informed about the protocol and their research-related duties and functions
  - Adequate facilities in which to perform study procedures
  - Availability of medical or psychological resources that participants may need as a consequence of the research
  - Access to a population that will allow recruitment of the necessary number of participants.
  - Make sure that the research application is consistent with the proposal for funding for extramural or intramural support.
  - Act as a liaison between the IRB and the research sponsor (e.g., notification of IRB review and approval).
  - Make sure that there are additional protections for research involving vulnerable populations as required.

- If your research involves entities within HonorHealth Network that are not under your control, you must ensure appropriate communication, education, and training of those staff.
- If your research has a therapeutic intent and/or involves clinical interventions, you must ensure that you have support from the following departments: Project Management, Regulatory Affairs, Data Management, Research Administration, Research Quality Regulatory and Compliance (RQRC). In addition, there must be at least 2 investigators (1 principal investigator and 1 sub-investigator) responsible for the study conduct.
- If your research is sponsored by a federal agency, foundation or other non-profit organization, you must ensure that you have support from Research Administration and Research Quality Regulatory Compliance (RQRC).
- If your research is an IIS, you must ensure that you communicate with Research Administration and RQRC for guidance and support.
- All contracts for research projects must be reviewed, approved and executed by the Institute's Legal Counsel. Project Management will coordinate this task.
- If your research involves investigational drugs or biologics, you must follow Investigational Pharmacy Procedures – please contact Karen Ansaldo, PharmD, [Karen.Ansaldo@honorhealth.com](mailto:Karen.Ansaldo@honorhealth.com) for more information.

**You may not sign any contracts with third parties that involve the Institute in any way, shape or form before consulting with Legal Counsel.**

## What financial interests do my staff and I need to disclose to conduct Human Subject Research?

You must follow the Institute's policy on disclosure of financial interests (AD1402 Conflict of Interest) and federal and state regulations regarding conflict of interest.

A conflict of interest occurs when an individual's private interest interferes in any way, or even appears to interfere, with the interests of the organization as a whole.

Conflicts are inevitable but they are manageable.

All individuals involved in the design, conduct and/or reporting of research are required to disclose whether they have any financial interests related to the research as follows:

- With submission of an initial review.
- At least annually as part of the project/study continuing review.

- Within 60 days of discovering or acquiring (e.g., through purchase, marriage, or inheritance) a new financial interest.

Researchers should provide an accurate description of the related financial interest to the IRB.

<b>Includes:</b>	<b>Excludes income as follows:</b>
Compensation – income from any consulting, employment, service on boards, service to non-profits, honoraria, research support/grants	U.S. institutions of higher education, academic teaching hospitals, medical centers, or research institutes affiliated with an institution of higher education
Equity interests, stock options	U.S. federal, state, or local government agency
Licensing agreements and royalties for inventions	Investment vehicles such as mutual funds, retirement accounts, and blind trusts
Travel – only applicable for PHS/NIH funding	

#### Federal Regulations:

<b>Topic</b>	<b>21 CFR Part 54</b>	<b>42 CFR Part 50</b>
Disclosure parameters	Any equity greater than \$50,000 during timeframe of study and one year after OR total payments greater than \$25,000	Greater or equal to \$10,000 over 12 months or equity greater than 5% or greater than \$10,000
Forms to be completed	FDA 3454 – Certification FDA 3455 – Investigator’s disclosure	None
Related parties	Investigator, spouse and dependent children	Investigator, spouse and dependent children
Retention time	2 years after the date of approval of application (NDA)	3 years from the date of submission of the final expenditures
Notifications	None	Annual disclosure required or as needed within 60 days of being identified
Federal Agency	FDA	NIH and any federal grants

Additionally any investigators who are also members of committees which set drug formularies and/or develop clinical practice guidelines, must disclose through a process in place by these organizations/thirds-party vendors, of the investigators’ involvement in study and non-study activities when they arise during the period the investigators serve on these committees.

## How do I know what federal regulations apply to my research?

Your research may be regulated by more than one federal agency, depending on the project funding and type of project. Regardless of funding source, all human participant research must meet the regulatory criteria for approval.

- If you are the IND holder, you are required to follow both the Investigator responsibilities and Sponsor responsibilities at 21 CFR 11, 21 CFR 54, 21 CFR 210, 21 CFR 312, 21 CFR 314, 21 CFR 320, 21 CFR 330, and 21 CFR 601. Refer to Appendix A.
- If your research is funded by a federal agency, you are required to follow Department of Health and Human Services (DHHS) regulations at [45 CFR Part 46](#). Also refer to Appendix B for more information.
- If your research involves the use of a device with an active Investigational Device Exception (IDE), you are required to follow FDA regulations at [21 CFR Part 812](#). Also refer to Appendix A for more information.
- If your research involves drugs or devices, you are required to follow Food and Drug Administration (FDA) regulations at 21 CFR 50 and 21 CFR 56. Also refer to Appendix A for more information.
- If your research involves the use of a drug with an active Investigational New Drug (IND) application, you are required to follow FDA regulations at [21 CFR Part 312](#). Also refer to Appendix A for more information.
- If you are the IDE holder, you are required to follow both the Investigator responsibilities and Sponsor responsibilities at 21 CFR 11, 21 CFR 54, 21 CFR 812, 21 CFR 814, 21 CFR 820, and 21 CFR 860.
- If your research involves the use of veterans, Veterans Health Administration (VHA) funding or other VA resources, you are required to follow regulations in VHA Handbook 1200.05. Also refer to Appendix D for more information.

## How do I develop a new idea into a Human Research Project?

The Institute's Incubator Program can assist you in developing your concept idea including guiding you through the grant proposal process.

Full HRI Member may receive full support in the following areas:

1. LOI writing
2. Grant opportunities referral
3. Protocol Development
4. Statistical design support
5. Protocol documents development
6. Access to Project Management Services (budget negotiation, contract development and assistance)
7. Access to Study Coordinator/Research Nurse services as applicable
8. Access to Regulatory Services (IRB submission, amendments, continuing reports, reportable events submission)
9. IND writing and support (FDA1571 and 1572 completion, annual FDA reporting, if applicable)

10. Access to Data Safety Monitoring Committee services, if applicable
11. Access to monitoring services for investigator-initiated study, if applicable
12. Manuscript writing, if applicable

Affiliate Member may receive support in the following areas:

1. Grant opportunities referral
2. Access to Project Management Services (budget negotiation, contract development and assistance)
3. Access to Study Coordinator/Research Nurse services as applicable
4. Access to Regulatory Services (IRB submission, amendments, continuing reports, reportable events submission)
5. Access to monitoring services for investigator-initiated study, if applicable
6. Provide clinical research guidance

Faculty Participant may receive support in the following areas:

1. Provide Full Member Principal Investigator/Sub-Investigator, as applicable.
2. If Investigator-Initiated Study with Full Member PI;
3. Protocol Development
4. Statistical design support
5. Protocol documents development
6. Access to Project Management Services (budget negotiation, contract development and assistance)
7. Access to Study Coordinator/Research Nurse services as applicable
8. Access to Regulatory Services (IRB submission, amendments, continuing reports, reportable events submission)
9. IND writing and support (FDA1571 and 1572 completion, annual FDA reporting, if applicable)
10. Access to Data Safety Monitoring Committee services, if applicable  
Access to monitoring services for investigator-initiated study, if applicable

If not IIS:

1. Provide IRB submission guidance
2. Provide regulatory and compliance guidance as applicable

Students, Residents, Fellows\* may receive support in the following areas:

1. Provide IRB submission guidance.
2. Provide regulatory and compliance guidance as applicable.
3. Other services on a case-by-case basis.
4. Access to monitoring/auditing services as applicable

\*(Faculty/Member Principal Investigator MUST be listed on the project)

For more information, please contact:

Maribeth Schade

Director, Research Administration,

HonorHealth Research Institute

[Maribeth.Schade@honorhealth.com](mailto:Maribeth.Schade@honorhealth.com)

### Additional Information

Nursing Research – If you are a nurse conducting a research study or evidence-based practice project, you must first contact the Network Nursing Research Council prior to starting the IRB process or submitting an application through [IRBNet](#). Please contact Dr. Melanie Brewer at The Center for Nursing Excellence at [TheCenter@HonorHealth.com](mailto:TheCenter@HonorHealth.com) or (480) 323-3388 for more information or assistance.

### Statistical Assistance

Dr. Kevin Gosselin, Director of Academics and Biostatistics at the HonorHealth Research Institute, offers statistical consulting services to support investigators who require assistance with projects. Services range from purely advisory assistance to comprehensive data analysis services. Support functions are also available for data management and study design. Dr. Gosselin can be reached by email at: [Kevin.Gosselin@honorhealth.com](mailto:Kevin.Gosselin@honorhealth.com)

Dr. Curt Bay is willing to assist in the design and evaluation of research projects. He is not an employee of HonorHealth, but has agreed to have his contact information listed. Investigators are responsible for negotiating any fee for service which might be required. Dr. Bay can be reached by e-mail at: [cbay@atsu.edu](mailto:cbay@atsu.edu).

Compassionate or Emergency Use Requests – Please contact HonorHealth IRB at [irb@honorhealth.com](mailto:irb@honorhealth.com) (480-323-3071; 480-323-4196) regarding this process.

Preparatory to Research – If you plan to do work in advance of submitting your research project to the IRB for review and that work involves the use of protected health information (PHI) as defined by HIPAA, please contact IRB at [irb@honorhealth.com](mailto:irb@honorhealth.com) or (480) 323-3388 for more information related to the Preparatory to Research Form.

## How do I submit new Human Research to the IRB?

The Institute's IRB uses an electronic database called [IRBNet](#). This system provides the research community with electronic protocol management, online submission, and a suite of tools for researchers and IRB staff. [IRBNet](#) is hosted at a secure, enterprise-class data center that supports and meets the strict requirements of federal regulations.

All studies which will require any involvement by HonorHealth, whether staff, facilities and/or resources must be submitted through IRBNet. Within IRBNet the Principal Investigator may request review by either the local IRB (HHIRB) or the Central IRB (WIRB).

