**PURPOSE:**

To outline the organization of clinical trials documents such as Regulatory Binders, IND Safety Reports (INDSRs), Investigator documents (e.g. CV, ML, FDF, and CITI Training), Patient Shadow Charts, and clinical trials manuals (e.g. Lab, Pharmacy, and Radiology Manuals), to ensure audit-readiness at all times. Federal regulation, institutional policy and good clinical practice (GCP) requires site maintenance of essential regulatory and clinical documentation related to all clinical study activity. Regulatory binders, Patient Shadow Charts, and other electronic and/or hard copy storage are used for the compliance, organization, and maintenance of these documents.

**DEFINITIONS/ABBREVIATIONS:**

- **Adverse Event (AE):** Any untoward medical occurrence encountered by an individual during the course of a clinical trial which may or may not be associated with the study drug, procedure, or device. An AE can include previously undetected symptoms, or the exacerbation of a pre-existing condition. When an AE has been determined to be related to the investigational drug, it is considered an Adverse Drug Reaction.
- **AE Reports:** Investigator reports of all adverse events (both serious sand non-serious), injuries, and deaths given to the sponsor, the IRB and the FDA or appropriate regulatory body.
- **Case Report Form (CRF):** A printed, optical, or electronic document designed to record all of the protocol-required information to be reported to the sponsor on each trial subject.
- **Collaborative Institutional Training Initiative (CITI):** Web-based Training Program providing ethics and Good Clinical Practice (GCP) education to all members of the research community.
- **Clinical Laboratory Improvement Amendments (CLIA):** Responsible for the regulations of laboratory testing and require clinical laboratories to be certificated by their state as well as the Center for Medicare and Medicaid Services (CMS) before they can accept human samples for diagnostic testing.
- **Clinical Research Nurse/Coordinator (CRC):** Clinical Trials staff responsible for oversight and coordination of assigned protocols.
- **Clinical Trials Office (CTO):** Centralized clinical trials staff, responsible for the conduct and support of SLUHN clinical trial functions.
- **College of American Pathologist (CAP):** The world's largest association responsible for the inspection and accreditation of medical laboratories under deemed authority of the Centers for Medicare & Medicaid Services (CMS), with a goal to improve patient safety by advancing the quality of pathology and laboratory services through education, standard setting, and ensuring laboratories meet or exceed regulatory requirements.
- **Curriculum Vitae (CV):** A written overview of a person's experience and other qualifications.
- **Delegation of Authority Log (DOAL):** A document used to record all study staff members' significant study-related duties, providing a comprehensive list of study staff members and the duties that have been delegated to them by the PI.

- **Data and Safety Monitoring Committee (DSMC):** an independent group of experts who monitor patient safety and treatment efficacy data while a clinical trial is ongoing.
- **Financial Conflict of Interest (FCOI):** Significant Financial Interest of an Investigator that could directly and significantly affect the design, conduct, or reporting of research.
- **Financial Disclosure Form (FDF):** A document giving financial details about a person or company.
- **Good Clinical Practice (GCP):** A standard for the design, conduct, performance, monitoring, auditing, recording, analyses, and reporting of research that provides assurance that the data and reported results are credible and accurate, and that the rights, integrity, and confidentiality of subjects are protected.
- **Investigational New Drug Safety Reports (INDSRs):** Sponsor notifications to the FDA and all participating investigators of potential serious risks, from clinical trials or any other source. In each INDSR, the sponsor must identify all INDSRs previously submitted to FDA concerning a similar suspected adverse reaction, and must analyze the significance of the suspected adverse reaction in light of previous, similar reports or any other relevant information.
- **Informed Consent Form (ICF):** IRB approved form outlining all aspects of a clinical trial in lay language, signed by the subject consenting to participate.
- **Institutional Review Board (IRB):** Independent ethics committee formally designated to approve, monitor, and review biomedical and behavioral research involving human subjects.
- **Investigator Brochure (IB):** A comprehensive document summarizing the body of information about an investigational product ("IP" or "study drug") obtained during a drug trial. The IB is a document of critical importance throughout the drug development process and is updated with new information as it becomes available. The purpose of the IB is to compile data relevant to studies of the IP in human subjects gathered during preclinical and other clinical trials.
- **Lab Normal Reference Ranges (LNRRs):** the range of values for a laboratory measurement in healthy persons, serving as a basis for comparison for a physician or other health professional to interpret a set of test results for a particular patient.
- **Medical License (ML):** A legal document for a person who is legally qualified to practice medicine; doctor of medicine.
- **Note to File (NTF):** Regulatory document used to confirm and document aspects of a clinical trial.
- **Principal Investigator (PI):** Lead investigator, responsible for the sound conduct of the project in accordance with the protocol and regulations.
- **Serious Adverse Event (SAE):** 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.

