Institutional Review Board Policy Manual

PRINCIPAL INVESTIGATOR RESPONSIBILITIES

PURPOSE: To outline the responsibilities of the Principal Investigators who conduct clinical research at McLeod Health.

POLICY: Principal investigators at McLeod Health must understand and accept their responsibilities for conducting research.

PROCEDURE:

Responsibilities of the Principal Investigator

The McLeod Health policy requires all individuals (PI, co-PI, research nurse, coordinator, and research staff) who are involved in the performance of clinical research to be educated in human research protection issues prior to their involvement in human subject research. Evidence of continuing education every three years must be submitted to the IRB.

It is important to have a strong, comprehensive educational program that ensures that any individual involved in the performance of human subject research at McLeod Health understands the ethical principles and regulatory requirements related to the protection of human subjects.

1. Each principal investigator (PI) will be required to review and sign a copy of an "Individual Investigator Agreement" (Attachment C - see page 8). The McLeod Health Institutional Review Board has approved utilizing the agreement suggested by our Federalwide Assurance (FWA). This agreement is an extension of our institution's FWA to cover a collaborating individual investigator. The detailed information is outlined in the agreement. The FWA is the only type of assurance of compliance accepted and approved by the Office for Human Research Protections (OHRP). Once the contracts are fully executed, an original will be returned to the PI for their files. This agreement will expire after 5 years from the date signed.

2. McLeod Health requires all individuals who conduct human subject research to be trained prior to beginning a protocol. The IRB has determined that the NIH, "Protecting Human Research Participants” online education1 is the required training. The only exception is if the PI has a current CITI training certificate, they can forward a copy of that document to the IRB in place of the NIH training. It must not expire before one year of submission.

3. Before a new PI (and co-PI), to the McLeod Health system, submits a new protocol application for a study to be reviewed, they must complete New Principal

1 NIH Link: http://phrp.nihtraining.com/users/login.php
Investigator Orientation. The PI must have adequate staff and resources available to comply with federal regulations and IRB policies and procedures. The PI and the research coordinator will meet with the IRB vice-chair and/or the IRB coordinator. During this meeting, documentation will be reviewed of the IRB Policies and Procedures (including, but not limited to the Principal Investigator Responsibilities), the forms utilized by the IRB, meeting and deadline submission dates, electronic submission process, etc. The PI will be provided with a copy of the IRB Policy and Procedure manual (also contains additional resources). In addition, a copy of the PI's CV and the research coordinator’s resume must be submitted to the IRB. If the PI obtains a new research coordinator, that individual must go through the required training with the IRB coordinator.

4. Requests for protocol review must be submitted by the principal investigator in writing. Upon receipt, the Chairperson or his or her designee will send the principal investigator a copy of the requirements of a proposed investigational plan (see #6).

5. The principal investigator cannot begin the protocol until written approval has been received from the Institutional Review Board (IRB).

6. The proposed investigational plan and the consent form submitted by the principal investigator to the IRB shall include at a minimum the following information:

- The name of the principal investigator and the principal investigator’s contact information.
- Purpose of the study to include but not limited to the intended use(s) of the device or drug.
- Plan or outline to include how the protocol will be monitored.
- Expected length and intensity of the protocol.
- Expected number of human subjects involved with the protocol and a description of the human subjects
- Expected results of the protocol.
- Possible adverse reactions by human subjects to the device or drug involved.
- Report of prior human subject investigation(s), and Investigational Drug Brochure if available.
- Copy of informed consent containing all of the current required elements. A translated consent should also be submitted if applicable.
- The process of obtaining the informed consent by the principal investigator.
- The submitted plans should include a "Financial Pro Forma" (see attachment A) to identify where, when, how, and what kind of transactions are a part of the "research". Note these items may also be listed in the sponsor contract agreement.
- The principal investigator shall be required to sign a “Physician/Presenter Financial Disclosure form” (see attachment B).
7. The principal investigator, co-investigator, or his/her designee, must attend a convened IRB meeting where the protocol has been placed on the agenda and must present the proposed protocol to the IRB. The IRB has the authority to request additional information from the principal investigator as needed for the review of the protocol or other matters.

8. The principal investigator is responsible for reporting to the IRB any expressed concerns that result in the findings regarding subject safety, compliance with the research protocol, informed consent violations, or the integrity of the research data.

