Study Management
SM – 302.00

STANDARD OPERATING PROCEDURE FOR
Interactions with the Institutional Review Board (IRB)

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(Signature and Date)

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I. INTRODUCTION AND PURPOSE

The primary responsibility of the Institutional Review Board (IRB) is to protect the rights and welfare of research subjects. Federal regulations require that the IRB ensure that certain criteria for approval of research are met prior to approving a study. The Investigator must provide the IRB with the information necessary to permit an informed decision on whether to approve, disapprove, or to require modifications prior to approval.

By signing the Form FDA 1572, the Investigator ensures that the IRB reviewing the research complies with the regulations. Additionally, the Investigator agrees to inform the IRB of any changes to the protocol and any materials used to recruit subjects, as well as any additional risks to subjects associated with the investigational article.

This SOP describes how Georgia CORE communicates with the central IRB on behalf of the Georgia CORE network sites who use a central IRB throughout the research process in order to ensure compliance with the regulations and to protect the safety and well-being of study subjects. Georgia CORE network sites that use a local IRB are responsible for following their standard operating procedures for interacting with the IRB. Georgia CORE will monitor the IRB interactions of the sites using local IRBs

2. SCOPE

This SOP applies to Georgia CORE's interactions with the central IRB responsible for research subject to investigational new drug (IND) regulations for drugs and biologics or those eligible for investigational new drug (IND) exemption during all phases of development carried out at the Georgia CORE network sites which use a central IRB. Georgia CORE will monitor the IRB interactions of the sites using local IRB and central IRBs. The central IRB refers to the non-federal IRBs used for industry clinical trials or investigator initiated trials in which Georgia CORE acts as a Site Management Organization (SMO). For NCI sponsored trials, the Central IRB (CIRB) refers to the federal IRB in which government sponsored trials are initiated.

3. APPLICABLE REGULATIONS AND GUIDELINES

21 CFR 312.32	IND safety reports
21 CFR 312.53	Selecting investigators and monitors
21 CFR 312.54	Emergency research
21 CFR 312.66	Assurance of IRB review
21 CFR 50	Protection of Human Subjects
21 CFR 56	Institutional Review Boards
45 CFR 46	Protection of Human Subjects
FDA Information	Frequently Asked Questions, Continuing Review After

Sheets, October 1998	Study Approval
October 2009	Guidance for Industry Investigator Responsibilities Protecting the Rights, Safety, and Welfare of Study Subjects
May 1997	International Conference on Harmonization; Good Clinical Practice: Consolidated Guideline

4. REFERENCES TO OTHER APPLICABLE SOPs

GA-102	Sponsor Responsibility and Delegation of Responsibility
SS-201	Assessing Protocol Feasibility
SS-204	Site Initiation Visit
SM-301	Communication
SM-303	Documentation and Records Retention
SM-304	Routine Monitoring Visits
SM-305	Closeout Visits
SM-306	Adverse Event Reporting

5. ATTACHMENTS

A. Checklist for IRB submission
B. Checklist for IRB submission of changes in research
C. Template letter for reporting IND safety reports to the IRB
D. Periodic report to the IRB

6. RESPONSIBILITY

This SOP applies to Georgia CORE staff members and others involved in communicating with the central IRB to ensure appropriate management of all study activity. This includes the following:

- President and CEO
- Georgia CORE staff and consultants

7. DEFINITIONS

The following definitions from the Code of Federal Regulations and the International Conference on Harmonization, Good Clinical Practice: Consolidated Guideline apply to this SOP.

Adverse event: Any untoward medical occurrence in a study subject administered a pharmaceutical product; it does not necessarily have to have a causal relationship with this treatment.

Approval in relation to Institutional Review Boards (IRBs): The affirmative decision of the IRB that the clinical trial has been reviewed and may be conducted at the institution site within the

constraints set forth by the IRB, the institution, good clinical practice (GCP), and the applicable regulatory requirements.

Informed Consent: A process by which a subject voluntarily confirms his or her willingness to participate in a particular trial, after having been informed of all aspects of the trial that are relevant to the subject's decision to participate. Informed consent is documented by means of a written, signed, and dated informed consent form.

Institutional Review Board (IRB): An independent body constituted of medical, scientific, and nonscientific members, whose responsibility it is to ensure the protection of the rights, safety, and well-being of human subjects involved in a trial by, among other things, reviewing, approving, and providing continuing review of trials, of protocols and amendments, and of the methods and material to be used in obtaining and documenting informed consent of the trial subjects.

Protocol: A document that describes the objective(s), design, methodology, statistical considerations, and organization of a trial. The protocol usually also gives the background and rationale for the trial, but these could be provided in other protocol referenced documents. Throughout the ICH GCP Guideline, the term protocol refers to protocol and protocol amendments.

Protocol Amendment: A written description of a change(s) to or formal clarification of a protocol.

