

INVESTIGATIONAL PROJECT GUIDELINES

Great Lakes College of Clinical Medicine

INSTITUTIONAL REVIEW BOARD

Rev. 3/00

Great Lakes College of Clinical Medicine

Investigational Project Guidelines

Table of Contents

Introduction	1 - 2
Project/Protocol Information	3 - 6
Informed Consent	8-10
Termination of a Project/Protocol	10
Continuing Review and serious adverse reactions.....	10
Charging for Investigational Devices, Drugs, and Biologics.....	11
Recruiting Study Subjects.....	12

Introduction

According to 45 CFR 46, any activity (whether funded or not) involving human subjects must be reviewed and approved by the Institutional Review Board. **This review and approval must be granted prior to beginning the proposed activity.**

The GLCCM IRB has been inspected by the FDA and is in applicable compliance of the FDA Regulations. The IRB does not "protect" investigators, it supervises and oversees approved activities of research studies.

One of the Institutional Review Board's main functions in reviewing such activity is to determine the degree of risk to subjects. Risk exists when a subject may be exposed to any possible, physical, psychological, or other harm as a result of an activity that is not an accepted and established method of meeting the subject's needs. In addition to the physical risk, any procedures involving discomfort, anxiety, invasion of privacy, or other threats to the subject's dignity fall under the purview of the Institutional Review Board. Thus, the Institutional Review Board will assess risk for:

1. **Experimental** activities, including surgery, biopsy, new devices, drugs, organ transplants, and other innovations.
2. Use of materials such as organs, body fluids and tissues, obtained during **routine** services.
3. Trainee education and/or demonstration projects.
4. Use of stored data, such as medical records, that may have been obtained for other purposes.

If the Institutional Review Board decides that an activity will expose a subject to risk, the Board will assure that:

1. The rights and welfare of the subject(s) are protected.
2. The methods used to obtain the subject's or subjects' informed consent are appropriate.
3. The potential benefit for the subject(s) and/or society, to knowledge, outweighs the risks.

The Institutional Review Board may request information on any aspect of a proposed activity. As part of the review process, the Institutional Review Board may seek the advice of consultants, supplementary information, and may request demonstration of the activity. **All criteria must be met for the Institutional Review Board to consider approval of the proposed biomedical or behavioral research activity.** The Institutional Review Board will request continuing review reports at the designated intervals for approved activities and immediate reporting of any unforeseen complications or adverse reactions.

To assure prompt review of your project/protocol by the Institutional Review Board, contact Betsey Angus, telephone 800-788-4627 or (419) 358-4627. **The material required for the IRB to review a project must be submitted six weeks prior to the Institutional Review Board meeting at which it will be reviewed. You will be notified of the date, time, and place of the Institutional Review Board meeting, and requested to attend.**

After the Board has reviewed the project/protocol, you will be notified in writing of its decision, and/or requested to submit supplemental information if necessary.

The determination IF a project requires an Investigational New Drug (IND) approval or requires approval as an Investigation Device Exemption (IDE) from the FDA or other agency, a copy of all correspondence, permits, and any other notification must be submitted to the Institutional Review Board PRIOR to final review of the IRB. A written statement signed by an official or documentation of a telephone call, including the date and time, the name and title of the FDA official spoken to, and a summary of the substance of the conversation, if an IDE or IND is not needed. For IND information contact the FDA at 301-827-4573 or <http://www.fda.gov/opacom/morechoices/fdaforms/idec.html>. For IDE information contact the FDA at 301-594-1190 or <http://www.fda.gov/cdrh/index.html>.

If a project is contingent upon funding, the Institutional Review Board is to be notified when funding is obtained and when the project will begin.

Please see the "Rules" sheet (enclosed) for full information about submission of your project.

For Institutional Review Board review of your project/protocol, **4 collated copies** initially of the following information will be required:

1. Completed **project/protocol information sheets**. (See pages 3-6).
2. Principal investigator's **Curriculum Vitae**, along with any additional information on the investigator's experience in this research area.
3. Copy of **formal protocol along with an abstract** to be utilized. If a medical device is used, information from the manufacturer will be required.
4. **Consent form(s)** to be used. (See pages 7-8).
5. **Submission fee** and the above material is to be submitted to Betsey T. Angus 122 Thurman Street, P.O. Box 248 - Bluffton, OH 45817 (419-358-7900), (If you have questions, the initial contact person is Betsey.)

