Standard Operating Procedures

Clinical Research Unit
Division of Gastroenterology, Hepatology and Nutrition
University of Louisville

Version 3.0
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STANDARD OPERATONAL PROCEDURES (SOP)

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Table of Contents

1. INTRODUCTION

1.1 Research Mission Statement

1.1.1 The Clinical Research Unit of the University of Louisville, Department of Medicine, Division of Gastroenterology, Hepatology and Nutrition is an organization of professionals dedicated to promoting digestive health through the pursuit of quality clinical research.

1.1.2 Goals for our Research Mission are the following:

(a) To conduct high-quality clinical research according to the International Conference on Harmonization (ICH) Guidelines for Good Clinical Practice (GCP) and be in compliance with local, state and federal regulations

(b) To promote and strengthen professional development of staff

(c) To become recognized as an outstanding site for industry-sponsored clinical research

(d) To advocate the value of research as a means to enrich and promote digestive health

(e) To provide personnel and infrastructure support for clinical research within the division

1.2 Purposes of the SOP

1.2.1 This SOP outlines the responsibilities of all personnel involved in conducting clinical research in the Division of Gastroenterology, Hepatology and Nutrition at the University of Louisville.

1.2.2 Goals of our SOP are the following:

(a) To provide guidance for planning, conducting, and managing clinical research

(b) To ensure compliance to the guidelines of ICH, GCP, and University of Louisville Human Subjects Protection Program Office (HSPPO).

(c) To allow appropriately qualified personnel, once trained, to perform the function and define accountability

(d) To establish procedures and standards to be followed for designated operations

2. ABBREVIATIONS

Abbreviations used in this SOP are listed below in alphabetical order

CFR	Code of Federal Regulation
CITI	Collaborative Institutional Training Initiative
CRF	Clinical Trial Forms
CRU	Clinical Research Unit
GCP	Good Clinical Practice
HIPAA	Health Insurance Portability and Accountability Act
HSPPO	Human Subjects Protection Program Office
IBC	Institutional Biosafety Committee
ICF	Informed Consent Form
ICH	International Conference on Harmonization
IRB	Institutional Review Board
MIRA	Multi-Institutional Research Application
MTA	Material Transfer Agreement
OIC	Office of Industry Contracts
ORI	Office of Research Integrity
PHI	Protected Health Information
PI	Principal Investigator
SAE	Severe Adverse Events
SOP	Standard Operating Procedure
Sub-I	Sub-Investigator

3. CLINICAL RESEARCH UNIT (CRU)

3.1 Role of the CRU

3.1.1 The role of CRU is to assist and provide resources for the Division to conduct clinical research.

3.1.2 A meeting of all CRU research staff will be held monthly for at least 9 meetings per year Attendance of CRU research staff is mandatory, unless previously excused. Research staff includes the principal investigator, sub-investigator, research coordinators, clinical trial coordinators (data managers), and Unit Business Managers. All doctors in the division are invited. Agenda and meeting minutes will be recorded and filed. The meeting minutes will also be sent to the group via e-mail.

3.1.3 An update on clinical research projects will be presented to the Division at least bimonthly during the division meeting.

3.1.4 The following data will be gathered, updated and maintained by the CRU:

(a) A study list, updated monthly, that consists of active clinical research studies within the Division, currently-enrolling studies, pending studies and studies closed to enrollment.

3.1.5 A Research Finance meeting (or informational e-mail correspondence) with the principal investigator or sub-investigator and the finance administrators will be held at least monthly for NIH studies and every 4 months for sponsored trials.

3.1.6 The Division's Clinical Research web site will be maintained with the following information:

(a) A selected list of active clinical studies. This list will contain basic study information which does not require IRB approval. This list will be updated. Each posted study should have a link to the corresponding posting on ClinicalTrial.gov (if available).

3.2 Role of the Research Team

3.2.1 Investigator Guide to Human Research for the University of Louisville and affiliated research institutions can be found on the web (link).

3.2.2 Role of Principal Investigator

(a) Understand protocol and agree to conduct study in accordance of investigational plan, good clinical practice, and applicable local, state, and federal regulations.

(b) Provide administrative oversight for the sub-investigators, coordinators, regulatory and budgeting staff participating in this study.

(c) Follow the study procedures as outlined in the protocol and to follow sponsor and IRB requirements.

(d) Manage the medical care of subjects by assuring that a qualified physician (PI or Subinvestigator) is responsible for all trial related medical decisions.

(e) Responsible for the conduct and compliance of the study.

3.2.3 Role of the Sub-Investigator

(a) Perform critical trial-related procedures and/or make important trial-related decisions. The Sub-Investigator is designated and supervised by the Principal Investigator.

3.2.4 Role of the Research Nurse/Coordinator

(a) Manage all aspects of conducting clinical trials.

(b) Have an in-depth knowledge of protocol requirements and good clinical practices as set forth by federal regulations.

(c) Act as liaison between the investigators, primary care providers, the Institutional Review Board (IRB) and the sponsor.

(d) Along with the Investigator, the research nurse/coordinator will screen, enroll and follow study subjects, ensuring protocol compliance and close monitoring while the subjects are on study.

(e) Be responsible for all data and source documentation, adverse experience reporting and maintenance of complete regulatory files.

(f) Ensure that any concerns regarding the conduct of the trial by any team member be brought to the attention of the PI.

4. GENERAL ADMINISTRATION OF SOP

4.1 Preparation and Revision

4.1.1 The SOP will be reviewed and revised if necessary on a yearly basis by the Director and the research staff of the CRU

4.2 Applicable Studies

4.2.1 The SOP is applicable to all research studies involving human subjects within the Division of Gastroenterology, Hepatology and Nutrition. Clinical research studies will be classified into the following:

(a) Industry-Sponsored Study: protocol written by the study sponsor

(b) Investigator-Initiated Study: protocol written by the investigators. Investigator-Initiated Study may be an academic study without sponsorship or may be sponsored by industry, society organization, or government agency.