Serious Adverse Event (SAE) or Serious Adverse Drug Reaction (Serious ADR): Any untoward medical occurrence that at any dose results in death, is life-threatening, requires inpatient hospitalization or prolongation of existing hospitalization, results in persistent or significant disability/incapacity, or is a congenital anomaly/birth defect or requires medical or surgical interventions to prevent any of the above outcomes.

Well-being of the trial subjects: The physical and mental integrity of the subjects participating in a clinical trial.

8. PROCESS OVERVIEW

A. Documenting IRB compliance
B. Communicating with the IRB at study start-up
C. Communicating with the IRB while the study is ongoing
D. Communicating with the IRB when the study is over

9. PROCEDURES

A. Documenting IRB compliance

Responsible Staff:	Procedure:
• Research Staff/Consultant	Ensure that the IRB is duly constituted and compliant with federal and state regulation which can be completed by checking that the

	IRB has been accredited by the Association for the Accreditation of Human Subject Research Protection Programs (AAHRPP) and/or obtaining a letter of compliance from the IRB. Request a copy of the IRB's guidelines for sponsors. Request a copy of the IRB membership list and the general assurance number (if available).

B. Communicating with the IRB at study start-up

• Research Staff/ Consultant	Using the IRB procedure manual (if available) and the appropriate form, complete the initial IRB submission. Include all attachments as directed, e.g., the protocol, investigator's brochure, informed consent form and advertisements (Attachment A, Checklist for IRB Submission). Submit the package for the next scheduled meeting.
• Research Staff/ Consultant	Obtain documentation of IRB approval for the protocol, informed consent, and other supporting material prior to study start. Copy Sponsor/CRO, if applicable, and network sites on correspondence. • Through direct contact with the central IRB for those sites using the central IRB • Through the network sites using local IRBs Maintain all documents in the appropriate study files.

C. Communicating with the IRB while the study is ongoing

• Research Staff/Consultant	Notify the IRB of any changes to the protocol and/or informed consent and of new information on the investigational product. (Attachment B, Checklist for IRB submission of changes in research) Obtain documentation of IRB approval of amendments and revisions to study-related documents, such as advertisements, prior to implementation except to eliminate apparent hazard to subject safety. Copy sponsor/CRO, if applicable, and site(s) on correspondence.
	Notify the IRB promptly of all serious or alarming events occurring during the approval period for the ongoing study according to the FDA and central IRB guidelines. (Note: Some IRBs do not require a report if changes to the study or informed consent are not proposed.) The report should include: • Adverse event description/treatment/outcome (including relevant dates)

	• Pertinent subject history • Why the event is considered "unanticipated" • Why the event is considered "a problem involving risks to human subjects or others", i.e., how does this event suggest that subjects or others are at greater risk of harm than was previously known? • What are the proposed changes to the consent form and/or protocol in order to protect the rights, welfare, and safety of the research subjects? If none are proposed, provide the rationale why changes are not needed, if the IRB requires a report when changes are not proposed. Submit to the Investigator all IND Safety Reports and MedWatch Reports received from the sponsor who will review the reports as described in SOP SM-306 Adverse Event Reporting, Attachment D, Algorithm for Review and Distribution of IND Safety and MedWatch Reports. Use Attachment C, Reporting IND Safety Reports to the IRB or the IRB's form when sending reports to the IRB. Report all AEs to the IRB as part of the periodic or annual reporting requirements. Submit periodic report form for renewal of protocol as requested (Attachment D, Periodic Report to the IRB can be used if the IRB does not provide a standard form to be completed). Maintain all documents in the appropriate study files.
• Research Staff/ Consultant	Obtain from each network site that is using a local IRB copies of all communications between the sites and respective IRB.

D. Communicating with the IRB when the study is over

• Research Staff/Consultant	Complete the study closure report as required by the IRB with a copy to the sponsor, if applicable, and to the site. The report should include: • Date study closed • Total subjects who signed the consent form • If there were any unanticipated problems involving risks to subjects or others at the site that were not previously reported to the central IRB • Any other pertinent comments about the study, including outcome results of the study, if known. Provide the network sites that used a local IRB with a copy of the central IRB report so the sites can submit a study closure report to their local IRB.

10. History of Changes

Version Number	Section Number	Modification	Approval Date
302.00	All	Original Version	
302.00	All	No change was necessary	09 March 2012
302.00	All	No change was necessary	01 July 2014
302.00	2	Clarification of CIRB versus NCI CIRB	17 March 2017

Attachment A

CHECKLIST FOR IRB SUBMISSION

- Central IRB initial review submission form*
- Study summary
- Research protocol*
- Investigator's brochure (if applicable)
- Proposed informed consent form*
- Proposed patient information (instructions, diaries, etc.)
- Up-to-date curriculum vitae of principal investigator
- Up-to-date curriculum vitae of sub investigator(s) or other staff listed on Form FDA 1572
- Copy of current medical license with expiration date for principal investigator and sub investigators (if applicable)
- Other supporting material (e.g., sample of any proposed advertising, questionnaires, subject diaries)*
- Copy of Form FDA 1572 (if required)
- Documentation from sponsor or FDA verifying the IND (Investigational New Drug) number if one is required for the research. In an IND is not required, provide the reason why in writing.