All Industry-Sponsored/Funded studies must be submitted for WIRB for review. Other studies may be reviewed by either IRB as per principal investigator preference.



Procedure:

## Login to IRBNet

1. Click on Create New Project
2. Complete basic project information page.
3. On the “Designer” page Select a Library
  - “Western IRB – for industry-sponsored/funded studies
    - Click on All WIRB forms and templates available here – will take you to WIRB document depository. Complete Initial Review submission form.
  - “Honor Health IRB – for non-therapeutic/non-interventional IIS.
4. These are smart forms. Simply follow the prompts and instructions as you move through the applications.
5. When you application is complete, you will be given a list of documents to submit with your application.
6. You can then print or preview your application.
7. Finally, click Save & Exit to save your completed form to your submission package.
8. You will then be able to upload additional documents as needed.

## How to create a new initial review submission for HonorHealth IRB in IRBNet using the Smart Form:

- Click on Create New Project and complete required fields. Click “Continue”.
- Scroll down to the bottom of the Designer page
- Click “Start a Wizard”.
- After clicking on this button the screen will move back up to the top, so you will need to scroll back down to the bottom of the page and click “Honor Health - Research Application” to select the application.
- The smart form will open up. Simply follow the prompts and instructions as you move through the application.
- When you application is complete, you will be given a list of documents to submit with your application.
- You can then print or preview your application.
- Finally, click Save & Exit to save your completed form to your submission package.
- You will then be able to upload additional documents as needed.
- Once all documents are uploaded please submit your package to the HonorHealth IRB for review.

The Principal Investigator will conduct the protocol in accordance with requirements in the INVESTIGATOR MANUAL listed in the section, “What are my obligations after IRB approval?”

- The Principal Investigator is qualified by education, training and experience to personally conduct and/or supervise the research described in the protocol.

- The Principal Investigator has completed all applicable institutional credentialing processes to conduct this research.
- The Principal Investigator has sufficient resources to carry out this research as proposed.
- The protocol is scientifically valid and employs research procedures which are consistent with sound research design.

The Principal Investigator and HonorHealth Full Member Senior Faculty Sponsor (if applicable) must electronically sign the Initial Submission.

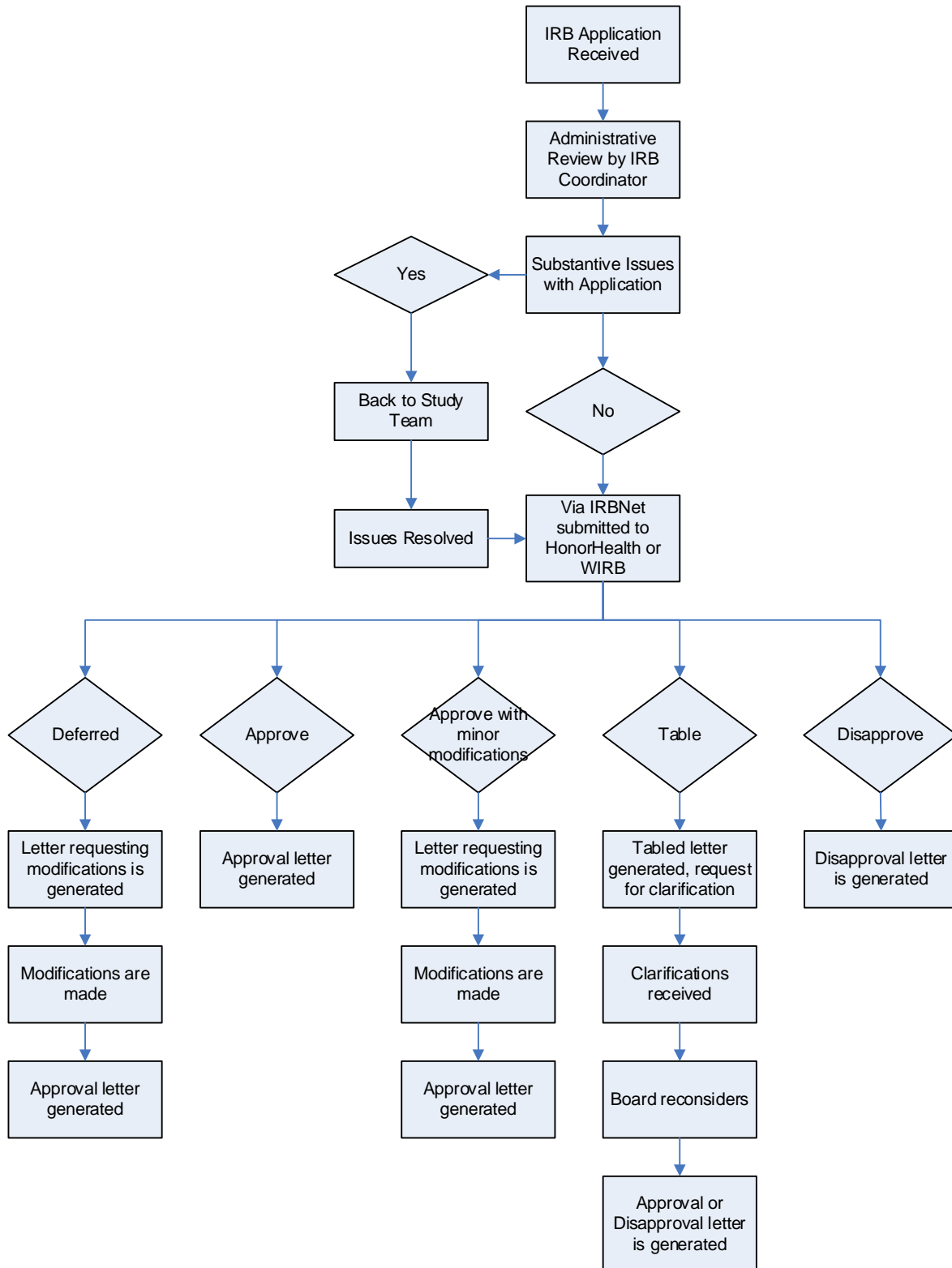
Review package before the completed packet is submitted to the IRB Administration. Maintain electronic copies of all information submitted to the IRB in case revisions are required.

Before submitting the research for initial review, you must determine whether any member of the research staff has a financial interest related to the research. If “yes”, you must report specific information about the related financial information as described in the section above, “What financial interests do my staff and I need to disclose to conduct Human Research?”

You must also ensure that every member of the research team who has interactions with participants, intervenes with participants, obtains consent or accesses identifiable private information for research purposes has completed the required training and received training on the procedures that s/he will conduct for this project.

The Institute’s IRB Coordinator will pre-review your submission for completeness (Diagram 1). If incomplete, the IRB Coordinator will communicate with the research team through the designated contact person(s) in IRBNet. When the submission is complete it will be directed it through the proper level of review. Some submissions will be reviewed by a designated reviewer (expedited review) and others will require review by a fully convened Committee.

## HonorHealth IRB Process



For definitions, please go to “What are the decisions the IRB can make when reviewing proposed research”?

## How do I write an Investigator Protocol?

In IRBNet under Forms and Templates use the “PROTOCOL TEMPLATE FOR RESEARCH PROJECT INVOLVING HUMAN SUBJECTS”, as a starting point for drafting a new Investigator Protocol.

Here are some key points to remember when developing an Investigator Protocol:

- Please complete sections as applicable.
- Delete all instructions within sections before submitting. These instructions are to guide you as you write the protocol.
- Certain sections of the template may not be applicable to your project. Please mark inapplicable sections with “N/A”.
- In some instances a project may appear to be human subject research when it does not meet the regulatory definitions of human subject research. If you need a formal determination from the IRB that your project is not human research, create and submit a new project in IRBNet.
- You may not include any individuals of the following populations as subjects in your research unless you indicate in your application the populations will be included.
  - Adults who lack the capacity to provide legally effective consent
  - Individuals who are not yet adults (infants, children, teenagers)
  - Pregnant women – to change when new Regulation comes into effect January 2018. After this date, pregnant women will not be considered vulnerable subjects
  - Prisoners (this type of research is not allowed at HonorHealth)

If you are conducting community-based participatory research, you may contact the IRB Coordinator for information about:

- Research studies using a community-based participatory research design
- Use of community advisory boards
- Use of participant advocates
- Partnerships with community-based Institutions

If you need assistance with statistical design, you may contact Kevin Gosselin, PhD at [Kevin.Gosselin@honorhealth.com](mailto:Kevin.Gosselin@honorhealth.com).

## Does my study require an IND

Regulations in 21 CFR Part 312 require sponsors who wish to study a drug or biological product in humans to submit an IND to the Agency. The regulation also provides criteria for the exemption of some studies from this requirements.

IND Exemption Criteria (21 CFR 312.2(b)(1))

1. The investigation is not intended to be reported to the FDA as a well-controlled study in support of a new indication for use nor intended to be used to support any other significant change in the labeling for the drug;
2. If the drug that is undergoing investigation is lawfully marketed as a prescription drug product, the investigation is not intended to support a significant change in the advertising for the product;
3. The investigation does not involve a route of administration or dosage level or use in a patient population or other factor that significantly increased the risk (or decreases the acceptability of the risks) associated with the use of the drug product;
4. The investigation is conducted in compliance with the requirements for institutional review set forth in part 56 and with the requirements for informed consent set forth in Part 50; and
5. The investigation is conducted in compliance with the requirements of § 312.7.

For a study to be IND exempt it must fit all five (5) criteria.

## Does my study require an IDE?

21 CFR Part 812 allows for investigational medical devices to be evaluated in human through clinical trials under and Investigational Device Exemption (IDE). A medical device is an instrument, apparatus, implement, machine, contrivance, implant, in vitro reagent, or other similar or related article, including any component, part, or accessory, which is

- Recognized in the official National Formulary, or the United States Pharmacopeia, or any supplement to them,
- Intended for use in the diagnosis of disease or other conditions, or in the cure, mitigation, treatment, or prevention of disease, in man or other animals, or
- Intended to affect the structure or any function of the body of man or other animals, and
- which does not achieve its primary intended purposes through chemical action within or on the body of man or other animals and which is not dependent upon being metabolized for the achievement of its primary intended purposes.