4.3 Applicable Research Personnel

4.3.1 This SOP is applicable to all personnel who are involved in clinical research within the Division of Gastroenterology, Hepatology and Nutrition.

(a) Principal Investigator (PI): PI must be a faculty member of the University of Louisville.

(b) Sub-investigator (Sub-I): Sub-I may be a faculty member, fellow, resident, intern, physician assistant, or a nurse practitioner.

(c) Research personnel: Research personnel may be a student, research coordinator, research administrator, or any support personal.

4.3.2 All applicable research personnel will be required to review the SOPs

4.4 Distribution

4.4.1 The most current version of the SOP will be posted on the division website . The SOPs are to be reviewed and acknowledged by all clinical research staff on an annual basis.

5. TRAINING REQUIREMENTS

5.1 Training Requirements for New Personnel

The training requirements listed below must be completed before any personnel can participate on a research study. If the new employee completed training within the last year, the training will not need to be repeated.

5.1.1 Human Subjects Protection Program Office (HSPPO)

(a) Instructions for Individuals Who Have Never Completed the CITI Basic Course

5.1.2 Health Insurance Portability and Accountability Act (HIPAA)

(a) HIPAA Privacy & Research Training using the "Blackboard @ U of L" is required for all research personnel.

5.1.3 Bloodborne Pathogen Training

(a) Bloodborne Pathogen Training is required for the principal investigator and any research personnel involved in handling biohazard materials such as blood, body fluid, tissue, cell culture involving human or animals.
(b) IATA training (if applicable)
(c) Basic Biosafety training

5.1.4 Significant Financial Interest

(a) An Attestation and Disclosure form (ADF) form must be completed by all research personnel.

5.1.5 Division of Gastroenterology, Hepatology and Nutrition SOP

(a) Review division SOP

5.2 Training Requirements for Renewal

The trainings listed below must be retaken every 12 months. Failure to renew the required HSPPO training is considered non-compliance by HSPPO. Personnel cannot participate on any study without completion or renewal of the required training.

5.2.1 Human Subjects Protection Program Office (HSPPO)

(a) For individuals with a current CITI username and password, who have completed the CITI Basic Course in the past, see web link

(b) For individuals who have completed the CITI Basic Course and need to re-register, see web link

5.2.2 Bloodborne Pathogen Training

(a) Bloodborne Pathogen Training is required for the Principal Investigator and any research personnel involved in handling biohazard material, such as blood, body fluid, tissue, cell culture involving human or animals.

5.2.3 Significant Financial Interest

(a) An Attestation and Disclosure form (ADF) form must be completed by all research personnel.

6. DEVELOPMENT OF STUDY PROTOCOL

6.1 Industry-Sponsored Study

Study protocol will be supplied by the sponsor.

6.2 Investigator-Initiated Study

Study protocol should contain the following components:

6.2.1 Title page with the following:

(a) Title of study

(b) Principal investigator, sub-investigators, coordinators and key personnel

(c) Contact information

(d) Sponsor name (if applicable)

6.2.2 Introduction

6.2.3 Hypothesis

6.2.4 Primary and secondary objectives: What is the primary and secondary research aims?

6.2.5 Primary and secondary endpoints: What are the primary and secondary measurable endpoints to support primary and secondary objectives stated above?

6.2.6 Study design: Define the study design. For example: prospective vs. retrospective, chart review, cohort study, randomized, placebo-controlled, etc.

6.2.7 Study methods

(a) List the detailed procedures step by step on how the study is to be conducted. The study procedure section should contain the following details (where applicable):

- Methods of identifying potential study subjects
- Inclusion and exclusion criteria
- Details on the information to be collected for a chart review
- Details on each study visit and procedures to be done
- Randomization schedule and method
- Study-related testing to be conducted or collected, randomization scheme, etc.

(b) A study algorithm and a study time-table may be included.

6.2.8 Data analysis

(a) Define the specific and measurable primary and secondary study endpoints

(b) List how the data will be analyzed based on primary and secondary endpoints

6.2.9 Statistical analysis

(a) List the statistical methods on the data analysis.

(b) Provide power analysis, if applicable, in estimating the number of subjects required to achieve the primary objective(s).

6.2.10 Potential risk-versus-benefit analysis

(a) State the potential risk versus potential benefit of participating in this study. Justify the risk in terms of the potential scientific yield and the anticipated benefit to the subjects.

6.2.11 References

6.2.12 Appendices

- Tables for inclusion and exclusion criteria
- Informed consent and HIPAA authorization form (see "Study Submission")
- Data collection forms

7. STUDY SUBMISSION

7.1 Human Study Protection Program Office

All studies must be submitted to HSPPO for approval before any study-related tasks or procedures can be conducted. Continuing annual review of these studies will be performed as defined by the IRB. This review will occur before the expiration date of the study. Any amendments or modifications to the protocol will be approved by the IRB before being instituted.

7.1.1 Some minimal-risk research studies may be exempt from full IRB review. The authority to determine exempt status rests with the IRB and not with the PI. Federal regulation 45 CFR 46.116(d), may allow research to be exempted from IRB review if the research falls into any one of the following categories:

(a) Research conducted in established or commonly-accepted educational settings, involving normal educational practices.

(b) Research involving the use of educational tests (cognitive, diagnostic, aptitude, achievement), survey procedures, interview procedures or observation of public behavior, unless:

- Information obtained is recorded in such a manner that human subjects can be identified, directly or through identifiers linked to the subjects;

AND

- Any disclosure of the human subjects' responses outside the research could reasonably place the subjects at risk of criminal or civil liability or be damaging to the subjects' financial standing, employability, or reputation. Surveys on sensitive or personal topics are not exempt from IRB review.

(c) Research involving the collection or study of existing data, documents, records, pathological specimens, or diagnostic specimens, if these sources are publicly available or if the information is recorded by the investigator in such a manner that subjects cannot be identified, directly or through identifiers linked to the subjects.

