SOP 12: Audits

I. Scope:
Audit of research studies performed at Centro Comprensivo de Cáncer UPR and for studies with approved IRB Reciprocity.

II. Overview/Procedure Description:

1. **Policy**: This Policy & Procedure applies to all on-going and future human participant research projects conducted by CCC-UPR, Hospital faculty, staff, or students or by anyone conducting a research activity supported by CCC-UPR Hospital or where CCC-UPR is considered to be engaged in the research. IRB oversees that the clinical studies conducted at the Consortium are given the highest priority in warranting the human rights of the research study subjects (welfare, beneficence, security, privacy, and confidentiality).

2. **Purpose**:
   a. To make sure that investigators follow all the necessary steps to warrant the safety of subjects participating in research studies.
   b. To warrant that investigation are performed according to approved protocols by the Institutional Review Board (IRB).

3. **Area(s) of Responsibility**: IRB, Investigators, and their staff.

4. **Terms and Definitions:**

   All parties to whom this policy applies (e.g., faculty, staff, IRB members) should consult the IRB Glossary.

5. **Regulations Applicable:**

   5.1. The Belmont Report

   5.2. 45 CFR 46.109(b), (c), & (e): IRB Review of Research, stating that (1) "[a]n IRB shall require that information given to subjects as part of informed consent is in accordance with §46.116. The IRB may require that information, in addition to that specifically mentioned in §46.116, be given to the subjects when in the IRB's judgment the information would meaningfully add to the protection of the rights and welfare of subjects;" (2) "[a]n IRB shall require documentation of informed consent or may waive

documentation in accordance with §46.117;" and (3) "[a]n IRB shall have the authority to observe or have a third party observe the consent process and the research."

5.3. 45 CFR 46.111(a)(4), (a)(5), & (b): Criteria for IRB approval of research, mandating that (1) informed consent "will be sought from each prospective subject or the subject's legally authorized representative, in accordance with, and to the extent required by §46.116," and "appropriately documented, in accordance with, and to the extent required by §46.117;" and

(2) "[w]hen some or all of the subjects are likely to be vulnerable to coercion or undue influence, such as children, prisoners, pregnant women, mentally disabled persons, or economically or educationally disadvantaged persons, additional safeguards have been included in the study to protect the rights and welfare of these subjects."

5.4. 45 CFR 46.116: General requirements for informed consent

5.5. 45 CFR 46.117: Documentation of informed consent

6. Procedure Details:

6.1- We will randomly select studies that received services from the IRB. The selected studies will be considered among the following categories but not limited to:

a. High risk
b. With poor follow-up or monitoring
c. Those studies for which the Program Director recommends an audit
d. Continuous or serious complaints from study participants or situations identified by the clinical personnel
e. Pilot studies
f. Protocols approved with IRB reciprocity

6.2- The Principal Investigator (PI) will receive a notification that their IRB-approved research study will be audited. This letter will contain the date of the audit and the necessary information about the process; the PI can receive this notification either by electronic mail or standard letter at least four weeks in advance of the audit date.

6.3 -This notification will include, although not necessarily limited to, the records and documents that will be audited. Within the elements that will be audited are the following:

g. Subjects' consent form and consent process note
h. Subjects' eligibility criteria
i. Adverse events:
    1. Occurrence of adverse events and serious adverse events
    2. Adverse events reporting to the following entities: Sponsor, IRB, Food and Drug Administration, among others

7. **Documents that can be revised in an audit** may include, but are not necessarily limited to the following:

    a. Regulatory binder (Approvals, Protocol, Amendments, Safety reports, submissions, correspondence, etc.)
    b. Protocol with IRB Reciprocity: the audit on the regulatory binder will be done only on the PI site (Reviewing IRB)
    c. Participant records
    d. Protocol with IRB Reciprocity: the audit on participant records will be done depending on where the documents are located. If all the participants' records are located on the PI site, a percent of the records will be randomly selected for review. If the participants records are located on both sites PI and Co-PI, a percent of the records will be randomly chosen to review on each site.
    e. Signed subject informed consent document
    f. Protocol with IRB Reciprocity: the audit on informed consent document (ICD) will be done depending on where the ICD is located. If all ICD are located on the PI site, a percent will be randomly selected for review. If the ICD are located on both sites PI and Co-PI (according to the recruitment process), a percent of the records will be randomly selected for review on each site.