Classes of medical devices:

- Class I – Subject only to general controls. Present lowest potential for harm (e.g., elastic bandages, exam gloves, hand-held surgical instruments)
- Class II – General controls alone are insufficient to ensure safety and effectiveness (e.g., powered wheelchairs, infusion pumps. Surgical drapes). May be subject to special controls identified by FDA.
- Class III – Insufficient information exists to determine that general or special controls are sufficient to ensure safety and effectiveness (e.g., replacement heart valves, silicone gel-filled breast implants, implanted cerebellar stimulators).

Types of devices:

- Significant Risk – presents a potential for serious risk to the health, safety or welfare of a subject (e.g., implants, stents, heart valves). **Requires IDE**
- Non-Significant Risk – does not meet the definition of a significant risk device. Determined by IRB. If IRB determines it is a significant risk device, sponsor/PI must submit IDE application to FDA for review.

HonorHealth Research Institute Regulatory Affairs may provide guidance and assistance in submitting to ClinicalTrials.gov. Please contact Fanny Zylstra ([Fanny.Zylstra@honorhealth.com](mailto:Fanny.Zylstra@honorhealth.com))

## How do I create a consent document?

Under Forms and Templates Use the “CONSENT TEMPLATE – FULL FORM” or “CONSENT TEMPLATE – SHORT FORM/INFORMATION SHEET” to create a consent document.

Note that long form consent documents and summaries for short form consent documents must contain all of the required and additional appropriate elements of informed consent disclosure (See Policy 1509 Research IRB Informed Consent).

The short form of consent intended for use in biomedical research when a potential non-English speaking participant is identified. The short form is available in several languages on the Consent Short Forms - Non English Speaking IRB Website.

If your study meets the requirements for EXPEDITED or EXEMPT research, you may use an abbreviated process for obtaining consent. A Consent Template – Short Form/Information Sheet is available in IRBNet for consent waivers or alterations of consent.

The following elements of informed consent should be included in consent forms or scripts as applicable:

- Subject rights: State that the activity involves research, participation is voluntary, and that participants may withdraw at any time without penalty or loss of benefits.
- Purpose of the study: Provide a brief non-technical explanation of the purpose(s) of the research. Explain why the subject is being asked to participate in the study (e.g., You are being asked to participate in this research study because...)
- Study tasks or procedures: Provide a complete description of procedures (including the order in which they take place). Identify and distinguish procedures that are being performed solely for research purposes from any activities that would otherwise occur. Include information about audio- or videotaping and/or any records that may be accessed (e.g., educational records).
- Duration of subject’s participation: Provide expected duration of the subject’s participation (e.g., time required to complete surveys). Ensure that the proposed time period is realistic for the procedures to be performed.

- Risks and Benefits, if any: Provide information regarding any risks and/or benefits that may be expected to participants in the research. If the study is minimal risk or less (such as an anonymous survey) it may be stated that there are no risks to participating in this research. If there are no benefits expected to the participant this should be stated: *“We cannot guarantee that you will experience any benefits from participating in this study. Others may benefit in the future from information we obtain while you are in this study.”*
- Confidentiality: Include a statement describing the extent, if any, to which confidentiality of the data/records will be maintained. Discuss the retention or disposition of participants’ data/records following conclusion of the research. Note: Do not interchange the terms “confidential” (i.e., maintained in a way that prevents inadvertent or inappropriate disclosure of participants’ identifiable information) and “anonymous” (i.e., identifiers were not collected or have been permanently removed).
- Provide the name and contact information of the Principal Investigator for questions, concerns, or complaints about the study. Include contact information for research staff, as applicable. The person(s) listed should be knowledgeable about the research. Include area code or international dialing codes for phone and fax numbers.
- Provide contact information for questions about subject rights and as a contact who is not part of the study team for participant concerns or complaints about the research: For questions about your rights as a participant in this study or to discuss other study-related concerns or complaints with someone who is not part of the research team, you may contact HonorHealth IRB at [irb@honorhealth.com](mailto:irb@honorhealth.com).
- Incentives: Explain payments or other incentives (e.g., class credit) to participate, including amount and schedule of payments. Compensation should be pro-rated (e.g., per session) and not contingent upon study completion. Explain the effect of a subject’s decision to withdraw from the research on compensation (e.g., a participant who is an ASU student will receive extra credit for enrolling in the study even if he/she withdraws). If payments are offered, include the following: By law, payments to subjects may be considered taxable income.
- Sponsor: Provide the name of the sponsor funding the research, when applicable.

It is required that you provide a version number and date for each revision of your consent documents to ensure that you use the most recent version approved by the IRB.

## What are the different requirements for each level of IRB review?

Submitted activities may fall under one of the following four regulatory classifications:

- Not “Human Research”: Activities must meet the Institutional definition of “Human

Research” to fall under IRB oversight. Activities that do not meet this definition are not subject to IRB oversight or review.

- **Exempt:** Certain categories of Human Research may be exempt from regulation but require IRB review. It is the responsibility of the Institution, not the investigator, to determine whether Human Research is exempt from IRB review. Review Policy RE1503 Research IRB Exempt Review for reference on the categories of research that may be exempt.
- **Review Using the Expedited Procedure:** Certain categories of non-exempt Human Research may qualify for review using the expedited procedure, meaning that the project may be approved by a single designated IRB reviewer, rather than the convened board. Review Policy RE1502 Research IRB Expedited Review for reference on the categories of research that may be reviewed using the expedited procedure.
- **Review by the Convened IRB:** Non-Exempt Human Research that does not qualify for review using the expedited procedure must be reviewed by the convened IRB.

## Does the IRB charge a fee to review research proposals?

Yes, both HonorHealth IRB and WIRB charge to review research proposals. These are subject to change at any time. For current HonorHealth IRB fees, please contact IRB Coordinator at [irb@honorhealth.com](mailto:irb@honorhealth.com). For current WIRB fees go to <https://ww.wirb.com>. If you use HonorHealth Project Management services, these should be included in the services provided (i.e., budget, contracts, etc.).

## What are the decisions the IRB can make when reviewing proposed research?

The IRB may approve research, require modifications to the research to secure approval, table research, or disapprove research:

- **Approval:** Made when all criteria for approval are met. See “How does the IRB decide whether to approve Human Research?” below.
- **Approval with minor modifications:** Made when IRB members require specific modifications to the research before approval can be finalized.
- **Deferred:** Made when the IRB determines that the board is unable to approve the research and the IRB suggests revisions that might make the research approvable. When making this motion, the IRB describes its reasons for this decision, describes modifications that might make the research approvable, and gives the investigator an opportunity to respond to the IRB in person or in writing.
- **Tabled:** Made when the IRB cannot approve the research at a meeting for reasons unrelated to the research, such as loss of quorum or the application or associated



documents are incomplete and/or do not provide enough information to allow the IRB to make a determination. When taking this action, the IRB automatically schedules the research for review at the next meeting and may provide comments, request revisions, or request additional information.

- **Disapproval:** Made when the IRB determines that it is unable to approve research and the IRB cannot describe revisions that might make the research approvable. When making this motion, the IRB describes its reasons for this decision and gives the investigator an opportunity to respond to the IRB in person or in writing.

For more information please see Policy RE1501 Research IRB Initial Review

## How does the IRB decide whether to approve Human Research?

The criteria for IRB approval can be found in Policy RE1501 Research IRB Initial Review. The IRB will conduct a full board review of all research involving more than minimal risk to human subjects. Specifically, this will include all research not described in the categories for EXEMPT or EXPEDITED .

In order for a research project to be approved, the IRB must find that:

- Risks to subjects are minimized. For example, the IRB evaluates whether procedures to be performed on subjects are consistent with sound research design and do not unnecessarily expose subjects to risk, and whether they are already being performed for diagnostic or treatment purposes.
- 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. In evaluating risks and benefits, the IRB should consider only those risks and benefits that may result from the research (as distinguished from risks and benefits of therapies subjects would receive even if not participating in the research). The IRB should not consider possible long-range effects of applying knowledge gained in the research (for example, the possible effects of the research on public policy) as among those research risks that fall within the purview of its responsibility.
- Selection of subjects is equitable, taking into account the purposes of the research study and the setting in which it will be conducted and being particularly cognizant of the special problems of research studies involving vulnerable populations.
- 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 appropriate state and federal regulations. See Policy RE1509 Research IRB Informed Consent.

- Informed consent will be appropriately documented as required by state and federal regulations.
- When appropriate, the research study makes adequate provision for monitoring the data collected to ensure the safety of subjects.
- When appropriate there are adequate provisions to protect the privacy of subjects and to maintain the confidentiality of data.
- Appropriate additional safeguards have been included to protect the rights and welfare of subjects who are likely to be vulnerable to coercion or undue influence (e.g., children, prisoners, pregnant women, mentally disabled persons, or economically or educationally disadvantaged persons).

The IRB may approve a research study involving children, fetuses and/or pregnant women only if it falls into one of the following categories noted in 45 CFR 46 Part B and D. Please contact the IRB at 480-323-3071 if you wish to include one or more of these populations in your research.

Pregnant women, neonates or fetuses may be involved in research if all of the following conditions are met:

- Where scientifically appropriate, preclinical studies, including studies on pregnant animals, and clinical studies, including studies on non-pregnant women, have been conducted and provide data for assessing potential risks to pregnant women and fetuses
- The risk to the fetus is caused solely by interventions or procedures that hold out the prospect of direct benefit for the woman or the fetus; or, if there is no such prospect of benefit, the risk to the fetus is not greater than minimal and the purpose of the research is the development of important biomedical knowledge which cannot be obtained by any other means
- Any risk is the least possible for achieving the objectives of the research
- If the research holds out the prospect of direct benefit to the pregnant woman, the prospect of a direct benefit both to the pregnant woman and the fetus, or no prospect of benefit for the woman nor the fetus when risk to the fetus is not greater than minimal and the purpose of the research is the development of important biomedical knowledge that cannot be obtained by any other means
- If the research holds out the prospect of direct benefit solely to the neonate (includes viable, non-viable and uncertain viability) or fetus then the consent of the pregnant

woman and the father is obtained in accord with the informed consent process, except that the father's consent need not be obtained if he is unable to consent because of unavailability, incompetence, or temporary incapacity or the pregnancy resulted from rape or incest

- Non-viable neonates after delivery may not be involved in research unless the following conditions are met:
  - Vital functions of the neonate will not be artificially maintained
  - The research will not terminate the heartbeat or respiration of the neonate
  - There will be no added risk to the neonate resulting from the research
  - The purpose of the research is the development of important biomedical knowledge that cannot be obtained by other means
- For children who are pregnant, assent and permission are obtained
- No inducements, monetary or otherwise, will be offered to terminate a pregnancy
- Individuals engaged in the research will have no part in any decisions as to the timing, method, or procedures used to terminate a pregnancy; and
- Individuals engaged in the research will have no part in determining the viability of a fetus or neonate.