Submission is performed via the internet using the HSPPO electronic submission program. Guidelines for submission are on the HSPPO website.

7.1.2 Studies being performed at the Louisville Veteran Administration Medical Center (VAMC) require a separate IRB process.

7.2 Multi-Institutional Research Application (MIRA)

7.2.1 A MIRA form is required to perform research at any of the hospital facilities owned by University of Louisville, Jewish Hospital, and Norton Hospital. Please see appendix for submission information for JHSMH.

7.2.2 Be certain to fill out the Billing Compliance Table completely, listing all research-related tests, procedures, services and supplies that will be used in the research study, including time points for distribution of medications, where necessary. When

listing labs that will be collected, be certain to list specific labs that are required. Do not list "safety labs".

7.2.3 An internal billing process for charges generated from research related procedures is in place at each institution (i.e. U of L Healthcare assigns a T Account number),

7.3 Institutional Biohazard Committee (IBC)

7.3.1 All research studies involving biohazard materials, such as blood, body fluid, tissue, cell culture involving human or animals, are required to submit documentation of IBC approval.

7.4 Office of Industry Contracts

7.4.1 Submission to University of Louisville Office of Industry Contracts (OIC) is required for all studies that will utilize any University of Louisville facilities or services. It is recommended that all NDA agreements should be signed by the University OIC office and not the PI. The TRIA form must be completed first and emailed to the OIC along with the following documents:

(a) Contact information of the sponsor

(b) Study protocol
(c) Clinical trial agreement with the sponsor

(d) Study budget: A preliminary draft can be submitted with the TRIA, but the final budget should be submitted after negotiations with the sponsor to obtain approval.

(e) Informed consent form (ICF): Can be a draft version of the ICF

7.5 Others Requirements

7.5.1 Additional requirements for an Industry-Sponsored Study

Sponsor submission of all sponsor-required documents such as: 1572, Financial Disclosure Forms, CVs, medical licenses, etc. for all investigators participating in the research study.

7.5.2 ClinicalTrials.gov

Registration with the FDA ClinicalTrials.gov is required if the clinical research meets the criteria listed below (in accordance with the International Committee of Medical Journal Editors (ICMJE) initiative): "Any research project that prospectively assigns human subjects to intervention and comparison groups to study the cause-and-effect relationship between a medical intervention and a health outcome. Medical intervention is defined as any intervention used to modify a health outcome. This definition includes drugs, surgical procedures, devices, behavioral treatments, process-of-care changes, and the like. A trial has to have at least one prospectively assigned concurrent control or comparison group in order to trigger the requirement for registration."

(a) Industry-Sponsored Study: Sponsor will register with ClinicalTrials.gov
(b) Investigator-Initiated Study: Investigator is responsible for registering with ClinicalTrials.gov

7.5.3 Materials Transfer Agreements

Materials Transfer Agreements (MTAs) are necessary any time a researcher at the University wishes to send or receive materials of a confidential or proprietary nature; material that is infectious, hazardous or subject to special regulations; material for which the provider is concerned about potential liability; or material for which the provider wishes to obtain rights to the results of the research in which the material or information is to be used (link).

8. PREPARING BUDGET

8.1 Industry-Sponsored Study

Proposed budget from the sponsor will be reviewed. The budget will be adjusted accordingly for our Division based on many factors, including but not exclusively the following:

8.1.1 Non-Refundable Start-up Fees

(a) Study administrative and preparation fee: cost of preparing the study for approval, time expended by administrative personnel during preparation of submission to IRB and OIC, budget negotiation, preparing study binders, sponsor site visit, obtaining approval from the hospital to set up T-accounts, attending the investigator meeting, monitoring visit after enrollment begins, etc.

(b) HSPPO new study submission fee

(c) HSPPO renewal fee (depends on the length of the study)

(d) Research Integrity Office application fee (University of Louisville Hospital)

8.1.2 Study Procedural Itemized Fees (if applicable)

(a) Investigator (PI and Sub-I): Time spent to perform the following duties (where applicable)

- Physical exam
- Pre-study visit
- Review questionnaire and lab tests
- Interview subjects to discuss informed consent
- Follow protocol
- Time spent for each study visit
- Regulatory interactions

(b) Coordinator: Time spent to perform the following duties (where applicable)

- Screen potential subjects by phone, reviewing charts, emails, etc.
- Copy, build source documents, binders/folders
- Recruitment of subjects
- Review and obtain medical records, medication list of subjects
- Obtain screening data
- Schedule requiring appointments, tests
- Obtain informed consent
- Set up time for subject's physical with physician
- Perform each study visit including filling out source documents, vital signs, any labs required, obtaining questionnaires, teaching regarding the subject requirements and any other needs related to the study.
- Collect and review lab, test results
- Complete case report forms
- Review adverse events, collect records, submit to sponsor and IRB as required.
- Attend conference calls, meetings regarding study
- Coordinate and be available for monitoring visits
- Complete data clarification forms as needed and collect any other information requested per the sponsor
- Coordinate regulatory tasks with the regulatory staff

(c) Diagnostic testing: Itemized fee for each diagnostic test

(d) Subject incentive (prorated to each study visit and procedure)

(e) Screen failure fee per subject

(f) Research medication storage fee

(g) Pharmacy fees, including any/all of the following:

- Pharmacy one-time set-up fee
- Pharmacy dispensing fee (dependent on the number of dose(s) being dispensed)
- Research one-time drug Storage ,dispensation and destruction fees

8.1.3 Overhead Research Cost for University of Louisville: Overhead cost is applicable to all items except advertisement and fees for HSPPO and ORI submission.

8.1.4 Other fees (where applicable)

(a) Study advertisement

(b) Submission of each protocol amendment for approval

(c) Fee for each UPIRTSO report submitted to IRB and the sponsor, as required

8.2 Investigator-Initiated Study

If applicable, budget may be similar to Industry-Sponsored Studies listed above. Budget should be reviewed by the CRU finance administrators.