After the initial submission is accepted and revisions are made if requested, 20 copies of the project ABSTRACT and 4 COMPLETE copies will need to be sent along with the PROCESSING FEE two weeks before the meeting. Please refer to the RULES.

PROJECT/PROTOCOL INFORMATION

Principal Investigator: _____

Address: _____

Telephone/Fax: _____

TITLE OF PROJECT/PROTOCOL: _____

Project/Protocol Sponsor: _____

Address: _____

Telephone: _____ Contact: _____

ABSTRACT:

PROJECT/PROTOCOL INFORMATION

Principal Investigator: _____

Address: _____

Telephone/Fax: _____

TITLE OF PROJECT/PROTOCOL: _____

Project/Protocol Sponsor: _____

Address: _____

Telephone: _____ Contact: _____

Funding agency to which project will be submitted and/or funding sources (if any):

Projected date of start up: _____

Indicate which of the following will be involved in your project/protocol.

___ Patients as experimental subjects

___ Data, medical records, etc.

___ Patients as control subjects

___ Radiation

___ Non-Patient volunteers

___ Subjects to be paid

___ Students as subjects

___ Charges incurred by subjects

___ Pregnant subjects

___ Charges to third parties

___ Subjects under 18 years old

___ Fetal or placental tissue

___ Mentally disabled subjects

___ Autopsy tissue

___ Filming, recording subjects

___ Surgical pathology tissue

___ Experimental drugs

___ Approved drugs for new uses

___ Placebos

Experimental devices

___ Questionnaires, psychological tests

___ Nonprescription nutritional substances

8. Will there be any cost to the participant and/or insurer as a result of participation?

9. What potential side effects or adverse reactions could arise from the subjects participation in the study?

10. How will medical care be provided in the event of an adverse reaction or problem arising from the subject's participation in the project/protocol? How will the patient contact the principal investigator at all times in the event of a medical emergency? Be specific and list phone numbers, etc.

11. How will confidentiality of data be maintained and how will data be stored and retained?

12. What provisions have been made for informing the subject's primary physician (if the investigator is not the primary physician) of the response of his/her patient?

13. Are results of prior investigations adequate to support a conclusion that it is reasonably safe to begin the study? (Provide full details and statistics).

14. What clinical laboratory facilities and medical support are available to assure that the study will be conducted properly and in conformance with the investigational plan and to assure the safety of the subjects?

INFORMED CONSENT

For each project/protocol, the Principal Investigator must submit to the Institutional Review Board the consent form(s) and/or the script for any verbal explanation given. All medical terms must be explained clearly in language that a non-medical person would understand. The investigator for must retain consent forms at least five (5) years (21 CR 56.195(b)). **Participation in a study will not be permitted unless the participant gives his/her written consent; retroactive consent will not be permitted.** The consent form(s) and verbal information should be clear, legible, and in simple terms, and contain the following:

1. Title of the project/protocol.
2. Date of preparation/revision.
3. Patient Bill of Rights as page 1: see below in italics

*Consent for _____
Are you participating in any other research project?*

_____ Yes _____ No

Experimental Subject Bill of Rights

Persons who participate in a medical experiment are entitled to certain rights. These rights include but are not limited to the subject's right to:

Be informed of the nature and purpose of the experiment:

Be given an explanation of the procedures to be followed in the medical experiment, and any drug or device to be utilized.

Be given a description of the any attendant discomforts and risks reasonably to be expected:

Be given a disclosure of any benefits to the subject reasonably to be expected, if applicable:

Be given a disclosure of any appropriate alternatives, drugs or devices that might be advantageous to the subject, their relative risks and benefits;

Be informed of the avenues of medical treatment, if any available to the subject after the experiment if any complications should arise;

Be given the opportunity to ask questions concerning the experiment or the procedures involved:

Be instructed that consent to participate in the medical experiment may be withdrawn at any time and the subject may discontinue participation without prejudice:

Be given a copy of the signed and dated consent form:

And be given the opportunity to decide to consent or not to consent to a medical experiment without the intervention of any element force, fraud, deceit, duress, coercion or undue influence on the subject's decision.

4. Pages numbered.
5. Space for the signatures and dating thereof by the investigator, person obtaining the consent, the participant, a witness, and (where appropriate) space for a minor to sign, in addition to his/her parent/guardian.
6. Notification that the participant will receive a copy of the signed consent form.

7. A statement that in the event the results of the project will be published as a study, that permission is granted from the patient to be included, provided that his/her privacy and confidentiality is protected.
8. The Great Lakes College of Clinical Medicine statement on compensation ("I also understand that Great Lakes College of Clinical Medicine has no policy to medically treat or compensate or physical injuries incurred as the result of participating in biomedical or behavioral research.") must be included in the consent form(s).