- **The Site Initiation Visit (SIV):** A meeting designed to prepare the study team for conducting the study that occurs prior to patient enrollment.
- **St. Luke's University Health Network (SLUHN)**
- **Unanticipated Problems Involving Risk (UAP):** Unanticipated Problems posing risks to subjects or others that are unforeseen and indicate that participants or others are at increased risk of harm.

**SCOPE:**

This SOP applies to all clinical research site personnel involved in the conduct of clinical research within the SLUHN CTO.

This policy describes the process:

- Starting from the time clinical trial documents are received
- Ending with final site closeout of the clinical trial

This policy is applicable to the following studies:

- All clinical trials run through the SLUHN CTO, including Industry-sponsored, Government-sponsored, and Investigator-Initiated Trials

**PERSONNEL RESPONSIBLE:**

This SOP applies to those members of the clinical research team involved in organizing and maintaining clinical trials documents. This includes the following:

- Principal Investigator (PI)
- Clinical Trials Management
- Research Nurse/Coordinator
- Study Start-up Project Coordinator
- Regulatory Coordinator
- Study Pharmacist
- Support staff

**ROLES:**

The following information describes which areas and associated roles that shall adhere to this policy:

**Director of Clinical Trials and Research:** The Director or designee shall be responsible for oversight of this policy.

**Clinical Trials Manager:** The Clinical Trials Manager or designee shall be responsible for ensuring all clinical trials documents are properly maintained and available when necessary for monitoring and auditing, and "audit-ready" at all times. The Clinical Trials Manager or designee shall also be responsible for ensuring that the Lab, Pharmacy, and Radiology/Imaging Manuals are requested at the time of internal feasibility review, or prior to the SIV at the latest.

**Study Start-up Project Coordinator:** The Study Start-up Project Coordinator shall be responsible for creating the regulatory binder and ensuring all regulatory documents are filed appropriately, as well as ensuring all Investigators are up-to-date on their CITI training, Financial Disclosure training and documentation, and that we have a current CV and ML. The Study Start-up Project Coordinator may assign binder development and filing to the Administrative Assistant or designee, but is responsible for the overall accuracy of the regulatory binders.

**Regulatory Coordinator:** The Regulatory Coordinator shall be responsible for updating and maintaining the regulatory binder and ensuring all regulatory files are available as necessary. The Regulatory Coordinator shall also be responsible for ensuring all regulatory items are up-to-date and accurate. The Regulatory Coordinator may assign filing and binder organization to the Administrative Assistant or designee, but is responsible for the overall maintenance of their assigned study binders. All essential documents, IRB submissions, and pertinent correspondence shall be filed in the regulatory binder.

**Research Nurse/Coordinator:** The CRC shall be responsible for ensuring all patient files are maintained appropriately with notations and source documentation, and that these files are available as necessary. The CRC shall also be responsible for dispersing and/or maintaining the Lab, Radiology/Imaging, and/or Pharmacy Manuals as necessary.

**Principal Investigator or designee:** The PI or designee shall be responsible for:

- Overall oversight and responsibility for clinical trial conduct at SLUHN
- Being available during Monitoring visits and Audits as needed
- Addressing any corrective action that is required

**Administrative Assistant:** The Administrative Assistant shall be responsible for the filing and maintenance of INDSRs, Investigator documents, or other regulatory documents as requested when necessary.

## PROCEDURES:

Regulatory Binders:

- The Study Start-up Project Coordinator or designee shall develop the Regulatory Binder and/or organize the sponsor-provided Regulatory Binder in line with institutional guidelines.
- The Study Start-up Project Coordinator or designee shall file all completed regulatory documents, as well as the Certification of Verification of Copies Form, within the appropriate tabs of the Regulatory Binder.
- The Regulatory Coordinator or designee shall update regulatory documents as necessary, and file and maintain them as necessary throughout the life of the trial until final closeout.
- The Regulatory Coordinator shall regularly review the binders for accuracy and completeness, and ensure all documents are available to monitors and auditors as necessary.