9. STUDY REGULATORY BINDER

9.1 Industry-Sponsored Study

Study Binder will be provided by the sponsor. They may include the following components:

9.1.1 Compliance Check List for the study

9.1.2 Protocol

9.1.3 Investigator's Brochure: Usually provided by the sponsor

9.1.4 Form FDA 1572

9.1.5 IRB (correspondence/approvals)

9.1.6 Financial Disclosure Forms

9.1.7 CV/ Medical License

9.1.8 Lab Information

9.1.9 Sponsor Correspondence

9.1.10 Internal and External Adverse Events

9.1.11 Training Log

9.1.12 Site Visit Log

9.1.13 Responsibility Log

9.1.14 Subject Screening/Enrollment Log (if applicable)

9.1.15 Hospital approval letters
9.1.16 Contract/award letter

9.2 Investigator-Initiated Study

A Study Binder must be maintained for each study and should contain components similar to the Industry-Sponsored Study, above, where applicable. Inclusion and exclusion criteria should be documented in the Clinical Trial Forms (CRF).

10. PROCEDURES FOR STUDY PREPARATION

10.1 Purpose

The initiation of a clinical study marks the beginning of subject accrual. Prior to enrolling the first subject, all regulatory and institutional requirements must be met and preparations for initiating protocol procedures must be complete. In addition, the research staff and others involved in recruitment, selection of subjects and enrollment must receive appropriate training. A suggested Compliance Check List for Study Preparation is provided in Part A of Attachment E.

10.2 Responsibility of Principal Investigator

In order to be the Principal Investigator (PI) of a clinical research study, the PI must agree to the following:

10.2.1 Understand the protocol and agree to conduct the study in accordance of the investigational plan and Good Clinical Practice, and in accordance with applicable local, state, and federal regulations.

10.2.2 Provide administrative oversight for the sub-investigators, coordinators, regulatory and budgeting staff participating in this study.

10.2.3 Follow the study procedures as outlined in the protocol and to follow sponsor and IRB requirements.

10.2.4 Sign and date all required documents and review for accuracy and oversights.

10.2.5 Implement all future study amendments in a timely fashion.

10.3 Training and Personnel on Study

10.3.1 If required, the PI and coordinator will attend the sponsor's investigator meeting and complete all required training for a study. If unable to attend the meeting, a Sub-I and/or the backup coordinator will attend in their places. If the Sub-I attends the investigator meeting, the PI will need to become familiar with the meeting contents and complete all required training for the study.

10.3.2 All personnel listed on the site delegation log require training on the protocol, and the trainer and trainee should be documented.

10.3.3 All investigators doing study-related procedures are listed on the 1572.

10.3.4 Personnel are trained in electronic data transfer and other technology for the study, as required.

10.3.5 Sponsor site initiation visit is performed.

10.4 Review of Protocol

10.4.1 Protocol procedures, inclusion/exclusion criteria, amendments, screening tools, and all aspects of the study are reviewed before beginning enrollment. Make sure the protocol procedures with all of the applicable amendment changes are being utilized.

10.4.2 The informed consent (ICF) will contain the most recent amendment changes.

10.4.3 Source documents will reflect the most recent protocol and amendments.

10.4.4 The Compliance Check List (Attachment E) can be used as a guide for preparation, screening, enrollment and compliance review.

10.5 Drug Accountability, Storage, Dispensing, Return and Destruction (if applicable)

10.5.1 Study drugs will be stored in a secure manner in a secured area in accordance with the sponsor, drug manufacturer (i.e. refrigerate, temperature controlled, etc.), IRB requirements and Federal requirements.

10.5.2 Transportation of study drug from the research study office or the hospital pharmacy to the location where the subject is being seen will be handled as follows:

(a) If the study drug requires refrigeration, the labeled study drug will be transported in an insulated cooler with a frozen ice pack to ensure a stable temperature during the transportation.

(b) If the study drug is to be maintained and transported at room temperature, the labeled drug will be hand carried by the coordinator in its original box/container.

(c) (c) If the site acts as the pharmacy the study drug will be used as packaged, but the date dispensed and date returned as well as the subject number will be listed on the product container.

10.5.3 Temperature logs are updated as required by the sponsor.

10.5.4 The research nurse/coordinator will ensure that each time study medication is dispensed and/ or returned, the drug accountability form is completed as per protocol.

10.5.5 Investigational medication may be destroyed on site with written permission from the sponsor or investigator under certain conditions. "Written permission" may be via a monitor log notation or letter or e-mail.

10.5.6 Conditions under which medication may be destroyed on site include:

(a) Relatively small volume of drug

(b) Facility has appropriate destruction method / container for drug (e.g., chemo)

(c) Drug is a non-hazardous substance

(d) All investigational medication (oral or injection) shall be disposed of in a puncture proof sharps container appropriate for the type of medication

(e) Destruction log shall be completed and verified by two qualified individuals:
- Pharmacist and technician
- Sponsor monitor and technician or pharmacist
- Two study coordinators or study coordinator and a technician or pharmacist

(f) Destruction log shall contain the following information:
- Medication name and strength / strength per volume
- Quantity
- Date
- Lot #, batch #, or other identification number(s) from packing slip
- Expiration date (if specified) per labeling information or per sponsor memo
- Initials of two qualified individuals
- Study information (title, protocol number, investigator, IRB#, site #)

In the event the drug cannot be destroyed on site, arrangements should be made with the study sponsor for the drug to be sent back and destroyed at their preferred location.

10.6 Blood and Specimen Transportation (if applicable)

10.6.1 The transportation of specimens (i.e. blood, urine, stool, etc.) from the location where the research subject was seen and the specimen was collected to the area where it will be packaged for shipment will be handled as follows:

(a) Per OSHA guidelines, universal precautions shall be observed to prevent contact with blood or other potentially infectious materials. All procedures involving blood or other potentially infectious materials shall be performed in such a manner as to minimize splashing, spraying, spattering, and generation of droplets of these substances.