*****Denotes documents typically required for approvable submission. (Approvable submission can be requested by the sponsor/CRO during the planning stages of a multi-center study. If the IRB finds the research acceptable, the submitter is issued a letter documenting the Board's determination, a redlined template consent form indicating the IRB's changes and appropriate documentation of the review of the other submitted subject materials. Certificate of Approval (COA) will not be issued, however, until the remaining appropriate investigator documents are received and reviewed by the IRB.)

Attachment B

CHECKLIST FOR IRB SUBMISSION OF CHANGES IN RESEARCH

Protocol Changes (Amendments, Administrative Changes, etc:

- Central IRB Change in Research and Subject Recruitment Submission Form
- A rationale for the change(s)
- Summary of changes for the new amendment to the protocol (or if previously submitted and approved, submit the amendment title page and signature page only)

Planned Protocol Deviation:

- Provide the details of the planned deviation.

Consent Form Modifications:

- Central IRB Change in Research and Subject Recruitment Submission Form
- Copy of the IRB approved consent form with changes marked and the rationale for the changes or submit a document detailing the requested changes. Note any changes to addresses (include an updated 1572, if applicable) or phone numbers.

Change of Principal Investigator:

- Written confirmation that the change is acceptable and has been approved by the sponsor, a letter from the original investigator relinquishing responsibility for the study, and a letter from the new investigator accepting responsibility for the study.
- Submit an IRB initial review submission form or the Investigator Submission Form for Multi-Center Protocols, license and CV for the new investigator, a modified 1572 (when applicable), and a request to modify the existing consent form to reflect the new investigator's name and contact information (when applicable).

Addresses and Phone Number Changes:

- An updated 1572 (if applicable) and a copy of the IRB's additional site form for each new or updated location

Change or Addition of Laboratory
Recruitment Materials:

- Copy of the IRB Change in Research and Subject Recruitment (Ads) Submission form
- If any of the recruitment materials have been previously approved by the IRB, attach a copy of the previously-approved item(s), even if they are from a different protocol
- Indicate if any submitted scripts will be used as Public Service Announcements, and whether they will be announcer-read (verbatim) or recorded
- If submitted materials reference a web site, attach a hard copy of the recruitment sections of the web site for IRB review
- If submitting written or verbal screening materials for screening subjects prior to enrollment in the research (such as telephone scripts, written or web-based questionnaires or pre-screening forms), describe the screening plan.
- A script for all audio and video materials

The above is not an exhaustive list of the changes in research that may need to be reported to the IRB. The IRB guideline should be used as a reference and/or the IRB should be contacted to obtain instructions.

Attachment C

TEMPLATE LETTER FOR REPORTING IND SAFETY REPORTS TO THE IRB

<Date>

<Name>
Chairperson
Institutional Review Board
<Hospital>
<City, State, Zip code>

RE: <Protocol Title>

Dear Chairperson:

Enclosed please find an IND Safety Report #_____, submitted to us by <sponsor> for the above referenced study. The federal regulations require that sponsors notify investigators of immediately reportable adverse events that have occurred worldwide in connection with the investigational drug. I am, in turn, notifying you of this event.

In my opinion, information contained in this IND Safety Report (does/does not) require a change to our approved informed consent form. (*Enclose revised consent form when a change is being requested)*

If you have any questions, please call.

Sincerely,

<Signature>

Copy: Study file

Attachment D

PERIODIC REPORT TO THE IRB

Protocol Title: _____ Date of Report: ____/____/____

❑ Interim Report

❑ Renew approval for the study

❑ The study has ended

- ❑ Completed Date ___/___/___
- ❑ Terminated Date ___/___/___
- ❑ Not Started
- ❑ Inactive

If the study is inactive, terminated or never started, please state the reason.

1. Study Summary

   a. Results obtained to date, if any.

   b. Have there been any significant new findings? ❑ Yes ❑ No

   c. Has there been an interim analysis? ❑ Yes ❑ No

   d. Have there been any changes to the approved protocol that have not been reviewed by the IRB? ❑ Yes ❑ No

2. Site Summary

   a. Number of subjects enrolled at this site _____

   b. Number of subjects who withdrew or discontinued participation for a reason other than an adverse event _____

c. Number of subjects who discontinued participation in the study because of an adverse event _____

d. Number of subjects who experienced a serious adverse event _____

e. Summarize serious adverse events that occurred in the study.

f. Explain why any subjects terminated their participation prematurely.

3. Have all serious adverse events, whether related to the study article or not, been reported to the IRB? (Please include reports of serious adverse events not reported, including sponsor-generated reports.) ❑ Yes ❑ No

4. Have all subjects signed the approved informed consent form? If not, please explain. ❑ Yes ❑ No

5. Have all subjects received a copy of the informed consent form? If not, please explain. ❑ Yes ❑ No

I certify that the information on this report and any attachments accompanying this report are correct.

Submitted by:_____on _____/_____/_____