INDSR Binders:

- The Regulatory Coordinator or designee shall develop and maintain the INDSR Binders throughout the life of the trial until final closeout.
- The Regulatory Coordinator or designee shall print and file all sponsor-provided full INDSRs.
- The Regulatory Coordinator or designee shall file all signed INDSR spreadsheets in the appropriate INDSR Binder.
- The Regulatory Coordinator shall regularly review the binders for accuracy and completeness, and ensure all documents are available to monitors and auditors as necessary.

Investigator Documents:

- The Administrative Assistant or designee shall scan and upload all required investigator documents to the Common Drive in their respective folders.
- The Administrative Assistant or designee shall provide a hard copy of the CITI training, FCOI Disclosure Form, and the FCOI Tutorial certificate to the IRB.
- The Regulatory Coordinator or designee shall file a copy of the current signed and dated CV and ML in the appropriate binder.
- The Regulatory Coordinator or designee shall regularly review the binders for accuracy and completeness, and ensure all documents are available to monitors and auditors as necessary.

Patient Shadow Charts:

- The CRC or designee shall maintain a shadow chart for each research subject that contains certified copies of relevant medical records.
- The CRC or designee shall ensure that shadow charts contain all the relevant pages from the medical records to serve as source documentation for all data reported, along with the Certification of Verification of Copies.
- The research shadow charts shall also contain the original signed consents, progress notes, AE/SAEs, and UAPs in addition to copies of source documents.

Radiology/Imaging Manual:

- If available from the Sponsor, the Radiology Manual shall be maintained in the CTO by the CRC, and dispersed to the Radiology department as well.
- If there are specific instructions for the Radiology Department, the CRC shall provide these instructions for imaging requirements to the Radiology department as necessary.
- Should the sponsor provide an updated radiology manual at any point during the study, the CRC shall provide any relevant imaging requirement changes to the Radiology department as necessary.

Pharmacy Manual:

- If available from the Sponsor, the Pharmacy Manual shall be given to the investigational pharmacist. The investigational pharmacist shall store the manual where the investigational product is stored.
- The Pharmacy Manual shall be maintained and available for the study monitor to review drug accountability.
- Should the sponsor provide an updated pharmacy manual, the CRC shall provide the updated version of the manual to the investigational pharmacist.

Lab Manual:

- If available from the Sponsor, the Lab Manual shall be given to the CRCor designee for review and maintenance.
- Should the sponsor provide an updated lab manual, the CRC or designee shall review and maintain the new version.

**ORGANIZATION OF REGULATORY BINDER**

| Role | Step | Activity |
|---|---|---|
| N/A | --- | **NOTE:** Specific steps with regard to the completion of regulatory documents will not be outlined in this SOP |
| Study Start-up Project Coordinator or designee | 1.0 | Assemble regulatory binder for studies supported by the CTO with labeled tabs listed in Step 1.1.<br><br>**NOTE:** Industry-sponsored trial binders will be used once provided, but shall be reorganized as outlined in Step 1.1. |
| Study Start-up Project Coordinator or Regulatory Coordinator or designee | 1.1 | Organize the following essential documents in the appropriate tabs in the regulatory binder (most recent always on top):<br>• **FDA Form 1572**<br>• **Financial Disclosure Forms (FDFs)**<br>• **Delegation of Authority Logs (DOALs)**<br>• **CVs/MLs/GCP Training**<br>• **Lab Documents**<br>• **Monitoring Visit**<br>  o Monitoring Visit Log<br>  o Monitoring Visit Confirmation Letters<br>  o Monitoring Visit Follow-up Letters<br>• **IRB**<br>  o IRB Submissions with DDOTS upload |

| | | |
| --- | --- | --- |
| | | notification email<br>o IRB Approval Letters (filed on top of corresponding IRB submission)<br>o Patient Materials (if applicable) filed within the IRB submission<br>o SAE and UAP Reports pulled from the Patient Chart and filed as an IRB submission<br>o AE and UAP Logs pulled from the Patient Chart and filed within the Periodic Review IRB submission<br>o DSMC and Audit Reports filed within the Periodic Review IRB submission<br>• **Documentation of Training/Site Training Log**<br>o SIV Slides<br>o Documentation of Training throughout life of study<br>• **Protocol**<br>o Protocol<br>o Copy of Protocol signature page (if applicable)<br>• **IB/Device Brochure**<br>o IB/Device Brochure or Package Insert<br>o IB/Device Brochure signature page if applicable<br>• **Informed Consent Tab**<br>o Original Stamped ICFs<br>o All current ICFs on top<br>• **Correspondence Tab**<br>o Sponsor correspondence<br>o General Correspondence<br>o IRB correspondence<br>o General NTFs<br>• **310 Form Tab** (National Clinical Trials Network "NCTN" Trials only)<br><br>**NOTE:** Non-essential correspondence at the discretion of the site will not be filed, with the exception of IDE studies which shall follow 21 CFR 812.140.<br><br>**NOTE:** NTFs shall be housed within the Regulatory |