Research involving, after delivery, the placenta; the dead fetus; macerated fetal material; or cells, tissue, or organs excised from a dead fetus, shall be conducted only in accord with any applicable federal, state, or local laws and regulations regarding such activities.

If information associated with this material is recorded for research purposes in a manner that living individuals can be identified, directly or through identifiers linked to those individuals, those individuals are research subjects and all regulations are applicable.

Studies determined to involve more than minimal risk involving children must hold out the prospect of direct benefit to the individual subject or likelihood to contribute to the subject's well-being.

- The risk is justified by the anticipated benefit to the subjects;
- The relation of the anticipated benefit to the risk is at least as favorable to the subjects as that presented by available alternative approaches;

- Adequate provisions are made for soliciting the assent of children and the permission of their parents (or legally authorized representative/guardians). Furthermore See Policy RE1509 Research IRB Informed Consent and Policy RE15010 Research IRB Assent.

## What are my obligations after IRB approval?

1. Do not start Human Research activities until you have the final IRB approval letter.
2. Do not start Human Research activities until you have obtained all other required institutional approvals, including approvals of departments or divisions that require approval prior to commencing research that involves their resources. For instance, when an investigational drug or biologic is involved, you are required to defer responsibility for accounting, storage, dispensing, etc. to the Investigational Pharmacy. Please contact Dr. Karen Ansaldo @ [Karen.Ansaldo@honorhealth.com](mailto:Karen.Ansaldo@honorhealth.com).
3. Ensure that there are adequate resources to carry out the research safely. This includes, but is not limited to, sufficient investigator time, appropriately qualified research team members, equipment, and space.
4. Ensure that Research Staff are qualified (e.g., including but not limited to appropriate training, education, expertise, credentials, protocol requirements and, when relevant, privileges) to perform procedures and duties assigned to them during the study.
5. Update the IRB office with any changes to the list of study personnel (other than PI and Co-PI) at time of continuing review, if applicable. To change the PI and/or Co-PI, a modification must be submitted and approved by the IRB before the new PI and/or CO-PI can engage in the research.
6. Personally conduct or supervise the Human Research.
  - a. Conduct the Human Research in accordance with the relevant current protocol as approved by the IRB.
  - b. When required by the IRB, ensure that consent or permission is obtained in accordance with the relevant current protocol as approved by the IRB.
  - c. Do not modify the Human Research without prior IRB review and approval unless necessary to eliminate apparent immediate hazards to subjects.
  - d. Protect the rights, safety, and welfare of subjects involved in the research.
7. Submit to the IRB:

- a. Proposed modifications as described in this manual. (See “How do I submit a modification?”)
  - b. A continuing review application as requested in the approval letter. (See “How do I submit continuing review?”)
  - c. A continuing review application when the Human Research is closed. (See “How do I close out a study?”)
8. Report to the IRB through a new package in IRBNet any of the information items in Appendices A, B, and C within five (5) to ten (10) business days as outlined in Appendices A, B, and C.
- a. The IRB will review to determine if any of the information items meet the definitions of serious noncompliance, continuing noncompliance or an unanticipated problem involving risks to subjects or others
  - b. Examples include:
    - i. Adverse events that are unexpected/unanticipated, involve new or increased risks to participants or others, and are related to the research.
    - ii. Changes made to the research without prior IRB approval in order to eliminate apparent immediate harm.
    - iii. Other unanticipated information that is related to the research and participants or others might be at increased risk of harm.
9. Submit an annual disclosure of financial interests. In addition submit an updated disclosure of financial interests within thirty days of discovering or acquiring (e.g., through purchase, marriage, or inheritance) a new financial interest.
10. Do not accept or provide payments to professionals in exchange for referrals of potential subjects (“finder’s fees.”)
11. Do not accept payments designed to accelerate recruitment that are tied to the rate or timing of enrollment (“bonus payments.”)
12. See additional requirements of various federal agencies in Appendix B. These represent additional requirements and do not override the baseline requirements of this section.

## How do I document consent?

Informed consent shall be documented with the use of a written informed consent form approved by the IRB and signed, dated by the subject or the subject’s legally authorized representative (LAR) and signed and date by the investigator designee at the time of consent

## Review Policy RE1509 Research IRB Informed Consent

The following are the requirements for long form consent documents:

- The subject or representative signs and dates the consent document.
- The individual obtaining consent signs and dates the consent document.
- Whenever required by the IRB or sponsor, the subject's or representative's signature is to be witnessed by an impartial individual who signs and dates the consent document.
- Whenever the IRB or the sponsor require an impartial witness to the oral presentation, the witness signs and dates the consent document.
- A copy of the signed and dated consent document is to be provided to the subject or LAR.

The following are the requirements for short form consent documents:

- The subject or representative signs and dates the short form consent document and the summary.
- The individual obtaining consent signs and dates the short form consent document and the summary.
- The impartial witness to the oral presentation signs and dates the short form consent document and the summary.
- Copies of the signed and dated consent document and summary are provided to the subject or LAR.

If the subject is a patient of HonorHealth Network, a copy of the signed and dated consent form along with written documentation of informed consent process must be placed in the subject's medical record.

Additionally the process of informed consent must be documented in the patient's record as follows in narrative form:

- Conducted in a private room/area
- State the protocol number and/or identifier
- Document if the patient is accompanied and if so, who is/are the companion(s)
- When and how was a copy of the informed consent form given to the patient to review?
- Patient was counseled about contraception during study participation, if applicable
- Summary of patient's questions
- Statement that questions were answered
- Patient (and companion, if applicable) expressed understanding
- Form signed together on (Date)
- Signed copy was given to patient

## What if I want to enroll non-English speaking participants in my study?

Participants who do not speak English should be presented with informed consent documents in a language understandable to them that includes all the required and additional elements for disclosure. Either the long form of the consent document needs to be translated in writing into the subject's language or the translated short form of consent may be provided to the subject (via certified translator) and the required elements of consent (IRB-approved English consent form) provided orally via a translator to the subject. The short form is available in several languages on [WIRB](#) website. Spanish-translated HIPAA form is available in IRBNet Consent Short Forms - Non English Speaking. Please do not use a subject's family English-speaking family member/friend as a translator.

In order to execute consent using the short form:

- the patient/LAR must sign the short form
- the translator must sign the short form and the IRB-approved English ICF
- the person obtaining consent must sign the IRB-approved English ICF

## Can I recruit subjects over the phone for my study?

No, unless the IRB has approved a recruitment tool (script) to use when reaching potential subjects via the telephone. Potential subjects may be provided with the NIH clinical trials website which contains information on clinical trials (<http://www.clinicaltrials.gov>), and OHRP that provides participant-friendly information for study participants [OHRP About Research Participation](#).

## What is ClinicalTrials.gov?

ClinicalTrials.gov is a registry and results database of publicly and privately supported clinical studies of human participants conducted around the world. In 1997 the Food and Drug Administration Modernization Act of 1997 (FDAMA) required the National Institutes of Health (NIH) to create a registry to include information about federally or privately funded clinical trials conducted under investigational new drug (IND) applications. As a result [www.ClinicalTrials.gov](http://www.ClinicalTrials.gov) was created. Title VIII of the Food and Drug Administration Amendments Act of 2007 (FDAAA) expanded the legal mandate to additionally report summary results in the registry. In 2015 FDAAA clarified the mandate which took effect January 18, 2017.

“Applicable Clinical Trials” must be registered in ClinicalTrials.gov

## What is an Applicable Clinical Trial (ACT)?

ACT testing drug therapy:

- Study type is interventional
- Study phase is NOT Phase 1
- Studies an FDA-regulated drug product (including biologic product)

- One or more of the following:
  - At least one US facility location
  - Product manufactured in and exported from the United States
  - Conducted under and FDA IND

ACT testing a device:

- Study type is interventional
- Primary purpose is NOT device feasibility
- Studies and FDA-regulated device product
- One or more of the following:
  - At least one US facility location
  - Product manufactured in and exported from the United States
  - Conducted under an FDA IDE

HonorHealth Research Institute Regulatory Affairs may provide guidance and assistance in submitting to ClinicalTrials.gov. Please contact Fanny Zylstra ([Fanny.Zylstra@honorhealth.com](mailto:Fanny.Zylstra@honorhealth.com))

## Can I advertise my study in the newspaper, radio, television, buses, road signs, etc.?

Yes, however, all information to be provided to potential subjects in the advertisements must be approved by the IRB prior to use.

## When can a consent waiver be used?

The IRB may approve a consent procedure which does not include, or which alter, some or all of the required elements of informed consent. Also, the IRB may approved a consent procedure which waives the requirements to obtain written informed consent if it finds either:

- That the only record linking the subject and the research would be the consent document and the principal risk would be potential harm resulting from a breach of confidentiality. Each subject will be asked whether the subject want documentation linking the subject with the research, and the subject's wishes will govern: or
- That 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.

In cases in which the documentation requirement is waived, the IRB may require the investigator to provide subjects with a written statement regarding the research.



## When can a HIPAA waiver be used?

The Health Insurance Portability and Accountability Act (HIPAA) regulates how protected health information can be used and disclosed. An investigator must obtain an authorization via a HIPAA authorization Form from all participants in research prior to the use or disclosure of protected health information (PHI) for any research-related purpose. PHI is any information in the medical record or designated record set that can be used to identify and individual. For templates for HIPAA Authorization Forms go to HIPAA Authorization Forms English and Spanish. The IRB can waive or alter the requirement for HIPAA Authorization for study recruitment purposes or for the entire study. For more information and to complete go to Waiver of HIPAA Authorization.