(b) Specimens of blood or other potentially infectious materials shall be placed in a container which prevents leakage during collection, handling, processing, storage, transport, or shipping.

(c) The container for storage, transport, or shipping shall be labeled with an orange or orange-red biohazard emblem and closed prior to being stored, transported, or shipped. When a facility utilizes Universal Precautions in the handling of all specimens, the labeling/color-coding of specimens is not necessary provided containers are recognizable as containing specimens. This exemption only applies while such specimens/containers remain within the facility. Labeling or color-coding in accordance with Occupational Safety and Health Administration Regulation when such specimens/containers leave the facility.

10.7 Destruction of Unused or Expired Lab Kits

10.7.1 Unused or expired lab kits will be destroyed as mandated by the sponsor. If the sponsor does not have specific guidelines for destruction of lab kits, the kits will be

donated to Supplies over Seas (Hand in Hand Ministries 502-736-6362) or the coordinator will destroy the kits by placing glass/sharps in a sharps container and discarding the remaining items.

11. PROCEDURES FOR SCREENING AND ENROLLMENT

11.1 Screening subjects

11.1.1 Referral source is documented for follow-up care in the research chart or the clinic chart/electronic records.

11.1.2 Relevant present and past medical and social histories are reviewed. Subject's current medications are reviewed. If appropriate, subjects will sign a release of information form so past medical records can be reviewed and compared for accuracy.

11.1.3 Screening labs and test results are reviewed by the investigator.

11.1.4 All source documents that are generated by our unit will be reviewed by staff to ensure accuracy and reflect the study protocol with all amendment changes.

11.2 Study Entry Criteria

11.2.1 Subject must meet all inclusion criteria and none of the exclusion criteria, including results from screening labs and tests to assure the subject's safety.

11.2.2 Waiver from the sponsor is required for enrollment outside of study criteria, and the waiver must be submitted to IRB.

11.2.3 In some cases, it may be up to PI's discretion regarding subject enrolling. PI's clinical judgment and communication with sponsor (if applicable) will be carefully documented if subject is to be enrolled.

11.3 Obtaining Informed Consent and Research Authorization

Detailed informed consent procedures are provided in Attachment A. A summary of the informed consent process follows:

11.3.1 Subject will be given the most current, approved, IRB-stamped informed consent (ICF) and Research Authorization to read.

11.3.2 PI and/or coordinator will review the ICF and Research Authorization with the subject to answer any questions the subject may have and help ensure subject has full understanding of his/her involvement prior to signing.

11.3.3 Subject will sign the most current, approved, IRB-stamped ICF and Research Authorization before any study-related procedures are done.

11.3.4 Subject and coordinator will complete the appropriate signature/date lines on the ICF. If an Investigator on the study did not obtain the ICF, PI must sign the ICF within 2 weeks.

11.3.5 Subject will be given a copy of the signed ICF and Research Authorization.

11.3.6 The process of obtaining ICF and RA will be documented.

11.3.7 If a subject requires a legal representative to sign the ICF, this process has to be approved by the IRB and sponsor during the initial approval process.

11.4 Protocol Procedures

11.4.1 Protocol procedures, sponsor's documentation requirements are followed and case report forms are filled out per the sponsor's guidelines.

11.4.2 Documentation is complete to reflect protocol compliance.

11.4.3 All investigators performing study-related procedures are listed on the 1572.

11.4.4 The study-related procedures will be performed in accordance with the Site Signature /Delegation log that is mandatory for each study.

12. PROCEDURES FOR COMPLIANCE REVIEW

12.1 Protocol Review after Enrollment

12.1.1 After randomization and enrolling the first subject, it is recommended that the PI and coordinator review inclusion/exclusion criteria, source documents, procedures, data entry, and all aspects of protocol to ensure compliance. A suggested guide for Study Maintenance is provided in Part C of the Study Compliance Check List (attachment E).

12.2 Deviation to protocol procedure for an Industry-Sponsored Study has to be pre-approved by the sponsor. The IRB will be notified if protocol deviation may affect subject safety. If an unintentional (and not pre-approved) deviation is found, it will be reported to the IRB **Sponsor Review (if applicable)**

12.2.1 After enrollment of first or second subjects, the sponsor will schedule a monitoring visit to ensure protocol compliance.

12.2.2 PI and/or coordinator will work with sponsor to ensure accuracy of electronic data collection and in agreement of source documents.

12.2.3 Coordinator should ask for preliminary verbal feedback during the site visit, to avoid delay in correcting any problems.

12.2.4 Sponsors routinely provide a follow up letter of their monitoring visit. Any outstanding items should be addressed ASAP. If a follow up letter is not automatically generated by the sponsor, the coordinator should ask for written feedback of the site visit ASAP and file the response in the regulatory binder.

12.3 Response to Monitor Visit (if applicable)

12.3.1 Applicable personnel will incorporate the sponsor-initiated changes and fulfill all sponsor requests.

12.3.2 queries will be completed ASAP. If any queries need additional information prior to being answered, the coordinator will discuss with the PI. If the query remains unresolved, the monitor for the study should be consulted.

12.4 Periodic Protocol Review

12.4.1 PI and the coordinator will hold periodic reviews to discuss and ensure study compliance.

12.4.2 All required documents are signed and dated on the day of document review. Back-dating is prohibited.

12.4.3 Subject will be re-consented per IRB requirement or sponsor request.

12.4.4 Site delegation log should be updated to add or remove study personnel.

12.4.5 PI and coordinator should ensure accuracy of the electronic data set and in agreement of source documents.

12.5 Voluntary Suspension

12.5.1 If any unanticipated problems occur, the Unanticipated Problem Involving Risks to Subjects and Others (UPIRTSO) form will be completed and reported to the IRB within 72 hours to 5 business days, depending on study requirements. The IRB has the authority to suspend the research if a UPIRTSO occurs. These incidents are reviewed on a case by case basis.