| | | |
|---|---|---|
| | | Binder with the corresponding items in which they verify (e.g. "FDA Form 1572 Box 6 Policy" NTF should be housed with the FDA Form 1572)<br><br>**NOTE:** A one-page explanation shall be used for the following items as applicable stating they are housed elsewhere (e.g. a centralized binder, electronically, in a different department, etc.) and shall include the location where they are housed.<br>• CVs, MLs, and GCP Training<br>• Clinical Trial Agreement/Budget<br>• Pharmacy<br>• GCP Training<br>• Screening/Enrollment Logs<br><br>**NOTE:** If the Regulatory Binder becomes full and needs to be separated into additional binders, please pull the following tabs as a separate binder:<br>• Protocol Tab<br>• IB/Device Brochure/Package Insert Tab<br>• IRB Tab |
| Regulatory Coordinator or designee | 1.2 | **NOTE:** This Step applies to Multi-site Investigator-Initiated Trials led by SLUHN ONLY. Otherwise, please skip to Step 1.3<br><br>Create a Regulatory Binder for each participating site to include the following tabs:<br>• Site Contact Information Sheet<br>• IRB<br>• Consents<br>• Patient Materials (if applicable)<br>• FDA Form 1572<br>• Financial Disclosure Forms<br>• CVs and MLs<br>• DOAL<br>• Documentation of Training<br>• Lab Documents (e.g. CAP, CLIA, Permits, LNRRs)<br>• Off-site SAEs/UAPs<br>• Correspondence |

| | | |
|---|---|---|
| Regulatory Coordinator or designee | 1.3 | File all documents that you receive for each study in the appropriate tab to keep the binder accurate and organized throughout the life of the trial |
| Regulatory Coordinator or designee | 1.4 | Check binders prior to each Monitoring Visit and/or Audit to make sure they are organized and all corresponding essential documents are filed in the appropriate tabs and are up-to-date and accurate. |

**IND SAFETY REPORTS**

| Role | Step | Activity |
|---|---|---|
| N/A | --- | **NOTE:** Specific steps with regard to the receipt and processing of INDSRs will not be outlined in this SOP. Please refer to ***SOP 204.*** |
| Administrative Assistant or designee | 2.0 | Develop and maintain INDSR binders as follows:<br><br>**Industry-Sponsored Studies:**<br>Separated by drug with a cover sheet to include the following information:<br>• Drug name<br>• Studies utilizing the drug<br>• Date range of reports contained within the binder<br><br>**National Clinical Trials Network (NCTN) Studies:**<br>Separated by NCTN Group (e.g. ECOG, GOG, RTOG, etc.) with drug specific tabs and a cover sheet to include the following information:<br>• NCTN Group<br>• Date range of reports contained within the binder |
| Regulatory Coordinator or designee | 2.1 | File the sponsor provided full INDSR in the pertinent INDSR binder |
| Regulatory Coordinator or designee | 2.2 | Maintain the signed INDSR spreadsheet in the pertinent INDSR binder<br><br>**NOTE:** The INDSR Spreadsheet shall be filed in the front of the binder (most recent on top).<br><br>**NOTE:** A copy of the INDSR spreadsheets shall be submitted to the IRB at the time of continuing review. |

**INVESTIGATOR DOCUMENTS**

| Role | Step | Activity |
|---|---|---|
| N/A | --- | **NOTE:** Specific steps with regard to the processing of these documents will not be outlined in this SOP. Please refer to *SOP 203*. |
| Regulatory Coordinator or designee | 3.0 | Develop and maintain CV and ML binder(s) with separate tabs for each investigator<br><br>**NOTE:** Tabs shall be organized by alphabetical order by last name. |
| Administrative Assistant or designee | 3.1 | Provide a hard copy of the CITI Training, FCOI Disclosure and FCOI Tutorial Certificate to the IRB. |
| Administrative Assistant or designee | 3.2 | Scan and upload the following documents to the Common Drive in their respective folders and upload the respective excel spreadsheets with current dates:<br>• CV and ML<br>• CITI Training<br><br>**NOTE:** Each of the above bullets is its own individual folder, and within each of those folders is the investigator's respective documents organized by alphabetical order by last name. |