## How do I submit a modification (amendment)?

In IRBNet choose the project and create a new package. Attach all requested supplements.

The PI may sign the submission electronically by using "Sign this Package" in IRBNet and typing their name and "Signed electronically" or print form, sign in ink, scan, and upload the document to IRBNet. The documents must be submitted through IRBNet.

Please note that research must continue without implementing the modifications until the IRB approves the modification submission, *unless the modification is intended to protect human subjects from imminent harm.*

Updates to the list of study personnel must be submitted at the time of the staffing change using the Key Personnel Change in IRBNet. If the study is funded, a completed Conflict of Interest form must be provided with the amendment request form. Each new individual must create a User Profile in IRBNet and upload the required training and credential document to their profile in order for their addition to the research team to be verified and accepted. If the staffing changes coincides with the continuing report, the Key Personnel Change may be submitted together.

Modifications are categorized into minor changes and significant changes. A 'minor' modification is a proposed change in research-related activities that does not significantly affect an assessment of the risks and benefits of the study and does not substantially change the specific aims or design of the study. Minor modifications may be reviewed using the expedited IRB procedure

A 'significant' modification is a proposed change in research-related activities that significantly affects an assessment of the risks and benefits of the study or substantially changes the specific aims or design of the study. Significant modifications require review by the full IRB Committee

## How do I submit continuing review?

In IRBNet choose the project and create a new package. Complete the continuing review request form. Submit all required supplements and documents through IRBNet.

The PI may sign the submission electronically by using "Sign this Package" in IRBNet and typing their name and "Signed electronically" or print form, sign in ink, scan, and upload the document to IRBNet.

Before submitting the research for continuing review, you must:

- If the study is funded, updated Conflict of Interest forms must be provided at the time of the continuing review submission. If it is determined that a member of the research staff has a financial interest related to the research, additional paperwork will need to be completed. The HonorHealth Conflicts of Interest Committee (COIC) will make a determination and provide the information to the IRB.
- Ensure that each member of the research team has completed the required Human Subjects Protection Training (CITI) and has been trained on the protocol procedures s/he will complete. If previously completed through another affiliation, please ensure that your CITI account is affiliated with HonorHealth. In addition, please ensure that the training is up to date and will not expire prior to the next continuing review approval period.

The continuing review application must be received at least 3 weeks prior to the expiration of IRB approval data as noted in the approval letter. This will allow for IRB pre-review and notification to submit missing items or make corrections prior to IRB review and avoid a temporary suspension of research activities.

If the continuing review application is not received by the *protocol expiration date* found in the approval letter, you will be required to develop and implement a suitable CAPA *and* will be restricted from submitting new Human Research until the completed continuing review application has been received and approved.

If the approval of Human Research expires, all Human Research procedures related to the protocol under review must cease, including recruitment, advertisement, screening, enrollment, consent, interventions, interactions, and collection or analysis of private identifiable information.

Continuing Human Research procedures during a lapse is a violation of the Institution's policy and, in some cases, federal regulations. If current subjects will be harmed by stopping Human Research procedures that are available outside the Human Research context, provide these on a clinical basis as needed to protect current subjects. If current subjects will be harmed by stopping Human Research procedures that are not available outside the Human Research

context, immediately provide a coded list of the currently enrolled subjects and describe in writing why they will be harmed by stopping Human Research procedures.

## How do I close out a study?

In IRBNet choose the project and create a new package. Complete the Final Report form and attach all requested supplements and documents.

The PI may sign the submission electronically by using "Sign this Package" in IRBNet and typing their name and "Signed electronically" OR print form, sign in ink, scan, and upload the document to IRBNet. Submit to the IRB Administration via IRBNet. Maintain electronic copies of all information submitted to the IRB in case revision are required.

If the final report application for closing out a Human Research study is not received by the *protocol expiration date* in the approval letter, you will be required to develop and implement a suitable CAPA *and* will be restricted from submitting new Human Research until the completed continuing review application has been received and approved. For students/fellows conducting research, it is the responsibility of the HonorHealth Full Member Senior Faculty Sponsor to complete close-out procedures in the event the student/fellow is no longer at HonorHealth.

## How long do I keep records?

Maintain your Human Research records, including signed and dated consent documents for at least 10 years after the end of the calendar year in which the research is completed, unless otherwise specified in the Clinical Trial Agreement (CTA) or other award agreement.

For further information on required retention and disposition of administrative records relating to research, please see Policy QM1305 Record Control Policy.

## What if I need to use an unapproved drug, biologic, or device and there is no time for IRB review?

Contact the IRB Coordinator or Chairperson of the IRB immediately to discuss the situation. Provide the following information in writing:

- A certification of why the case is an emergency describing the life threatening or severely debilitating

Upon receipt of the request, the Chairperson of the IRB or his/her designee will review the protocol to ensure the request is consistent with IRB guidelines. If the guidelines are met, the IRB Chairperson or designee will approve the use of the drug or device without prospective IRB review. Any subsequent use of the investigational product with another human subject at HonorHealth will require IRB review and approval.

In addition to obtaining the prior approval of the IRB Chairperson or his/her designee, informed consent is required to be signed by the patient or the patient's legal representative unless the following requirements are met and documented:

- The patient is confronted by a life-threatening situation (as defined above) necessitating the use of the test article
- Informed consent cannot be obtained because of an inability to communicate with, or obtain legally effective consent, from the subject
- Time is not sufficient to obtain consent from the subject's legally authorized representative and,
- No alternative method of approved or generally recognized therapy is available that provides an equal or greater likelihood of saving the subject's life (21 CFR 50.23(a)).

If obtaining informed consent is not possible from the patient or the patient's legal representative, the treating physician and a physician not otherwise involved in the study of the test article must certify in writing to the IRB that the above four conditions were met:

- If, in the treating physician's opinion, immediate use is required to preserve the patient's life and if time is insufficient to obtain an independent physician's determination that the above four conditions are satisfied, the treating physician must, within five (5) working days, have the use reviewed and evaluated in writing by an independent physician as to whether the above four conditions were met at the time of the emergency use. Policy RE1517 Research IRB Emergency Use of Test Articles.
- If you believe you may need to use the test article in an emergency use situation you must submit a new project for initial review with a protocol and IRB application

If you do not comply with the 2 prior bullet points, you will be restricted from submitting new Human Research until the post emergency use requirements are met.

Emergency use of an unapproved drug or biologic in a life-threatening situation without prior IRB review is "research" as defined by FDA, the individual getting the test article is a "subject" as defined by FDA, and therefore is governed by FDA regulations for IRB review and informed consent. Emergency use of an unapproved device without prior IRB review is not "research" as defined by FDA. However, FDA guidance recommends following similar rules as for emergency use of an unapproved drug or biologic.

Individuals getting an unapproved drug, biologic, or device without prior IRB review cannot be considered a "subject" as defined by DHHS and their results cannot be included in prospective "research" as the term is defined by DHHS.

## What other internal reviews are also involved in the protection of human subject research?

Conflict of Interest Committee (COIC) – Any actual or perceived conflict of interest as defined by institutional policy, consistent with applicable federal and state regulations is

required to be reported to and reviewed by the Conflict of Interest Committee (COIC). The COIC will inform the IRB when investigators conducting human research have significant financial interests that constitute a financial conflict of interest.

The IRB has the final authority and may grant final approval of research studies with a disclosed conflict of interest, provided that the Principal Investigator has taken appropriate steps to eliminate or manage the conflict, consistent with the Conflict of Interest Committee determination (Policy AD1402 Conflict of Interest). Should the IRB or the Conflict of Interest Committee require changes in the research study to mitigate a conflict; the Principal Investigator will be required to submit the revised documents for IRB review and approval.

You department may require other approvals prior to submission to IRB. Please check with your respective departments.

## Monitoring versus Auditing

Conducting clinical studies is a complex endeavor, involving oversight of clinical investigators with respect to the protocol, Good Clinical Practices (GCP), governing regulations, conditions of Institutional Review Boards and/or Ethics Committees, and institutional Standard Operating Procedures before, during and after conduct of the study. Clinical study data that are generated must be of the highest quality; data must be accurate and evaluable in support of marketing clearance/product approval and collected in a manner that protects the rights, safety and welfare of properly consented trial participants.

*Auditing* is a formal approach, independent, objective. Audits are performed by someone who has no vested interest in the outcomes or business area being reviewed. Audits have established approaches and methodology for sampling. Audits involve formal communication with recommendations and corrective-action measures, followed by a documented follow-up of corrective actions

*Monitoring* is a less structured than auditing, although some audit techniques are occasionally employed. Monitoring involves day to day reviews. It is not necessarily independent of business unit, therefore it can involve self-reviews, peer reviews, etc. The approach may be informal. It does not necessarily include documentation for corrective actions, although by the nature of continuous day to review, it may involve follow-up.

HonorHealth Research Institute Research Compliance & Regulatory Compliance Department offers Full members and Affiliate members monitoring and auditing services for a fee. Please contact Dr. Aurea M. Flores, Director RQRC [Aurea.Flores@honorhealth.com](mailto:Aurea.Flores@honorhealth.com) (480) 323-4196 for further information.

## What if the FDA wants to inspect my research?

The Food & Drug Administration (FDA) conducts clinical investigator inspections to determine if the clinical investigators are conducting clinical studies in compliance with applicable statutory and regulatory requirements. Clinical investigators who conduct FDA-regulated clinical investigations (under an IND/IDE) are required to permit FDA investigators to access, copy, and verify any records or reports made by the clinical investigator with regard to, among other records, the disposition of the investigational product and subjects' case histories.

If you are conducting a clinical study under and IND or IDE, you may be subject to either an announced or unannounced inspection by an FDA investigator. It is important that you conduct clinical research in compliance with all applicable regulatory requirements at all times. For an announced visit, an FDA representative will contact the principal investigator to let the study team know when the FDA investigator will be stopping by. For unannounced visit, there is no call and the investigator will show up to the address on record found in the FDA Form 1572.