12.6 Protocol Deviations

12.6.1 Protocol deviations, if any, will be reported to the sponsor and the IRB Major deviations within 5 business days of the event, minor deviations can be reported with the annual continuing review.

12.6.2 Any deviations identified by this check list will be corrected and the sponsor and/or IRB will be notified, if needed, within 10 business days of the event.

12.7 Study Termination Visit

This visit should be scheduled as soon as possible after the last patient has completed all scheduled visits associated with the study. A mutually convenient date and time should be arranged with the study monitor, PI and coordinator.

12.7.1 The PI and the coordinator will:

(a) Ensure all regulatory documentation and case report forms (not previously monitored) are complete and available for review.

(b) Ensure all data queries have been resolved

(c) Ensure the appropriate patient medical records will be available for review (if applicable).

(d) Inform the study pharmacist (if applicable) of the study termination visit date so study drug can be inventoried and drug accountability records can be assessed for completeness. If a research pharmacist was not utilized, the coordinator will ensure the study drug is returned to the sponsor or, if approved by the sponsor, destroyed on site (see 10.5.5 for drug destruction policy).

12.7.2 Study Termination Visit Check List (Attachment D) can be used as a guide for this visit.

13. PROCEDURES FOR STUDY FINANCE

It is the policy of Uof L to accurately capture and invoice the correct payer for services provided during the research study. For performing the study at the University of Louisville Hospital, each study, with or without a budget, requires a T-account number from the Office of Research Integrity (ORI). Study-related procedures are to be billed under the T-account according to protocol requirements. The T-account covers study related procedures as designated in the Billing Compliance Table.

13.1 Procedures for Coordinator

13.1.1 Complete the Research Subject/Healthy Volunteer Admission Form (applicable only for University of Louisville Hospital). This form is provided by the ORI after the MIRA is approved. This form is used for all study specific procedures performed at University Hospital and should be sent along with the order for EACH procedure. It should not be used for standard of care procedures.
13.1.2 Kentucky One Health-Fill out the Research Encounter Notification Form. This form is provided by JHSMH Research Center once the protocol has the approval of the research office.

14. STORAGE OF PAPER AND ELECTRONIC RESEARCH DATA

14.1 Active Research Data

14.1.1 Paper Data

(a) Storage of paper data, such as study forms, study folders, etc., will be in a secured locked area and as required per the sponsor and the IRB.

14.1.2 Electronic Data

(a) Research data containing Protected Health Information (PHI) has to be stored on computers or computer systems located in a facility owned by University of Louisville. Definition of PHI is provided in Attachment B.
(b)
Before research data containing PHI can be stored on computers or computer systems at University of Louisville Physicians Group, a Business Associate

Agreement has to be in place between University of Louisville and University of Louisville Physicians Group. If this was to occur, the privacy office needs to be notified to ensure the data is secured.

(c) Electronic data has to be secured. Data files, such as Microsoft® Excel, Access, or SPSS, will be password protected and/or on a password-protected computer in a secured area.

(d) Research data files with PHI will not be transferred electronically through emails, unless the data files are encrypted with methods approved by the University Information Security Office.

(e) University's Information Security Office (ISO) Policies and Standards caution against storing data containing PHI on personal computer devices unless, the owner is personally able to configure the device to meet the University's security standards.

(f) Encryption of data files containing PHI is required on portable devices used outside the approved facility or during transit between the University Medical Associates and the Uof L research office. Methods of encryption should be approved by the University Information Security Office.

14.2 Archive Research Data

14.2.1 Paper Data

(a) Storage of paper data, such as study forms, study folders, etc., will be in a secured locked area and as required by the sponsor and the IRB.

(b) Research documents should be kept a minimum of five years after submission or publication of the final project report for which the data were collected, whichever is longer. If retention requirements specified by a funding agency are longer, the agency requirements will apply. In addition, at the discretion of the university, some data may be retained longer for use in subsequent projects. Therefore, study record retention above the minimum time requirement and final disposition is at the discretion of the PI.

(c) If space does not allow for long-term storage of closed study documents, the documents will be sent to archive. This is located in the basement of the Ekstrom Library on Belknap Campus.archive

14.2.2 Electronic Data

(a) Same procedures apply as in Active Research Electronic Data

ATTACHMENT A **PROCEDURES FOR OBTAINING AN INFORMED CONSENT**

Department:	Clinical Research Unit Division of Gastroenterology, Hepatology and Nutrition University of Louisville
Revised Date:	March 21, 2009
Title	Informed Consent Process

INTRODUCTION: The Informed Consent process applies to all clinical trials (and clinical trial related activities, i.e. quality of life survey research, phone surveys, etc) conducted by the Clinical Research Unit, unless an informed consent is deemed unnecessary according to federal and local regulations (ex: waste specimen trials, retrospective analysis studies). The FDA, the ICH, GCP and the University of Louisville HSPPO require that subjects (18 years and older) voluntarily confirm their willingness to participate in a particular trial. Confirmation of the Informed Consent process is documented by means of approved, written, signed, and dated Informed Consents. Phone consents are not acceptable.

PURPOSE: The Informed Consent ensures that each subject is provided with complete information regarding the investigational trial. Responsibility for ensuring that the process is carried out properly lies with the Principal Investigator, but it may be delegated to another member of the research staff.

PREREQUISITIONS TO THE INFORMED CONSENT: The Informed Consent process may not begin until all other trial-related documents/contracts (required by the sponsor, U of L, or other entity) are given signed approval and placed in the study Regulatory Binder. Research staff responsible for obtaining the ICF must be listed as such on the Site Responsibility Log in the study binder.

INFORMED CONSENT APPROVAL: Before the Informed Consent process is carried out with a potential subject, the ICF must be approved by the HSPPO, stamped and dated. The original ICF and HSPPO approval letter are to be maintained in the study Regulatory Binder. The most recent approved ICF must be used when enrolling patients in a study.

