DHR HEALTH INSTITUTE FOR RESEARCH & DEVELOPMENT
POLICY AND PROCEDURE

SUBJECT: Project Management	Policy #: CRP-1022
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DEPARTMENT: DHR Health Institute for Research & Development	EFFECTIVE: 02/19
APPROVED BY: Sohail Rao, MD, D.PHIL, President & Chief Executive Officer (Institutional Official, OHRP, DHHS)	REVIEWED/REVISED: 02/19, 02/20, 11/20, 01/21, 04/21, 05/21

Purpose:
Federal regulations require documentation of all study-related activities. The regulatory files and subject records, which are periodically reviewed by the sponsor and upon request by the FDA, serve as the site's record of compliance with good clinical practice (GCP).

This policy describes the steps for fulfilling all regulatory, and clinical requirements for collecting, filing and storing study-related documents and records.
Implementation of GCP is essential in ensuring compliance and communication with regulatory authorities from all study personnel.

Applies To:
This policy applies to the following potential research investigator; Physician staff employed by RMF and its affiliates; staff employed by DHR Health and its affiliates; faculty, fellows, residents, students of academic institutions with a current affiliation agreement with DHR Health Institute for Research & Development; staff and physicians of non-academic institutions with a current affiliation agreement with DHR Health Institute for Research & Development; Physicians with privileges to practice medicine in DHR Health, Physicians and staff employed by Starr County Memorial Hospital and its affiliates; faculty, fellows, residents, students of academic institutions with a current affiliation agreement with Starr County Memorial Hospital and its affiliates; staff and physicians of non-academic institutions with a current affiliation agreement with Starr County Memorial Hospital and its affiliates; Physicians with privileges to practice medicine in Starr County Memorial Hospital and its affiliates.

Definition:
A. Good Regulatory Practice is defined as the appropriate and effective management of regulatory documentation maintaining compliance and communication with regulatory authorities.

Policy:
This policy applies to the activities involved in maintaining the regulatory and subject records for all clinical studies conducted at DHR Health Institute for Research & Development subject to applicable local, state, and federal regulations for drugs, devices, and biologics during all phases of development.

Procedure:
Study Start Up:
Protocol Feasibility Assessment
A. Protocol Coverage Analysis
- Sponsor will send an initial budget offer, sometimes with an itemized breakdown of the protocol.
- The Research Coordinator will review the protocol and identify procedures to be itemized based on previous and current standard charge codes.
- The designated staff in DHR Health Institute for Research & Development will review, edit and approve the draft before submitting the offer to the sponsor.

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B. Budget & Contract Negotiation
- Sponsor will send a contract and an initial offer, sometimes with a breakdown of protocol procedures.
- The Research Coordinator will ensure the breakdown has all required procedures accounted for, identify which procedures are paid by whom (patient or Institution), ensure that the estimated time involvement for the project is covered by the budget and draft the first counter offer.
- Designated staff in DHR Health Institute for Research & Development will review, edit and approve first counter offer of the budget.
- Once the contract has been reviewed, edited, and approved by designated staff in DHR Health Institute for Research & Development will send both the contract and the budget to the sponsor.
- Sponsor will counter offer, request edits, or approve the budget & contract.
- This process will be repeated until a reasonable budget and contract have been approved by both parties. If not reasonable, then the protocol is not financially feasible for our institution.

Routine Monitoring Visits:

A. Scheduling the monitoring visit
- The sponsor Monitor will contact the PI and lead coordinator to schedule a Visit.
- The lead coordinator will work with the sponsor monitor and PI to schedule a mutually convenient date and time to conduct the monitoring visit.
- Upon confirmation from the sponsor monitor, the lead clinical research coordinator will book the conference room for the allotted time requested by the sponsor monitor.
- Have Wi-Fi passwords on hand if LAN connection is not available.

B. Preparing for the monitoring visit
- Ensure that all regulatory documentation and case report forms are complete and available for sponsor monitor review. Start at least a week in advance. Use the *Regulatory Binder Review Tool* and the *Subject Binder Review* Tool to ensure all aspects of the investigator file and subject binder is reviewed by the lead coordinator.
- Ensure all data queries received to date have been resolved to the extent possible. Queries should typically be resolved within the week.
- Ensure that Subject materials, lab supplies, and Investigational Product (IP) have been inventoried (if they have arrived) and expired materials have been disposed of.
- The appropriate patient medical records should be available for review at the time of the monitoring visit if applicable. All copied medical records or faxed medical records must be certified by delegated staff.
- Ensure all informed consent forms are signed and dated, and that the original is in the subject's file.

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- All CRFs and source documents must be complete, and signed as required.
- Up to date IRB approvals and copies must be appropriately filed in the Investigator site file/Regulatory binder.
- File correspondence accordingly in the regulatory binder. For example, sponsor newsletters and Safety reports.