9. The principal investigator is responsible for maintaining for each study protocol a current file/binder. It must contain, at a minimum, an approved IRB protocol; approved informed consent form; approved recruiting material; approved study materials (i.e. surveys, questionnaires); IRB approval and action letters; pertinent correspondence from the IRB (and sponsor if applicable); the Investigator Brochure for study. The investigator is responsible for the safe and secure storage of research data (both paper and electronic) and protecting the confidentiality of the data.

10. The principal investigator will submit a status report of all studies approved by the IRB (continuing review form) at the end of twelve (12) months or more often as determined by the IRB. These reports will specify the number of human subjects in the protocol to date, the number of human subjects withdrawn, etc. and any adverse reactions or complications by the human subjects to the drug or device employed.

11. The principal investigator shall submit to the IRB a request (revision, addendum, etc. form) for any change in the original protocol. Before any change can be implemented, the written approval of the IRB must be obtained. (Unless the change is necessary to eliminate immediate hazards to the health or welfare of human subjects involved with the protocol).

12. The principal investigator may request expedited review by the IRB of minor changes in previously approved research or changes that involve no more than minimal risk as allowed by the FDA. This review shall be carried out by the Chairperson of the IRB or his/her designee. All expedited reviews shall be listed on the full board agenda at the next scheduled convened IRB meeting.

13. The principal investigator must report in writing to the IRB within ten (10) days of its discovery, any unexpected serious adverse event(s) (SAE) that may reasonably be regarded as probably caused by the drug or device, and which was/were not anticipated in the original proposal. This must be completed and submitted on the serious adverse event form (SAE).

A SAE is any sign, symptom or medical condition that emerges during treatment or during a post-treatment follow-up period that (1) was not present at the start of treatment
and it is not a chronic condition that is part of the patient's medical history, OR (2) was present at the start of treatment or as part of the patient's medical history but worsened in severity and/or frequency during therapy, AND that meets any of the following regulatory serious criteria:

- Results in death
- Is life-threatening
- Requires or prolongs inpatient hospitalization
- Is disabling
- Is a congenital anomaly/birth defect
- Is medically significant or requires medical or surgical intervention to prevent one of the outcomes listed above

14. The principal investigator will notify the IRB of the completion or discontinuance of the protocol within ten (10) days of completion or discontinuance. A final protocol report (permanent closure form) is required to be completed and submitted to the IRB upon protocol completion or discontinuance. These forms will be provided to the principal investigator and are located on the McLeod Health Intranet.

15. The principal investigator will document enrollment of the human subjects into inpatient investigational studies by placing a copy of the signed informed consent in the inpatient record, or a physician order in the chart or a note in the human subject’s history and physical. These charts will be randomly reviewed by the IRB to ensure full compliance with this requirement.

16. The principal investigator shall have as a part of the informed consent, that the following individuals have access to the research information:
   - PI and co-PI(s) participating in the study
   - FDA
   - Research Protocol Sponsor (Manufacturer, Drug Company, etc.)
   - McLeod Health, to include the IRB.

17. The principal investigator shall refrain from exerting undue influence upon potential research human subjects.

18. The principal investigator shall have available for the nurses who are called upon to administer investigational drugs the following information: basic pharmacologic information concerning the drug(s), including dosage, strengths, actions, uses, side effects and symptoms of toxicity.

19. In case of a potential adverse event from a device, that staff should contact the principal investigator if questions arise. A complete chain of custody as far as practical be established for each device under the direction of the Risk Manager for McLeod Health.
20. The principal investigator agrees the McLeod Regional Medical Center Pharmacy Department will provide storage for all investigational drugs and will also provide for the proper labeling and dispensing according to the principal investigators written order. All essential information related to investigational drugs for inpatient and outpatient studies will be maintained and made available in the McLeod Regional Medical Center Pharmacy Department.

For principal investigators in a physician office (MPA), all investigational drugs are to be stored in a safe and secure storage area. Investigational drugs being used at other McLeod Health hospitals are to be stored at the appropriate Pharmacy for that campus. Investigational devices are to be stored in a secured area as well (i.e. Cath Lab, Surgical Services). It is the responsibility of the PI to provide these safety measures.

When a person who is actively participating in a protocol that has not been approved by the McLeod Health IRB is admitted to McLeod Regional Medical Center (and all other McLeod Health hospitals) and needs to continue their protocol medication, the principal investigator is responsible for providing/obtaining the following information for use by the Pharmacy and the appropriate Research Department:

- Copy of the protocol
- Copy of the signed informed consent (approved through another external IRB)
- Copy of the pharmacology information for Pharmacy and Nursing personnel.