PROCEDURE: Prior to signing the informed consent, the following issues will be discussed with the subject. This information regarding the trial must be reviewed with the subject, making sure he/she understands that the study involves research.

- Explain who is sponsoring the clinical trial.
- Explain who is conducting the clinical trial.
- Give the purpose of the study, trial treatment and probability for random assignment to each treatment.
- Explain in simple language the procedures to be followed, including invasive procedures.
- Explain the responsibilities of the subject.
- List the expected risks or inconvenience to the subject
- List the expected benefits, making clear if there is no intended clinical benefit to the subject.
- List the alternative treatment that may be available to the subject.
- List the treatment(s) available in the event of a study-related injury.
- Let the subject know that the trial is voluntary and that he/she may refuse to participate or can withdraw at any time.
- Explain methods used to ensure confidentiality.
- Provide the location of patient visits.
- Explain the circumstances and/or reasons the PI may terminate the subject's participation in the trial.

- After explaining the above information, allow the subject time to ask questions. When all questions have been answered to the satisfaction of the subject, the signature page must be completed with dated signatures of the subject, the Principal Investigator, and the person administering the informed consent.
- The written informed consent form and any other written information provided to subjects should be revised whenever important new information becomes available that may be relevant to the subject. Any revised written informed consent form and written information should be approved by the IRB before use. The subject or the subject's legally-acceptable 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. This communication should be documented in the chart.

SIGNED INFORMED CONSENT RECORDS:

- The original, signed ICF is filed with the source documentation.
- A signed copy is given to the subject or guardian.
- A signed copy is placed in a shadow chart, or clinic chart.

DOCUMENTATION: To confirm that all the requirements of the Informed Consent have been met prior to the subject signing, a note must be placed/written in the subject's medical record/source document stating this.

ATTACHMENT B DEFINITION OF PROTECTED HEALTH INFORMATION

Department:	Clinical Research Unit Division of Gastroenterology, Hepatology and Nutrition University of Louisville
Revised Date:	March 21, 2009
Title	Definition of Protected Health Information

The following identifiers are considered Protected Health Information. These identifiers of the individual or of relatives, employers, or household members of the individual must be removed for information to be considered de-identified under the safe harbor:

- Names, including initials
- All geographic subdivisions smaller than a State, including street address, city, county, precinct, zip code, and their equivalent geocodes, except for the initial three digits of a zip code if, according to the current publicly available data from the Bureau of the Census:
- All elements of dates (except year) for dates directly related to an individual, including birth date, admission date, discharge date, date of death; and all ages over 89 and all elements of dates (including year) indicative of such age, except that such ages and elements may be aggregated into a single category of age 90 or older
- Telephone numbers
- Fax numbers
- Electronic mail addresses
- Social security numbers
- Medical record numbers
- Health plan beneficiary numbers
- Account numbers
- Certificate/license numbers
- Vehicle identifiers and serial numbers, including license plate numbers
- Device identifiers/serial numbers
- Web Universal Resource Locators (URLs)
- Internet Protocol (IP) address numbers
- Biometric identifiers, including finger and voice prints
- Full face photographic images and any comparable images
- Any other unique identifying number, characteristic, or code

ATTACHMENT C PROTOCOL START UP CHECK LIST

Documents required

- o Signed Form FDA 1572
- o CV's/licenses of Investigator listed on Form FDA 1572
- o Financial disclosure forms
- o Signed protocol title page
- o Investigator's Brochure
- o IRB approval letter
- o IRB approved consent form
- o Laboratory certification and range of normal values
- o MIRA
- o Budget
- o Contract
- o U of L Hospital approval letter/T account number (if applicable)

Protocol preparation

- o Review regulatory files for completeness
- o Patient logs (screening, enrollment and follow-up)
- o Protocol summary sheets (purpose, inclusion/exclusion criteria)
- o Study drug administration sheets (adverse effects, administration)
- o Create source documents (if not provided by sponsor)
- o Delegation of responsibilities log
- o Study specific training (EDC, IVRS, etc)

Ancillary staff in-service

- o Pharmacy _____(Contact name)
- o Nursing _____(Contact name)
- o Physicians _____(Contact name)
- o Laboratory _____(Contact name)

Inventory

- o Study drug supplies
- o Laboratory supplies (central and/or hospital)
- o Case report forms

ATTACHMENT D **STUDY TERMINATION VISIT CHECK LIST**

Sponsor Protocol Number _____

HSC#_____

DATE	DONE BY	
_____	_____	All data queries resolved or designated unresolvable
_____	_____	Regulatory files reviewed for completeness
_____	_____	Study drug returned to sponsor/CRO or destroyed
_____	_____	Any instances of emergency unblinding appropriately documented
_____	_____	IRB notified that study has terminated
_____	_____	Report submitted to IRB
_____	_____	Sponsor copied on IRB correspondence
_____	_____	All study supplies no longer needed are returned or destroyed
_____	_____	Final payment received
_____	_____	Any equipment on loan returned
_____	_____	Study files prepared for long term storage