*** A. *Basic elements of informed consent.* In seeking informed consent, the following information shall be provided to each subject.

1.* A statement that the study involves research, an explanation of the purposes of the research, the ***expected duration of the subjects' participation, a description of the procedures to be followed and identification of any procedures which are experimental.

2.* A description of any reasonably foreseeable risks or discomforts to the subject.

3.* A description of any benefits to the subject or to others which may reasonably be expected from *** the research.

4.* A disclosure of appropriate alternative procedures or courses of treatment, if any, that might be *** advantageous to the subject.

* A statement describing the extent, if any, to which confidentiality of records identifying the subject ***will be maintained and that notes the possibility that the Food and Drug Administration may inspect the records.

* For research involving more than minimal risk, an explanation as to whether any compensation and *** an explanation as to whether any medical treatments are available if injury occurs and, if so, what they consist of or where further information may be obtained.

*** An explanation of whom to contact for answers to pertinent questions about the research and *** research subjects' rights, and whom to contact in the event of a research-related injury to the subject.

* A statement that participation is voluntary, that refusal to participate will involve no penalty or loss *** of benefits to which the subject is otherwise entitled, and that the subject may discontinue participation at any time without penalty or loss of benefits to which the subject is otherwise entitled.

*** B. *Additional elements of informed consent.* When appropriate, one or more of the following elements of information shall also be provided to each subject:

A statement that the particular treatment or procedure may involve risks to the subject (or to the embryo or fetus, if the subject is or may become pregnant) which are currently unforeseeable.

2. Anticipated circumstances under which the subject's participation may be terminated by the investigator without regard to the subject's consent.
3. Any additional costs to the subject that may result from participation in the research.
4. The consequences of a subject's decision to withdraw from the research and procedures for orderly termination of participation by the subject.
5. A statement that significant new findings developed during the course of the research, which may relate to the subject's willingness to continue participation, will be provided to the subject.
6. The approximate number of subjects involved in the study.

C. The informed consent requirements in these regulations are not intended to preempt any applicable Federal, State, or local laws which require additional information to be disclosed for informed consent to be legally effective.

D. Nothing in these regulations is intended to limit the authority of a physician to provide emergency medical care to the extent the physician is permitted to do so under applicable Federal, State, or local laws.

* Required per 45 CFR 46.103(c)

** Required per the compensation element which was added 1/12/79 as the seventh element of consent [45 CFR 46.103(c)(7)], revised 2/23/96 using the current version.

*** Required per 21 CFR 50.25

Termination of a Project/Protocol

If a project is completed, discontinued, or other circumstances arise requiring the Principal Investigator to withdraw from an approved study, the Institutional Review Board is to be notified, in writing, of such completion, discontinuation, or withdrawal within thirty (30) days. Any termination by the IRB will include a statement to the investigator of the reasons for the IRB's actions. The IRB must inform the FDA of a termination. The investigator may finish with the active patients but not enroll new patients. Any final data must be submitted to the IRB to close the file.

Continuing Review

The approval will be determined by the degree of risk, not to exceed one year. The *INVESTIGATOR* is responsible for submitting the annual continuing review. The IRB will send a continuing review form, but if it is not received, the investigator **MUST** submit the continuing review to the IRB **PRIOR** to the approval expiration date.

Adverse Reactions

All serious adverse reactions and deaths must be reported to the FDA and a written detailed form reported to the IRB.

**Great Lakes College of Clinical Medicine
Institutional Review Board**

CHARGING FOR INVESTIGATIONAL DEVICES, DRUGS AND BIOLOGICS

Charging for Investigational Medical Devices and Radiological Health Products.

The investigational Device Exemption (IDE) regulations allow sponsors to charge for an investigational device, however, the charge should not exceed an amount necessary to recover the costs of manufacture, research, development, and handling of the investigational device [21 CFR 812.7 (b)]. A sponsor justifies the proposed charges for the device in the IDE application, states the amount to be charged, and explains why the charge does not constitute commercialization [21 CFR 812.20 (b)(3)]. FDA generally allows sponsors to charge investigators for investigational devices, and this cost usually is passed on to the subjects.

Charging for Investigational Drugs and Biologics.