C. Managing the monitoring visit
- The monitor and delegated staff must sign the monitoring visit log.
- Delegated site staff should be readily available for the sponsor monitor to answer questions and complete open action items as they arise.
- Towards the conclusion of the visit, the PI should meet with the sponsor monitor to discuss any issues or trends that arose during the visit.
- The PI will also be advised by the sponsor monitor if needed.

D. Following up after the monitoring visit
- Upon receiving the Monitoring Visit Follow up Letter, file letter accordingly in the Regulatory Binder.
- Delegated staff and/or PI should complete open items/issues as soon as possible.
- Notify Sponsor Monitor, by correspondence, on the status of items/issues as they are completed.
- File correspondence with sponsor monitor accordingly in the regulatory binder.
- All open items/issues must be resolved before the next monitoring visit.

FDA Audit/FDA Warning Letter (FDA483):

A. Inform sponsor/CRO promptly if notified by FDA of impending inspection.
- Clinical Research Coordinator must immediately inform Trial Project Manager and assigned Clinical Research Associate/Monitor of impending inspection and file correspondence in Investigator Site File.

B. Provide copies of all FDA documentation (Form FDA 483, letters) generated as a result of the inspection to Trial Sponsor.

Study Closeout Visit:

A. The PI and research coordinator must ensure that the documentation is complete, accurate, and ready for review for the monitor's termination visit.

B. The Investigator and/or appropriately delegated staff, prepares the final report for Institutional Review Board (IRB), notifying them that the study is closed. A copy of the report is sent to the Sponsor and filed in the regulatory documentation binder.

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C. The Clinical Research Coordinator reviews the regulatory documentation binder and recovers any missing documents. If documents cannot be found, the Sponsor is notified and a memorandum will be placed in the regulatory documentation binder.
D. The Clinical Research Coordinator arranges for secure storage of the CRFs, source documents, and regulatory documentation binder, and informs the Sponsor of the storage location.
E. If the trial is terminated prematurely or suspended for any reason, the investigator and research staff will promptly inform the subjects via phone call or in person. If these attempts fail, then an attempt will be made with a certified letter.
F. If the trial is terminated prematurely by the sponsor for any reason, the Investigator and research coordinator will inform the institution and IRB.
G. If the IRB terminates, suspends or places the study on enrollment hold, the PI will inform the sponsor and provide a copy of the IRB notice/determination.

Specimen Collection and Handling:
Prior to handling specimens, ensure all personnel packaging/shipping specimens have completed Dangerous Goods Training within the past 24 months.

A. Collecting the specimens
   a. Collect the appropriate specimens identified in the study protocol.
   b. In the subject's record, note the date and time of the collection as well as any other relevant information pertaining to the subject's status at the time of the collection.
   c. Label the test tubes or other containers with the subject identifier, date, time and any other information required by the study protocol.

B. Processing the specimens
   a. Process the specimens according to the processing procedures defined in the study protocol.
   b. Centrifuge samples and transfer the specimens to the appropriate transport tube(s) as required by the study protocol.
   c. Ensure all study-specific test tubes and containers are labeled appropriately as defined in the study protocol.
   d. Complete lab requisition slip
      i. One copy with the specimens being shipped
      ii. One copy for the subject's record.

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C. Preparing the specimens for shipment to the testing laboratory

a. Prepare and package the specimens according to the shipping instructions specified in the study protocol and/or laboratory procedure manual.
b. Retain a copy of the shipping receipt and file with the subject's record.

Inventory/IP Management:

A. Receipt of Inventory/IP

Immediately upon receipt, supplies must be checked against any shipment form to ensure what has been received corresponds with what has been sent. The following checks should be made:

- Ensure supplies are correctly addressed
- Ensure all packaging intact
- Ensure that the quantity, batch/serial numbers, correspond with shipment form. The person who received the supplies should sign the shipment form. The date the supplies were received and the date they were checked should be on the form. One copy of the appropriate form should be retained in the site file and another copy returned to the sponsor as according to their instructions. If required, approve shipment has been received on Interactive Web Response System Portal.

B. Storage of Inventory/IP

- Immediately after checking the supplies received at site they should be stored in appropriate conditions as specified by the sponsor. Required equipment needed to store IP should be readily functioning and available at all times.
- The drug storage area should be secure. It should be locked where appropriate and access to the supplies limited where possible to investigators, research nurse and clinical research study coordinator.
- The temperature of the storage area should be monitored weekly and a temperature log maintained.

C. Dispensing Inventory/IP

1. Ensure that each time Inventory Item / Investigational Product is dispensed; the appropriate accountability form is completed. Documentation will include:
    - Amount (and lot number, if appropriate) dispensed,
    - Name of individual dispensing study drug,
    - Subject's number,
    - Subject's initials, if appropriate
    - Date (and time, if appropriate) of dispensing,
    - Date and time, if appropriate, amount of study drug returned,
    - Amount of study drug returned.