ATTACHMENT E STUDY COMPLIANCE CHECK LIST

STUDY TITLE: _____

A. Study Preparation	Coordinator		PI	
	Signature	Date	Signature	Date
1. Responsibility of PI: I agree to assume the following responsibilities: a. Understanding of protocol and agreeing to conduct study in accordance of investigational plan, good clinical practice, applicable local, state, and federal regulations. b. Provide administrative oversight for the sub-investigators, coordinators, regulatory and budgeting staff participating in this study. c. Follow the study procedures as outlined in the protocol and to follow sponsor and IRB requirements. d. Sign and date all required documents after reviewing for accuracy and oversights. e. Implement all future study amendments in a timely fashion.				
2. Training and Personnel: a. PI and coordinator to attend the investigator meeting and complete all required training. If the Sub-I attends the investigator meeting, PI still has to be familiar with what was discussed and complete all required training. b. Everyone listed on the site delegation log needs training on the protocol, and the trainer and trainee should be documented. c. All investigators doing study-related procedures are listed on the 1572. d. Personnel are trained in electronic data transfer/other technology for study. e. Sponsor site initiation visit is performed.				
3. Protocol Review: a. Protocol procedures, inclusion/exclusion criteria, amendments, screening tools, and all aspects of study are reviewed. b. Informed consent (ICF) will contained most recent amendment changes. c. Source documents reflect the most recent protocol and amendments.				
4. Drug Storage: a. Study drugs are stored in a secure manner (locked cabinet) in accordance with sponsor and IRB requirements. b. If study drug has to be refrigerated, it will be transported from office to subject in an insulated cooler with a frozen ice pack to ensure a stable temperature. If study drug can be at room temperature, it will be hand carried in its original box/container. c. Temperature logs are updated as required per the IRB or sponsor.				
B. Screening-Enrollment (To be done after Screening 1st subject)	**Coordinator**		**PI**	
	Signature	**Date**	**Signature**	**Date**
1. Screening: a. Referral source is reviewed for follow-up care. b. Relevant present and past medical/social history is reviewed prior to enrolling subject. Subject's				

	current medications are reviewed. c. Screening labs and test results are reviewed by the investigator. d. All source documents should be reviewed to ensure accuracy and reflect protocol and amendment changes. Sponsor may review the source documents if necessary.				
2.	Study Entry Criteria: a. Subject must meet all inclusion criteria and no exclusion criteria, including screening lab and test results, before enrollment to assure subject's safety. b. Waiver from the sponsor is required for enrollment outside of study criteria, and the waiver must be submitted to IRB. c. In some cases, it may be up to PI's discretion regarding enrollment. PI's clinical judgment and sponsor communication should be documented.				
3.	Obtaining Informed Consent and Research Authorization: a. Subject will be given most recently approved IRB-stamped informed consent (ICF) and Research Authorization (RA) to review, including most recent amendment changes. b. PI and/or coordinator will review ICF and RA with the subject. c. Subject will be given the opportunity to ask questions and receive answers. d. Subject will sign most recent, approved, ICF and RA before any study-related procedures are done. e. Subject and coordinator will sign the appropriate signature/date lines. If PI did not obtain the ICF, PI has to sign ICF within 2 weeks. f. Subject will be given a copy of the signed ICF and RA. g. The process of obtaining ICF and RA should be documented. h. Any subject requiring a legal representative to sign the ICF has to be pre-approved by IRB and sponsor.				
4.	Protocol Procedures: a. All protocol procedures, sponsor's documentation requirements, and case report forms are followed. d. Documentation is complete to reflect protocol compliance. e. All investigators doing study-related procedures are listed on 1572. f. Investigator who performs the study-related procedure will sign source document and will interpret results.				

C. Compliance Review (To be done after Enrolling 1st subject)	Coordinator		PI	
	Signature	Date	Signature	Date
1. Protocol Review after Enrollment: a. After initial enrollment of subjects, PI and coordinator should review the inclusion/exclusion criteria, source documents, procedures, data entry, and all aspects of protocol of this subject to ensure compliance. b. Deviation to protocol procedure for an Industry-Sponsored Study has to be pre-approved by the sponsor. The IRB will be notified if protocol deviation may affect subject safety.				
2. Sponsor Review: a. After enrollment of study subjects, coordinator should request the sponsor to come for a site monitor visit to ensure protocol compliance. b. PI and/or coordinator will work with sponsor to ensure accuracy of electronic data collection and in agreement of source documents. c. Coordinator should ask for preliminary verbal feedback during the site visit, to avoid delaying correction of any problems. d. Coordinator should ask for written feedback of site visit ASAP and file the response in the regulatory binder.				
3. Response to Monitor Visit: a. PI and coordinator will incorporate sponsor-initiated changes and fulfill all sponsor requests. b. Outstanding queries should be completed.				
4. Periodic Protocol Review: a. PI and coordinator should hold periodic reviews to discuss and ensure study compliance. b. Required documents are reviewed and signed. Back-dating is not allowed. c. Subject will be reconsented if there is a change of study risk in the Informed Consent or the sponsor request to reconsent the subjects. d. Update site delegation log for personnel (add or remove). e. PI should ensure accuracy of the electronic data set and in agreement of source documents.				
5. Voluntary Suspension: a. Voluntary suspension, if any, will be reported to the IRB within 72 hours to 5 business days, depending on requirement, using an Unanticipated Problem Involving Risks to Subjects and Others (UPIRTSO) form.				

6. Deviations Identified by this Check List: a. Protocol deviations, if any, will be reported to the sponsor and the IRB within 10 business days. b. Any deviations identified by this check list will be corrected and the sponsor and/or IRB will be notified if needed within 10 business days.				

Research Encounter Notification Form

This form must be submitted to the JHSMH Research Center **PRIOR** to any study visit where research procedures are being performed. Please email completed forms to: ResearchOffice@KentuckyOneHealth.org. **If a NEW subject, please include a copy of the subject's signed Informed Consent form with the RNF submission, or once all signatures are obtained.**

Protocol: **Research Center#:** **PI:**

Study Title:

****

Date of Consent: **Date of Service:**

Subject Name:

DOB: **Visit Name:** (Week/Cycle/Day):

JHSMH Record #: **Subject #:**

Physician Providing Services:

JHSMH Facility Location: ☐ Downtown ☐ Sts. Mary & Elizabeth ☐ Other _____

****

- ☐ **Gastric Emptying Test**
- ☐ **Upper GI Test**
- ☐ **Glucose Monitor Fingerstick**
- ☐ **ANA**
- ☐ **CBC w/ Diff**
- ☐ **Comprehensive Metabolic**
- ☐ **CRP**
- ☐ **Glycated HGB/Hg A1c**
- ☐ **Lipid Risk**
- ☐ **SED Rate**
- ☐ **TSH**
- ☐ **Vitamin D, 1-25**
- ☐ **Vitamin B-12**

Comments:

_____

Clinical Coordinator: _____ **Date:** _____