The Investigational New Drug (IND) regulations [21 CFR 312.7 (d)] permit a sponsor to charge for an investigational drug or biologic that has not been approved for marketing, only under the conditions outlined below. In both a clinical trial and a treatment IND, the charge should not exceed an amount that is necessary to recover the costs associated with the manufacture, research, development, and handling of the investigational drug or biologic. FDA may withdraw authorization to charge if the Agency finds that the conditions underlying the authorization are no longer satisfied.

i) Clinical Trials Under an IND

A sponsor may not charge for an investigational drug or biologic in a clinical trial under an IND without the Agency's prior written approval. In requesting such approval, the sponsor must explain why a charge is necessary, i.e. why providing the product without charge should not be considered part of the normal cost of conducting a clinical trial [21 CFR 312.7 (d)(1)].

ii) Treatment Protocol or Treatment IND

A sponsor or investigator may charge for an investigational drug or biologic for a treatment use under a treatment protocol or treatment IND, as outlined in 21 CFR 312.34 and 312.35, provided: (1) there is adequate enrollment in the ongoing clinical investigations under the authorization IND; (2) charging does not constitute commercial marketing of a new drug for which a marketing application has not been approved; (3) the drug or biologic is not being commercially promoted or advertised; and (4) the sponsor is actively pursuing marketing approval with due diligence. FDA must be notified in writing prior to commencing any such charges. Authorization for charging goes into effect automatically 30 days after receipt of the information by FDA, unless FDA notifies the sponsor to the contrary [21 CFR 312.7 (d)(2)].

There is no specific regulatory requirement that the Investigators' Brochure be submitted to the IRB. There are regulatory requirements for submission of information, which normally is included in the Investigator's Brochure. It is common that the Investigators Brochure may be part of the investigational plan that the IRB reviews when reviewing medical device studies.

Great Lakes College of Clinical Medicine
Institutional Review Board

RECRUITING STUDY SUBJECTS

FDA requires that an Institutional Review Board (IRB) review and have authority to approve, require modifications in, or disapprove all research activities covered by the IRB regulations [21 CFR 56.109(a)]. An IRB is required to ensure that appropriate safeguards exist to protect the rights and welfare of research subjects [21 CFR 56.107(a) and 56.111]. In fulfilling these responsibilities, an IRB is expected to review all the research documents and activities that bear directly on the rights and welfare of the subjects of proposed research. The protocol, the consent document, and, for studies conducted under the Investigational New Drug (IND) regulations, the investigator's brochure are examples of documents that the IRB should review. **The IRB should also review the methods that investigators propose to use to recruit subjects.**

Direct advertising for research subjects, i.e., advertising that is intended to be seen or heard by prospective subjects, is not in and of itself an objectionable recruitment practice. Direct recruiting advertisements are seen as part of the informed consent and subject selection processes. [21 CFR 50.20, 50.25, 56.111(a)(3) and 812.20(b)(11)]. **IRB review is necessary to ensure that the information is not misleading to subjects.** This is especially critical when a study may involve subjects who are likely to be vulnerable to undue influence.

Web Site Advertising: All information on web sites are considered advertising and must be approved by the IRB.

When direct advertising is to be used, **the IRB should review the information contained in the advertisement and the mode of its communication**, to determine that the procedure for recruiting subjects is **not coercive** and **does not state or imply a certainly of favorable outcome** or other benefits beyond what is outlined in the consent document and the protocol certainty of favorable outcome. **The IRB should review the final copy of printed advertisements** to evaluate the relative size of type used and other visual effects. When advertisements are to be **taped for broadcast**, the IRB should review the **final audio/video tape**. The IRB may review and approve the wording of the advertisement prior to taping to preclude re-taping because of inappropriate content. The review of a taped message prepared from IRB approved text **may be accomplished through expedited procedures.**

No claims should be made, either explicitly or implicitly, that the drug, biologic or device **is safe or effective** for the purposes under investigation. or that the test article is known to be equivalent or superior to any other drug, biologic or device. Such representation would

not only be misleading to subjects but would also be a violation of the Agency's regulations concerning the promotion of investigational drugs [21 CFR 312.7(a)] and of investigational devices [21 CFR 812.7(d).]

Advertising for recruitment into investigational drug, biologic or device studies **should not use terms such as "new treatment," "new medication" or "new drug"** without explaining that the test article is investigational. A phrase such as "receive new treatments" implies that all study subjects will be receiving newly marketed products of proven worth.