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2. After use by the study subject, return all used containers/units, if appropriate, to the study pharmacist. If any containers/units are missing, document the reasons.
3. Note any discrepancies between amounts used by subjects and amounts expected to be returned and document the reasons.
4. Ensure that study supplies are adequate and within an appropriate expiration date.
5. Alert the monitor when additional supplies will be required.
6. If emergency breaking of the study drug blind is medically necessary, document all circumstances appropriately.

D. Return/destruction of Inventory/IP

Return of Unused Inventory/Investigational Product

1. After the study has been completed, a comprehensive inventory of the product / devices is completed before returning them to the Sponsor. (ONLY at the instruction of the Sponsor should any IP be destroyed). Any discrepancies in the beginning and ending inventory are noted and explained. A copy of the post-study inventory and all study subject dispensing logs will be kept in the study files at DHR Health Institute for Research & Development, and a copy is placed in the box of IP being returned to the Sponsor.
2. The manner of shipment of used or unused IP must be defined by the Sponsor and followed by site personnel. Returned IP must be packed and shipped with the documentation provided by Sponsor. The manner of shipment must have mechanism of being traced.

Disposal of Used Inventory/Investigational Product

1. All IP used and unused must be accounted for by the Study Monitor. Disposal of used or unused IP must be initiated only after the written instruction from the Sponsor/Study Monitor had been obtained.
2. Once accounted for, if the sponsor does not request that drugs need to be returned, then the products may be disposed of. The procedure for destroying used study drugs is as follows:
   A. Environmental Services must be contacted (phone #956-362-7917) to arrange for pickup of used or unused IP for disposal as biomedical waste.
   B. Prepare accounted drug and place them in a biohazard bag. Secure and tape the bag closed.
   C. Keep bag with investigational product locked at site until it may be released to biomedical waste management personnel.
   D. Document that drugs were disposed of according to policy.

3. Documentation shall be maintained concerning the disposal of the Investigational Product which shall contain:
   A. The quantity of the Investigational Product disposed of;
   B. The date and manner of disposal;
   C. The staff member who conducted the disposal;
4. A copy of this documentation shall be sent to the sponsor and kept in the pharmacy binder.

E. Inventory/IP Issues

Temperature Excursion

Temperature Excursions can happen for many reasons, it is important to document the excursion as appropriate and follow the procedures below to ensure the IP is safe for use.

1. Remove all affected IP from excursion area and place in an appropriate temperature location (quarantine).
2. Inventory all affected IP on the Sponsor provided form.
3. Document temperature ranges, MAX and MIN, and how long the IP was exposed to the temperature excursion on the Sponsor provided form.
4. Do not dose or dispense affected IP to any subjects and notify sponsor immediately. Document inability to dose accordingly in source documents.
5. Notify all Sponsors, whose IP was affected, of the excursion as per Sponsor protocol.
6. Do not use IP until sponsor clears it or sends new IP.
   a) If cleared by sponsor, remove IP from quarantine and dispense accordingly
   b) If deemed unusable, follow sponsor protocol for destruction of IP or destroy as per DHR Health Institute for Research & Development policy
7. Label affected IP appropriately in *IP Accountability log* and sponsor IWRS.
8. File all Sponsor Correspondence and documentation accordingly in Investigator Site File or subject chart.

Damaged Inventory/IP

Investigational Product may be damaged in transit or damaged during dosing. Follow procedure below:

1. Inventory all affected IP on the Sponsor provided form or *IP Accountability Log*.
2. Follow sponsor protocol for disposal of IP or dispose as per DHR Health Institute for Research & Development policy (V-PM- 502-F)
3. Do not dose or dispense affected IP to any subjects. Document inability to dose accordingly in source documents.

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4. Notify all Sponsors, whose IP was affected, as per Sponsor protocol to obtain replacement(s) IP.
5. When replacement is obtained, dose or dispense to subject.
6. File all Sponsor Correspondence and documentation accordingly in Investigator Site File and subject chart.

Project Accounting:

A. Project Accounting Tool
- ***Protocol Coverage Analysis Template***, ***aka Project Log*** will aid the Principal Investigator and the Research Coordinator in maintaining project financial accountability.
- Upon approval of the budget and contract, the Template will be pre-populated with the approved amounts in order to track subject visit status and Project balance.

B. Project Invoicing & Billing
- According to the final sponsor approved contract, the invoicing requirements will be laid out.
- Using the tool ***Protocol Coverage Analysis Template***, ***aka Project Log***, the Coordinator will invoice as per contract requirements.
- The designated staff of DHR Health Institute for Research & Development will review, edit and approve the draft before submitting the offer to the sponsor.

C. Interim Contract re-negotiation
- Some billing issues may arise during the conduct of the project that was overlooked or un-accounted for during study start up negotiations.
- The Research Coordinator will notify the designated staff of DHR Health Institute for Research & Development of the need for a re-negotiation or amendment to the contract.
- Designated staff of DHR Health Institute for Research & Development will either approve or deny the need for an amendment or re-negotiation.
- If approved, designated staff of DHR Health Institute for Research & Development will send the amendment to the contract or the budget to the sponsor.
- Sponsor will approve or deny the amendment