If you receive a call from the FDA announcing a visit, and the study is being conducted within HonorHealth System it is important that you contact Aurea M. Flores, PhD, Director Research Quality & Regulatory Compliance (RQRC), [Aurea.Flores@honorhealth.com](mailto:Aurea.Flores@honorhealth.com) (480) 323-4196 immediately. RQRC will guide through the process of an FDA inspection.

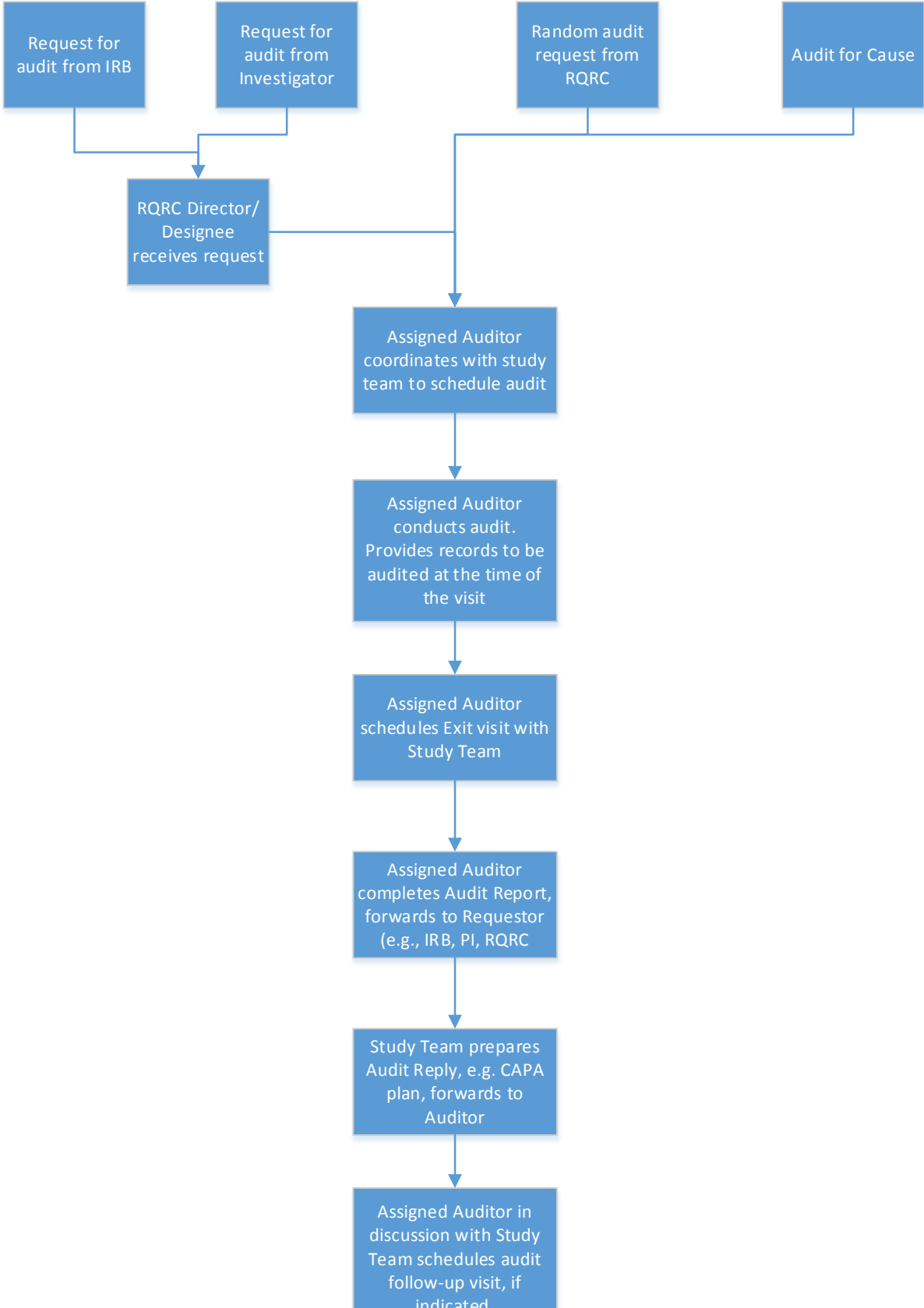
Similarly, if you are conducting clinical research regulated by the European Medicines Agency (EMA), they can also conduct investigations of your activities. If the EMA contacts you for a visit, please contact RQRC for guidance.

Furthermore, RQRC offers FDA/EMA audit preparation services. In this case, an RQRC auditor will conduct an audit similar to what the FDA/EMA will conduct, and provide you with the results where you can implement corrective and preventive actions.

RQRC conducts audits as follows:

- Request by the IRB of record for the study,
- Request by the study principal investigator
- For cause (as a result of a Compliance Hotline report).

In addition RQRC conducts random audits of HonorHealth System clinical research activities.



## What happens if I leave HonorHealth

If you are planning to conclude your relationship with HonorHealth, IRB must be notified. You can either have another HonorHealth investigator assume Principal Investigator responsibilities or you can close each of your research studies with the IRB.

You must also notify the IRB in writing of the plan for either destroying the data or transferring the data to another Principal Investigator. The original research study documents are the property of the Institute and must remain at HonorHealth.

If your research involves De-Identified Data, or a Limited Data Set under a Data Use Agreement, you may continue to use the data for the purposes of analyses and publication only. The identifiable source data is the property of HonorHealth.

### ***How do I get additional information and answers to questions?***

This document and the policies and procedures for the Human Research Protection Program are available on the HonorHealth [Website](#) .

If you have any questions or concerns about the Human Research Protection Program, contact IRB at:

Email: [irb@honorhealth.com](mailto:irb@honorhealth.com)

Phone: (480) 323-3071



## Appendix A: Additional Requirements for FDA-Regulated Research

1. When a subject withdraws from a study:
  - a. The data collected on the subject to the point of withdrawal remains part of the study database and may not be removed.
  - b. An investigator may ask a subject who is withdrawing whether the subject wishes to provide continued follow-up and further data collection subsequent to their withdrawal from the interventional portion of the study. Under this circumstance, the discussion with the subject would distinguish between study-related interventions and continued follow-up of associated clinical outcome information, such as medical course or laboratory results obtained through non-invasive chart review, and address the maintenance of privacy and confidentiality of the subject's information.
  - c. If a subject withdraws from the interventional portion of the study, but agrees to continued follow-up of associated clinical outcome information as described in the previous bullet, the investigator must obtain the subject's informed consent for this limited participation in the study (assuming such a situation was not described in the original informed consent form). IRB approval of informed consent documents is required.
  - d. If a subject withdraws from the interventional portion of a study and does not consent to continued follow-up of associated clinical outcome information, the investigator must not access for purposes related to the study the subject's medical record or other confidential records requiring the subject's consent.
  - e. An investigator may review study data related to the subject collected prior to the subject's withdrawal from the study, and may consult public records, such as those establishing survival status.
2. For FDA-regulated research involving investigational drugs:
  - a. Investigators must abide by FDA restrictions on promotion of investigational drugs:
    - i. An investigator, or any person acting on behalf of an investigator, must not represent in a promotional context that an investigational new drug is safe or effective for the purposes for which it is under investigation or otherwise promote the drug.
    - ii. This provision is not intended to restrict the full exchange of scientific information concerning the drug, including dissemination of scientific findings in scientific or lay media. Rather, its intent is to restrict promotional claims of safety or effectiveness of the drug. The investigator must also assure that he or she will promptly report to the IRB all changes in the research activity and all unanticipated problems involving risk to human participants or others, and that he or she will not make any

- changes in the research without IRB approval, except where necessary to eliminate apparent immediate hazards to human participants.
- b. Follow FDA requirements for inspection of investigator's records and reports
    - i. An investigator must upon request from any properly authorized officer or employee of FDA, at reasonable times, permit such officer or employee to have access to, and copy and verify any records or reports made by the investigator pursuant to 312.62.
    - ii. The investigator is not required to divulge subject names unless the records of particular individuals require a more detailed study of the cases, or unless there is reason to believe that the records do not represent actual case studies, or do not represent actual results obtained.
  - c. Follow FDA requirements for handling of controlled substances
  - d. If the investigational drug is subject to the Controlled Substances Act, the investigator must take adequate precautions, including storage of the investigational drug in a securely locked, substantially constructed cabinet, or other securely locked, substantially constructed enclosure, access to which is limited, to prevent theft or diversion of the substance into illegal channels of distribution.
3. For FDA-regulated research involving investigational devices:
- a. General responsibilities of investigators.
    - i. An investigator is responsible for ensuring that an investigation is conducted according to the signed agreement, the investigational plan and applicable FDA regulations, for protecting the rights, safety, and welfare of participants under the investigator's care, and for the control of devices under investigation. An investigator also is responsible for ensuring that informed consent is obtained in accordance with 21 CFR §50.
  - b. Specific responsibilities of investigators
    - i. Awaiting approval: An investigator may determine whether potential participants would be interested in participating in an investigation, but must not request the written informed consent of any subject to participate, and must not allow any subject to participate before obtaining IRB and FDA approval.
    - ii. Compliance: An investigator must conduct an investigation in accordance with the signed agreement with the sponsor, the investigational plan, and other applicable FDA regulations, and any conditions of approval imposed by an IRB or FDA.
    - iii. Supervising device use: An investigator must permit an investigational device to be used only with participants under the investigator's

supervision. An investigator must not supply an investigational device to any person not authorized to receive it.