Attachments

Project Pro Forma
Physician/Presenter Financial Disclosure Form
Individual Investigator Agreement

Applicable Regulations and Guidelines Referenced:

The Belmont Report
Title 45 CFR 46
ICH Guideline for Good Clinical Practice

Expedited review procedures for certain kinds of research involving no more than minimal risk, and for minor changes in approved research. 45 CFR 46.110

Approved: 10/08
Revised: 7/12, 9/16
18039.IRB.P-10

This Policy has been reviewed and approved for:
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Project Pro Forma

Principal Investigator’s Name: ________________________________

Study Name: ________________________________

Revenue

Primary Sponsor Research Project
   Per Subject Registered _______
   Per Subject Visit _______
   Per Subject Data Captured _______

Global Project Fee _______
Reimbursement for Equipment for Project _______

Other Revenue Sources from Research Project
1 _______
2 _______
3 _______

Total Revenue/Compensation _______

Expenses

Office Expenses above Routine Items
1 _______
2 _______
3 _______

Equipment Purchases
1 _______
2 _______
3 _______

Hospital Services above Standard of Care
1 _______
2 _______
3 _______

Office & Miscellaneous Expenses
1 _______
2 _______
3 _______

Total Expenses Covered _______

Net Income from Research Project _______

______________________________  ___________________________
Signature                                      Date

10/08
Physician/Presenter Financial Disclosure Form

It is the policy of McLeod Health to ascertain potential conflicts of interests of its medical staff, speakers and/or presenters, and to determine whether financial relationships and/or other interests affect the rights and welfare of McLeod's patients. In certain circumstances federal law requires such disclosure. This disclosure is intended to ensure that financial interests and arrangements of clinical investigators that could affect the reliability of data submitted to FDA are identified, disclosed, and addressed appropriately; that products and pharmaceuticals are appropriately evaluated for independency and safety; and that other arrangements would not compromise the safety or well being of patients. McLeod Health physicians may have such interests reviewed by McLeod's Institutional Review Board, Pharmacy and Therapeutics Committee, the Products and Evaluation Committee, and/or any other committee as McLeod deems appropriate.

Please indicate below if you, (including your spouse or dependent children) have any of the following disclosable financial arrangements:

Yes ☐ No ☐ Has any compensation been made to you in which the value of compensation could be affected by a study/case's outcome?

Yes ☐ No ☐ Do you have a proprietary interest in a tested product, drug, biologic product, or device, including, but not limited to, a patent, trademark, copyright or licensing agreement?

Yes ☐ No ☐ Do you have any equity interest in the sponsor of a covered study, i.e., any ownership interest, stock options, or other financial interest whose value cannot be readily determined through reference to public prices or any equity interest in a publicly held company that exceeds $10,000 in value? (The requirement applies to interests held during the time the clinical investigator is carrying out the study and for one (1) year following completion of the study.)

Yes ☐ No ☐ Do you have any financial incentive or advantage to gain by using a particular product, service, drug, biological product or device as opposed to using an alternative product, service, drug, biological product or device?

Yes ☐ No ☐ Have you been or are you currently responsible for the design, conduct, or reporting of any research or do you have or have you had an economic interest in, or acted as an officer or a director of any outside entity whose financial interests would reasonably appear to be affected by conducting a particular research study, utilizing a particular product, service, drug, biological product or device?

If you answered "yes" to any of the questions above, please provide the name of the associated study, case, product, service, drug, biological product and the company or companies with whom the financial relationship exists or existed (add attachments if necessary).

____________________________________________________________________________________
____________________________________________________________________________________
____________________________________________________________________________________

Signature ___________________________ Date ___________ Print Name ___________________________
DEFINTIONS

**Clinical Investigator** - Any listed or identified investigator or sub-investigator who is directly involved in the treatment or evaluation of research subjects. The term also includes the spouse and each dependent child of the investigator.

**Conflict of Interest** - An actual, potential or perceived conflict of interest occurs in those circumstances where an individual's judgment could be affected because the individual has a personal interest in the outcome of a decision over which the individual has control or influence. A personal interest exists when an individual colleague or a member of his or her family stands to directly or indirectly gain as a result of a decision.

**Covered clinical study** - Any study of a drug, biological product or device in humans submitted in a marketing application or reclassification petition that the applicant or FDA relies on to establish that the product is effective (including studies that show equivalence to an effective product) or any study in which a single investigator makes a significant contribution to the demonstration of safety. This would, in general, not include phase I tolerance studies or pharmacokinetic studies, most clinical pharmacology studies (unless they are critical to an efficacy determination); large open safety studies conducted at multiple sites, treatment protocols, and parallel track protocols. The Sponsor of the Clinical Study or the IRB may consult with FDA as to which clinical studies constitute "covered clinical studies" for purposes of complying with financial disclosure requirements.