Advertisements **should not promise "free medical treatment,"** when the intent is only to say subjects will not be charged for taking part in the investigation. IRBs should consider if the promise of treatment without charge is coercive to financially constrained subjects. **Advertisements may state that subjects will be paid, but should not emphasize the payment or the amount to be paid.**

If a clinical investigator decides to begin advertising for subjects after the study has received IRB approval, the advertising may be **considered as an amendment to the ongoing study**. When such advertisements are easily compared to the consent, the IRB may choose to review and approve the advertisement using expedited procedures. When the comparison is not obvious or other complicating issues are involved, the advertisement should be reviewed at a convened meeting.

Generally, FDA believes that **any advertisement to recruit subjects should be limited to the information the prospective subjects need to determine their eligibility and interest**. When appropriately worded, the following items may be included in advertisements. It should be noted, however, that FDA **does not require inclusion of the listed items**.

1. the name and address of the clinical investigator and/or research facility;
2. the condition under study and/or the purpose of the research;
3. in summary form, the criteria that will be used to determine eligibility for the study;
4. a brief list of participation benefits, if any (e.g., a no-cost health examination);
5. the time or other commitment required of the subjects; and
6. the location of research and the person or office to contact for further information.

RULES

INSTITUTIONAL REVIEW BOARD

Great Lakes College of Clinical Medicine

GLCCM IRB is located in the secretary's office-Dr. Chappell, Bluffton, Ohio

GLCCM office is located in Chicago, IL.

1. The Investigator **must** be an active member of GLCCM and attend at least one GLCCM meeting per year. An **application form is enclosed**. For more information contact GLCCM, Jack Hank, Executive Director, Great Lakes College of Clinical Medicine - 1407-B North Wells Street - Chicago, IL 60610. The telephone number is 800-286-6013, and the fax number is (312) 266-3685.
2. Write the project following written IRB guidelines and fill out the questionnaire and return.
3. Provide the IRB with an updated Curriculum Vitae, and copy of Medical License.
4. In order to be considered for review at the next meeting, (7:00 a.m. September 4, 2000 Pittsburgh, PA) Betsey Angus (secretary to L. Terry Chappell, M.D.) must receive your project at least six weeks (Aug. 4th) in advance of the meeting.

Please contact either Betsey or the Executive Director of GLCCM for more information about when and where the meetings are to be held. The **investigator is REQUIRED** to attend the IRB meeting in which your project will be discussed to answer any questions the members have.

5. **FEES:** When you first submit your project and abstract (4 copies), an initial submission fee is required (450.00). An initial review of your project will be done by at least two IRB members. They may make suggestions or ask for clarifications on your project. You will be contacted about any needed revisions prior to the meeting. Your revised project (along with 20 copies of the abstract and 4 complete copies) will then need to be sent to Betsey at least two weeks prior to the meeting (Sept. 1st). At this time a processing fee(750.00) is required. If you have more than one project you wish reviewed, and you submit them at the same time there are no additional fees required. An expedited review of minimal risk study will be approved by Dr. Chappell or a designated member.

Project fees: \$ 450.00 submission fee (Aug.4)

\$ 750.00 processing fee(Sept 1)

TOTAL \$ 1200.00 Please make check for IRB fees payable to the GLCCM IRB.

6. It is recommended that first time submitters purchase the **videotape**, which includes written guidelines, the **purchase price is \$25.00**. This was prepared for GLCCM by Dr. Virginia Ktsanes of Tulane University. To order contact Betsey Angus (address under number 9 below).
7. Within two weeks after the meeting we will notify you on letterhead stationery of the IRB decision. If approved you will receive **an expiration date, and a degree of risk for a device**.
8. When approved, you are required to submit a **continuing review in writing two weeks prior to the expiration date**. Any study exceeding one year without approval will be terminated.
9. Any correspondence or questions should be directed to Betsey Angus - Celebration of Health Center - 122 Thurman Street - P.O. Box 248 - Bluffton, OH 45817. Phone (419) 358-4627 extension 120. The fax number is (419) 358-1855. Please mark all faxed materials to the attention of Betsey.
10. Please submit the proper forms, which are supplied at the appropriate time: adverse reactions/death form, request to make revisions to protocol or informed consent.

CHECKLIST FOR SUBMITTING A PROJECT:

IF NOT A CURRENT GLCCM MEMBER SEND IN APPLICATION (enclosed) to GLCCM in *Chicago*

SEND TO THE GLCCM IRB IN OHIO: QUESTIONNAIRE. CURRICULM VITAE, COPY OF MEDICAL LICENSE. PROCESSING FEE \$ 450.00 and 4 COPIES OF THE STUDY WITH ABSTRACT.