- iv. Financial disclosure:
  - a. A clinical investigator must disclose to the sponsor sufficient accurate financial information to allow the applicant to submit complete and accurate certification or disclosure statements required under 21 CFR §54.
  - b. The investigator must promptly update this information if any relevant changes occur during the course of the investigation and for 1 year following completion of the study.
- v. Disposing of device: Upon completion or termination of a clinical investigation or the investigator's part of an investigation, or at the sponsor's request, an investigator must return to the sponsor any remaining supply of the device or otherwise dispose of the device as the sponsor directs.
- c. Maintain the following accurate, complete, and current records relating to the investigator's participation in an investigation:
  - i. All correspondence with another investigator, an IRB, the sponsor, a monitor, or FDA, including required reports.
  - ii. Records of receipt, use or disposition of a device that relate to:
    - a. The type and quantity of the device, the dates of its receipt, and the batch number or code mark.
    - b. The names of all persons who received, used, or disposed of each device.
    - c. Why and how many units of the device have been returned to the sponsor, repaired, or otherwise disposed of.
  - iii. Records of each subject's case history and exposure to the device. Case histories include the case report forms and supporting data including, for example, signed and dated consent forms and medical records including, for example, progress notes of the physician, the individual's hospital charts, and the nurses' notes. Such records must include:
    - a. Documents evidencing informed consent and, for any use of a device by the investigator without informed consent, any written concurrence of a licensed physician and a brief description of the circumstances justifying the failure to obtain informed consent.
    - b. Documentation that informed consent was obtained prior to participation in the study.
    - c. All relevant observations, including records concerning adverse device effects (whether anticipated or unanticipated),

information and data on the condition of each subject upon entering, and during the course of, the investigation, including information about relevant previous medical history and the results of all diagnostic tests.

- d. A record of the exposure of each subject to the investigational device, including the date and time of each use, and any other therapy.
  - iv. The protocol, with documents showing the dates of and reasons for each deviation from the protocol.
  - v. Any other records that FDA requires to be maintained by regulation or by specific requirement for a category of investigations or a particular investigation.
- d. Inspections<sup>8</sup>
- i. Entry and inspection: A sponsor or an investigator who has authority to grant access must permit authorized FDA employees, at reasonable times and in a reasonable manner, to enter and inspect any establishment where devices are held (including any establishment where devices are manufactured, processed, packed, installed, used, or implanted or where records of results from use of devices are kept).
  - ii. Records inspection: A sponsor, IRB, or investigator, or any other person acting on behalf of such a person with respect to an investigation, must permit authorized FDA employees, at reasonable times and in a reasonable manner, to inspect and copy all records relating to an investigation.
  - iii. Records identifying participants: An investigator must permit authorized FDA employees to inspect and copy records that identify participants, upon notice that FDA has reason to suspect that adequate informed consent was not obtained, or that reports required to be submitted by the investigator to the sponsor or IRB misleading.
- e. Prepare and submit the following complete, accurate, and timely reports<sup>15</sup>
- i. Unanticipated adverse device effects. An investigator must submit to the sponsor and to the reviewing IRB a report of any unanticipated adverse device effect occurring during an investigation as soon as possible, but in no event later than 10 working days after the investigator first learns of the effect.
  - ii. Withdrawal of IRB approval. An investigator must report to the sponsor, within 5 working days, a withdrawal of approval by the reviewing IRB of the investigator's part of an investigation.

- iii. Progress. An investigator must submit progress reports on the investigation to the sponsor, the monitor, and the reviewing IRB at regular intervals, but in no event less often than yearly.
- iv. Deviations from the investigational plan:
  - a. An investigator must notify the sponsor and the reviewing IRB of any deviation from the investigational plan to protect the life or physical well-being of a subject in an emergency.
  - b. Such notice must be given as soon as possible, but in no event later than 5 working days after the emergency occurred.
  - c. Except in such an emergency, prior approval by the sponsor and the IRB is required for changes in or deviations from a plan, and if these changes or deviations may affect the scientific soundness of the plan or the rights, safety, or welfare of human participants, FDA approval also is required.
- v. Informed consent. If an investigator uses a device without obtaining informed consent, the investigator must report such use to the sponsor and the reviewing IRB within 5 working days after the use occurs.
- vi. Final report. An investigator must, within 3 months after termination or completion of the investigation or the investigator's part of the investigation, submit a final report to the sponsor.
- vii. Other. An investigator must, upon request by a reviewing IRB or FDA, provide accurate, complete, and current information about any aspect of the investigation.

## Appendix B: Additional Requirements for DHHS-Regulated Research

1. When a subject decides to withdraw from a clinical trial, the investigator conducting the clinical trial should ask the subject to clarify whether the subject wishes to withdraw from all components of the trial or only from the primary interventional component of the trial. If the latter, research activities involving other components of the clinical trial, such as follow-up data collection activities, for which the subject previously gave consent may continue. The investigator should explain to the subject who wishes to withdraw the importance of obtaining follow-up safety data about the subject.
2. Investigators are allowed to retain and analyze already collected data relating to any subject who chooses to withdraw from a research study or whose participation is terminated by an investigator without regard to the subject's consent, provided such analysis falls within the scope of the analysis described in the IRB-approved protocol. This is the case even if that data includes identifiable private information about the subject.
3. For research not subject to regulation and review by FDA, investigators, in consultation with the funding agency, can choose to honor a research subject's request that the investigator

destroy the subject's data or that the investigator exclude the subject's data from any analysis.

4. When seeking the informed consent of participants, investigators should explain whether already collected data about the participants will be retained and analyzed even if the participants choose to withdraw from the research.

## Appendix C: Additional Requirements for Clinical Trials (ICH-GCP)

### Investigator's Qualifications and Agreements

- The investigator should be qualified by education, training, and experience to assume responsibility for the proper conduct of the trial, should meet all the qualifications specified by the applicable regulatory requirements, and should provide evidence of such qualifications through up-to-date curriculum vitae and/or other relevant documentation requested by the sponsor, the IRB, and/or the regulatory authorities.
- The investigator should be thoroughly familiar with the appropriate use of the investigational product, as described in the protocol, in the current Investigator's Brochure, in the product information and in other information sources provided by the sponsor.
- The investigator should be aware of, and should comply with, GCP and the applicable regulatory requirements.
- The investigator/institution should permit monitoring and auditing by the sponsor, and inspection by the appropriate regulatory authorities.
- The investigator should maintain a list of appropriately qualified persons to whom the investigator has delegated significant trial-related duties.

### Adequate Resources

- The investigator should be able to demonstrate (e.g., based on retrospective data) a potential for recruiting the required number of suitable participants within the agreed recruitment period.
- The investigator should have sufficient time to properly conduct and complete the trial within the agreed trial period.
- The investigator should have available an adequate number of qualified staff and adequate facilities for the foreseen duration of the trial to conduct the trial properly and safely.
- The investigator should ensure that all persons assisting with the trial are adequately informed about the protocol, the investigational product, and their trial-related duties and functions.

### Medical Care of Trial Participants

- A qualified physician (or dentist, when appropriate), who is an investigator or a sub-investigator for the trial, should be responsible for all trial-related medical (or dental) decisions.
- During and following a subject's participation in a trial, the investigator/institution should ensure that adequate medical care is provided to a subject for any adverse events, including clinically significant laboratory values, related to the trial. The investigator/institution should inform a subject when medical care is needed for intercurrent illnesses of which the investigator becomes aware.
- It is recommended that the investigator inform the subject's primary physician about the subject's participation in the trial if the subject has a primary physician and if the subject agrees to the primary physician being informed.
- Although a subject is not obliged to give his/her reasons for withdrawing prematurely from a trial, the investigator should make a reasonable effort to ascertain the reasons, while fully respecting the subject's rights.

#### Communication with IRB

- Before initiating a trial, the investigator/institution should have written and dated approval opinion from the IRB for the trial protocol, written informed consent form, consent form updates, subject recruitment procedures (e.g., advertisements), and any other written information to be provided to participants.
- As part of the investigator's/institution's written application to the IRB, the investigator/institution should provide the IRB with a current copy of the Investigator's Brochure. If the Investigator's Brochure is updated during the trial, the investigator/institution should supply a copy of the updated Investigator's Brochure to the IRB.
- During the trial the investigator/institution should provide to the IRB all documents subject to review.

#### Compliance with Protocol

- The investigator/institution should conduct the trial in compliance with the protocol agreed to by the sponsor and, if required, by the regulatory authorities and which was given approval opinion by the IRB. The investigator/institution and the sponsor should sign the protocol, or an alternative contract, to confirm agreement.
- The investigator should not implement any deviation from, or changes of the protocol without agreement by the sponsor and prior review and documented approval opinion from the IRB of an amendment, except where necessary to eliminate an immediate hazards to trial participants, or when the changes involves only logistical or administrative aspects of the trial (e.g., change in monitors, change of telephone numbers).

- The investigator, or person designated by the investigator, should document and explain any deviation from the approved protocol.
- The investigator may implement a deviation from, or a change of, the protocol to eliminate an immediate hazard to trial participants without prior IRB approval opinion. As soon as possible, the implemented deviation or change, the reasons for it, and, if appropriate, the proposed protocol amendments should be submitted: a) to the IRB for review and approval opinion, b) to the sponsor for agreement and, if required, c) to the regulatory authorities.

#### Investigational Product

- Responsibility for investigational product accountability at the trial site rests with the investigator/institution.
- Where allowed/required, the investigator/institution may/should assign some or all of the investigator's/institution's duties for investigational product accountability at the trial site to an appropriate pharmacist or another appropriate individual who is under the supervision of the investigator/institution.
- The investigator/institution and/or a pharmacist or other appropriate individual, who is designated by the investigator/institution, should maintain records of the product's delivery to the trial site, the inventory at the site, the use by each subject, and the return to the sponsor or alternative disposition of unused product. These records should include dates, quantities, batch/serial numbers, expiration dates (if applicable), and the unique code numbers assigned to the investigational product and trial participants. Investigators should maintain records that document adequately that the participants were provided the doses specified by the protocol and reconcile all investigational product received from the sponsor.
- The investigational product should be stored as specified by the sponsor and in accordance with applicable regulatory requirements.
- The investigator should ensure that the investigational product are used only in accordance with the approved protocol.
- The investigator, or a person designated by the investigator/institution, should explain the correct use of the investigational product to each subject and should check, at intervals appropriate for the trial, that each subject is following the instructions properly.
- Randomization Procedures and Unblinding: The investigator should follow the trial's randomization procedures, if any, and should ensure that the code is broken only in accordance with the protocol. If the trial is blinded, the investigator should promptly document and explain to the sponsor any premature unblinding (e.g., accidental unblinding, unblinding due to a serious adverse event) of the investigational product.