**Financial Interest** - A financial interest includes income or other remuneration, as well as investments and ownership interests in excess of 5% of the total interest. It does not include stocks, bonds, and other securities sold on a national exchange, but does include mutual funds, or certificates of deposits and other depository accounts at financial institutions.

**References:**

McLeod Health Administrative Conflict of Interest Policy

McLeod Health Medical Staff Bylaws


564 Physician Financial Disclosure Form
Individual Investigator Agreement

Name of Institution with the Federalwide Assurance (FWA): McLeod Health IRB

Applicable FWA #: 00007828

Individual Investigator’s Name: ________________________________

Specify Research Covered by this Agreement: ____________________

(1) The above-named Individual Investigator has reviewed: 1) The Belmont Report: Ethical Principles and Guidelines for the Protection of Human Subjects of Research (or other internationally recognized equivalent; see section B.1. of the Terms of the Federalwide Assurance (FWA) for International (Non-U.S.) Institutions); 2) the U.S. Department of Health and Human Services (HHS) regulations for the protection of human subjects at 45 CFR part 46 (or other procedural standards; see section B.3. of the Terms of the FWA for International (Non-U.S.) Institutions); 3) the FWA and applicable Terms of the FWA for the institution referenced above; and 4) the relevant institutional policies and procedures for the protection of human subjects.

(2) The Investigator will complete the educational training required by the Institution and/or the IRB prior to initiating research covered under this Agreement. The Investigator (and the research coordinator) will complete: 1) The NIH computer-based training course entitled “Protecting Human Research Participants”. This will expire after 3 years from date taken. A copy of the certificate(s) of completion will be forwarded to the IRB Research office for their files. If you have a current CITI (Collaborative Institutional Training Initiative) certificate you may submit a copy of that. It will expire on the date of the certificate.

(3) The Investigator understands and hereby accepts the responsibility to comply with the standards and requirements stipulated in the above documents and to protect the rights and welfare of human subjects involved in research conducted under this Agreement.

(4) The Investigator will comply with all other applicable federal, international, state, and local laws, regulations, and policies that may provide additional protection for human subjects participating in research conducted under this agreement.

(5) The Investigator will abide by all determinations of the Institutional Review Board (IRB) designated under the above FWA and will accept the final authority and decisions of the IRB, including but not limited to directives to terminate participation in designated research activities.
(6) The Investigator will report promptly to the IRB any proposed changes in the research conducted under
this Agreement. The investigator will not initiate changes in the research without prior IRB review and
approval, except where necessary to eliminate apparent immediate hazards to subjects.

(7) The Investigator will report immediately to the IRB any unanticipated problems involving risks to
subjects or others in research covered under this Agreement.

(8) The Investigator, when responsible for enrolling subjects, will obtain, document, and maintain records
of informed consent for each such subject or each subject’s legally authorized representative as required
under HHS regulations at 45 CFR part 46 (or any other international or national procedural standards
selected on the FWA for the institution referenced above) and stipulated by the IRB.

(9) The Investigator acknowledges and agrees to cooperate in the IRB’s responsibility for initial and
continuing review, record keeping, reporting, and certification for the research referenced above. The
Investigator will provide all information requested by the IRB in a timely fashion.

(10) The Investigator will not enroll subjects in research under this Agreement prior to its review and
approval by the IRB.

(11) Emergency medical care may be delivered without IRB review and approval to the extent permitted
under applicable federal regulations and state law.

(12) This Agreement does not preclude the Investigator from taking part in research not covered by this
Agreement.

(13) The Investigator acknowledges that he/she is primarily responsible for safeguarding the rights and
welfare of each research subject, and that the subject’s rights and welfare must take precedence over the
goals and requirements of the research.

Investigator Signature: ___________________________________________ Date _______________

Name: ___________________________ Degree(s): _______
  (Last) (First) (Middle Initial)

Address: ___________________________ phone #: ______________

_________________________ SC ___________________________ (City) (State/Province) (Zip/Country)

FWA IRB Chairman Signature: ___________________________ Date _____________

Name: ___________________________ Title: IRB Chair
  (Last) (First) (Middle Initial)

Address: ___________________________ phone #: 843-777-2808

__________________ P. O. Box 100551 ___________________________ (City) (State/Province) (Zip/Country)

Florence, SC 29502

1/05, 3/11, 9/16