    *** After the audit is finished a debriefing of the findings will be discussed***

8. **Classification of audit findings**: Audit findings will be documented in a written report. Results will be assigned to one of the following categories:

    Category 1 – No deviation from regulations or no findings were identified.

    Category 2 – Minor deviation(s) or minor findings that may require corrective action. The following findings are considered category 2: Incomplete or expired IRB documentation (although solved before the audit is finalized). Expired Training Certificates in Research

    Category 3 – Major deviation(s) from regulations or serious findings that may affect the study and participants' safety (need corrective action). The following findings are considered category 3 if they do not represent a study deviation pattern:

        1. Failure in obtaining participants' informed consent(s) before beginning with the study procedures or amendment.
        2. Participants sign an incorrect version of the consent.
        3. Failure in obtaining IRB approval for the initial protocol and amendments informed consents.
        4. Failure to obtain annual IRB approvals.
        5. Failure to report to the IRB and regulatory agencies serious adverse events.
        6. Files not available for audit.
        7. Inadequate credentials of the study personnel.

Category 4 – Serious deviation(s) from regulations or serious findings that may affect the study and safety of the participants (there is a need for immediate corrective actions).
The following findings are considered category 4:

1. All the findings considered category 3 that represent a pattern throughout the evaluated files.
2. Suspecting falsification or fabrication of study data.
3. Protocol violations that represent risk to the safety and welfare of participants.

9. Time frame for audit report and response:

Category 1 & 2: No deviation or Minor deviation

The IRB will make a written report within 10 working days after the audit is finalized. The report will include the findings and/or recommendations.

Category 3: Major deviation

1. The IRB will discuss the findings with the Investigator and staff at the end of the audit. This discussion with the Investigator and staff will be documented in the written report.
2. The IRB will do a written report in a period of not greater than ten (10) working days after the audit is finalized. This preliminary report will include audit findings and/or recommendations.
3. The IRB will request from the Investigator a written action plan.
4. The Investigator will have a period of not greater than 15 working days to answer the report; once the 15 days period has elapsed without any response, the following actions will take place:
5. The IRB Chair will discuss with the principal Investigator the unresolved situation and, between all the involved parties, will establish the action(s) to follow. This action may include, but is not necessarily limited to, temporarily stopping the study until the Investigator presents a written corrective plan.

Category 4: Serious deviation

6. The IRB will discuss the findings with the Investigator and staff at the end of the audit. The discussion with the Investigator and staff will be documented in the written report.
7. The IRB will do a written report in a term not greater than ten (10) working days after the audit is finalized. This preliminary report will include findings and recommendations.
8. The RKS will request from the Investigator a written action plan.
9. The Investigator will have a period not greater than 15 working days to answer the report; once the 15 days period has elapsed without any response, the following actions will take place:

10. The IRB Chair will discuss with the Program Director the unresolved situation and between all the involved parts will establish the action(s) to follow. This action may include, but is not necessarily limited to:
11. Temporarily stopping the study until the Investigator presents a written corrective plan.
12. Report the situation to the federal and regulatory agencies (e.g., Food and Drug Administration, National Institutes of Health, etc.)
13. Permanently stopping the study (if findings are of such magnitude that the participants' security is compromised, and the integrity of the data is adversely impacted).

10. Confidentiality: Audits' reports will be kept confidential in a locked archive to which only the IRB chair and coordinator will have access. During the audits, IRB will do everything possible to maintain the confidentiality of the subjects' identity as well as the information that belongs to the study sponsors.