#### Informed Consent of Trial Participants



- In obtaining and documenting informed consent, the investigator should comply with the applicable regulatory requirements, and should adhere to GCP and to the ethical principles that have their origin in the Declaration of Helsinki. Prior to the beginning of the trial, the investigator should have the IRB's written approval opinion of the written informed consent form and any other written information to be provided to participants.
- The written informed consent form and any other written information to be provided to participants should be revised whenever important new information becomes available that may be relevant to the subject's consent. Any revised written informed consent form, and written information should receive the IRB's approval opinion in advance of use. The subject or the subject's legally authorized representative should be informed in a timely manner if new information becomes available that may be relevant to the subject's willingness to continue participation in the trial. The communication of this information should be documented.
- Neither the investigator, nor the trial staff, should coerce or unduly influence a subject to participate or to continue to participate in a trial.
- None of the oral and written information concerning the trial, including the written informed consent form, should contain any language that causes the subject or the subject's legally authorized representative to waive or to appear to waive any legal rights, or that releases or appears to release the investigator, the institution, the sponsor, or their agents from liability for negligence.
- The investigator, or a person designated by the investigator, should fully inform the subject or, if the subject is unable to provide informed consent, the subject's legally authorized representative, of all pertinent aspects of the trial including the written information and the approval opinion by the IRB.
- The language used in the oral and written information about the trial, including the written informed consent form, should be as non-technical as practical and should be understandable to the subject or the subject's legally authorized representative and the impartial witness, where applicable.
- Before informed consent may be obtained, the investigator, or a person designated by the investigator, should provide the subject or the subject's legally authorized representative ample time and opportunity to inquire about details of the trial and to decide whether or not to participate in the trial. All questions about the trial should be answered to the satisfaction of the subject or the subject's legally authorized representative.
- Prior to a subject's participation in the trial, the written informed consent form should be signed and personally dated by the subject or by the subject's legally authorized representative, and by the person who conducted the informed consent discussion.
- If a subject is unable to read or if a legally authorized representative is unable to read, an impartial witness should be present during the entire informed consent discussion. After the written informed consent form and any other written information to be provided to

participants, is read and explained to the subject or the subject's legally authorized representative, and after the subject or the subject's legally authorized representative has orally consented to the subject's participation in the trial and, if capable of doing so, has signed and personally dated the informed consent form, the witness should sign and personally date the consent form. By signing the consent form, the witness attests that the information in the consent form and any other written information was accurately explained to, and apparently understood by, the subject or the subject's legally authorized representative, and that informed consent was freely given by the subject or the subject's legally authorized representative.

- Both the informed consent discussion and the written informed consent form and any other written information to be provided to participants should include explanations of the following:
  - That the trial involves research.
  - The purpose of the trial.
  - The trial treatments and the probability for random assignment to each treatment.
  - The trial procedures to be followed, including all invasive procedures.
  - The subject's responsibilities.
  - Those aspects of the trial that are experimental.
  - The reasonably foreseeable risks or inconveniences to the subject and, when applicable, to an embryo, fetus, or nursing infant.
  - The reasonably expected benefits. When there is no intended clinical benefit to the subject, the subject should be made aware of this.
  - The alternative procedures or courses of treatment that may be available to the subject, and their important potential benefits and risks.
  - The compensation and/or treatment available to the subject in the event of trial related injury.
  - The anticipated prorated payment, if any, to the subject for participating in the trial.
  - The anticipated expenses, if any, to the subject for participating in the trial.
  - That the subject's participation in the trial is voluntary and that the subject may refuse to participate or withdraw from the trial, at any time, without penalty or loss of benefits to which the subject is otherwise entitled.
  - That the monitors, the auditors, the IRB, and the regulatory authorities will be granted direct access to the subject's original medical records for verification of clinical trial procedures and/or data, without violating the confidentiality of the subject, to the extent permitted by the applicable laws and regulations and that, by signing a written informed consent form, the subject or the subject's legally authorized representative is authorizing such access.
  - That records identifying the subject will be kept confidential and, to the extent permitted by the applicable laws and/or regulations, will not be made publicly

- available. If the results of the trial are published, the subject's identity will remain confidential.
- That the subject or the subject's legally authorized representative will be informed in a timely manner if information becomes available that may be relevant to the subject's willingness to continue participation in the trial.
  - The persons to contact for further information regarding the trial and the rights of trial participants, and whom to contact in the event of trial related injury.
  - The foreseeable circumstances and/or reasons under which the subject's participation in the trial may be terminated.
  - The expected duration of the subject's participation in the trial. xx. The approximate number of participants involved in the trial.
- Prior to participation in the trial, the subject or the subject's legally authorized representative should receive a copy of the signed and dated written informed consent form and any other written information provided to the participants. During a subject's participation in the trial, the subject or the subject's legally authorized representative should receive a copy of the signed and dated consent form updates and a copy of any amendments to the written information provided to participants.
  - When a clinical trial (therapeutic or non-therapeutic) includes participants who can only be enrolled in the trial with the consent of the subject's legally authorized representative (e.g., minors, or patients with severe dementia), the subject should be informed about the trial to the extent compatible with the subject's understanding and, if capable, the subject should sign and personally date the written informed consent.
  - A non-therapeutic trial (i.e. a trial in which there is no anticipated direct clinical benefit to the subject), should be conducted in participants who personally give consent and who sign and date the written informed consent form.
  - Non-therapeutic trials may be conducted in participants with consent of a legally authorized representative provided the following conditions are fulfilled:
    - The objectives of the trial cannot be met by means of a trial in participants who can give informed consent personally.
    - The foreseeable risks to the participants are low.
    - The negative impact on the subject's well-being is minimized and low.
    - The trial is not prohibited by law.
    - The approval opinion of the IRB is expressly sought on the inclusion of such participants, and the written approval opinion covers this aspect. Such trials, unless an exception is justified, should be conducted in patients having a disease or condition for which the investigational product is intended. Participants in these trials should be particularly closely monitored and should be withdrawn if they appear to be unduly distressed.

- In emergency situations, when prior consent of the subject is not possible, the consent of the subject's legally authorized representative, if present, should be requested. When prior consent of the subject is not possible, and the subject's legally authorized representative is not available, enrolment of the subject should require measures described in the protocol and/or elsewhere, with documented approval opinion by the IRB, to protect the rights, safety and well-being of the subject and to ensure compliance with applicable regulatory requirements. The subject or the subject's legally authorized representative should be informed about the trial as soon as possible and consent to continue and other consent as appropriate should be requested.

### Records and Reports

- The investigator should ensure the accuracy, completeness, legibility, and timeliness of the data reported to the sponsor in the CRFs and in all required reports.
- Data reported on the CRF, that are derived from source documents, should be consistent with the source documents or the discrepancies should be explained.
- Any change or correction to a CRF should be dated, initialed, and explained (if necessary) and should not obscure the original entry (i.e. an audit trail should be maintained); this applies to both written and electronic changes or corrections. Sponsors should provide guidance to investigators and/or the investigators' designated representatives on making such corrections. Sponsors should have written procedures to assure that changes or corrections in CRFs made by sponsor's designated representatives are documented, are necessary, and are endorsed by the investigator. The investigator should retain records of the changes and corrections.
- The investigator/institution should maintain the trial documents as specified in
- Essential Documents for the Conduct of a Clinical Trial and as required by the applicable regulatory requirements. The investigator/institution should take measures to prevent accidental or premature destruction of these documents.
- Essential documents should be retained until at least 2 years after the last approval of a marketing application in an ICH region and until there are no pending or contemplated marketing applications in an ICH region or at least 2 years have elapsed since the formal discontinuation of clinical development of the investigational product. These documents should be retained for a longer period however if required by the applicable regulatory requirements or by an agreement with the sponsor. It is the responsibility of the sponsor to inform the investigator/institution as to when these documents no longer need to be retained.
- The financial aspects of the trial should be documented in an agreement between the sponsor and the investigator/institution.

- Upon request of the monitor, auditor, IRB, or regulatory authority, the investigator/institution should make available for direct access all requested trial related records.

#### Progress Reports

- The investigator should submit written summaries of the trial status to the IRB annually, or more frequently, if requested by the IRB.
- The investigator should promptly provide written reports to the sponsor, the IRB and, where applicable, the institution on any changes significantly affecting the conduct of the trial, and/or increasing the risk to participants.

#### Safety Reporting

- All serious adverse events (SAEs) should be reported immediately to the sponsor except for those SAEs that the protocol or other document (e.g., Investigator's Brochure) identifies as not needing immediate reporting. The immediate reports should be followed promptly by detailed, written reports. The immediate and follow-up reports should identify participants by unique code numbers assigned to the trial participants rather than by the participants' names, personal identification numbers, and/or addresses. The investigator should also comply with the applicable regulatory requirements related to the reporting of unexpected serious adverse drug reactions to the regulatory authorities and the IRB.
- Adverse events and/or laboratory abnormalities identified in the protocol as critical to safety evaluations should be reported to the sponsor according to the reporting requirements and within the time periods specified by the sponsor in the protocol.
- For reported deaths, the investigator should supply the sponsor and the IRB with any additional requested information (e.g., autopsy reports and terminal medical reports).
- Premature Termination or Suspension of a Trial If the trial is prematurely terminated or suspended for any reason, the investigator/institution should promptly inform the trial participants, should assure appropriate therapy and follow-up for the participants, and, where required by the applicable regulatory requirements, should inform the regulatory authorities. In addition:
  - If the investigator terminates or suspends a trial without prior agreement of the sponsor, the investigator should inform the institution where applicable, and the investigator/institution should promptly inform the sponsor and the IRB, and should provide the sponsor and the IRB a detailed written explanation of the termination or suspension.
  - If the sponsor terminates or suspends a trial, the investigator should promptly inform the institution where applicable and the investigator/institution should promptly inform the IRB and provide the IRB a detailed written explanation of the termination or suspension.

- If the IRB terminates or suspends its approval opinion of a trial, the investigator should inform the institution where applicable and the investigator/institution should promptly notify the sponsor and provide the sponsor with a detailed written explanation of the termination or suspension.
- Final Reports by Investigator: Upon completion of the trial, the investigator, where applicable, should inform the institution; the investigator/institution should provide the IRB with a summary of the trial's outcome, and the regulatory authorities with any reports required.