**PATIENT SHADOW CHARTS**

| Role | Step | Activity |
|---|---|---|
| Research Nurse/Coordinator or designee | 4.0 | Prepare research shadow chart with tabs to include, but not limited to:<br>• Face sheet<br>• Signed Consent(s)<br>• Progress notes<br>• AE Log<br>• UAP Log<br>• Medication log<br>• Any other pertinent documents<br><br>**NOTE:** If sponsor provides patient charts/binders, utilize the sponsor's provided materials. |
| Research Nurse/Coordinator or designee | 4.1 | Print records for the shadow chart that include screening procedures/tests and all subsequent |

| | | |
|---|---|---|
| | | visits. |
| Research Nurse/Coordinator or designee | 4.2 | Ensure AE logs are complete, signed, submitted yearly with the IRB periodic reviews, and maintained in the research shadow chart. |
| Research Nurse/Coordinator or designee | 4.3 | Ensure SAE forms are complete, signed, submitted to the Sponsor and the IRB, and maintained in the research shadow chart. |
| Research Nurse/Coordinator or designee | 4.4 | Ensure UAP forms are complete, signed, submitted to the IRB as necessary, and maintained in the research shadow chart. |
| Research Nurse/Coordinator or designee | 4.5 | Document all UAPs and AEs on the UAP log and AE Log, respectively, to be submitted yearly with IRB periodic reviews, and maintain the both logs in the research shadow chart. |
| Research Nurse/Coordinator or designee | 4.6 | Ensure all pertinent information from the EMR is printed and maintained in the patient shadow chart for the monitoring visits.<br><br>**NOTE:** An original signed Certification of Verification of Copies form shall be filed in the research shadow chart |

**RADIOLOGY/IMAGING MANUAL**

| Role | Step | Activity |
|---|---|---|
| Clinical Trials Manager or designee | 5.0 | Request Radiology/Imaging Manual from the sponsor during the internal feasibility review process or prior to SIV at the latest. |
| Research Nurse/Coordinator or designee | 5.1 | Provide Radiology/Imaging Manual and any other pertinent radiology documents to the radiology department prior to study activation if necessary, and maintain a copy within the CTO. |
| Research Nurse/Coordinator or designee | 5.2 | Provide the radiology department any new updated radiology manuals or information throughout the study as necessary. |

**PHARMACY MANUAL**

| Role | Step | Activity |
|---|---|---|
| Clinical Trials Manager or designee | 6.0 | Request the Pharmacy Manual from the sponsor during the internal feasibility review process or prior to SIV at the latest.<br><br>**NOTE:** If the sponsor provides an electronic |

| | | |
|---|---|---|
| | | manual (e.g. a USB of the Pharmacy documents), make every effort to request a hard copy. |
| Research Nurse/Coordinator or designee | 6.1 | Provide the Pharmacy Manual to the investigational pharmacist. |
| Investigational Pharmacist or designee | 6.2 | Maintain the Pharmacy Manual with the investigational product and ensure all is appropriately updated and available during the monitoring visit. |
| Research Nurse/Coordinator or designee | 6.3 | Provide the updated Pharmacy Manual to the investigational pharmacist as necessary throughout the study. |

**LAB MANUAL**

| Role | Step | Activity |
|---|---|---|
| Clinical Trials Manager or designee | 7.0 | Request Lab Manual from the sponsor during the internal feasibility review process or prior to SIV at the latest. |
| Research Nurse/Coordinator or designee | 7.1 | Provide the Lab Manual to the Clinical Research Associate or designee for review and maintenance. |
| Research Nurse/Coordinator or designee | 7.2 | Provide the updated Lab Manual to the Clinical Research Associate or designee as necessary throughout the study. |

**RESOURCES**:

21 CFR 54.15 Proposed Obligations of Clinical Investigators
21 CFR 312.50 General Responsibilities of Sponsors
21 CFR 312.60 General Responsibilities of Investigators
21 CFR 312.62 Investigator Recordkeeping and Record Retention
21 CFR 312.64 Investigator Reports
21 CFR 312.68 Inspection of Investigator's Records and Reports
ICH GCP Consolidated Guidelines (Part 5.18 Monitoring)

**Endorsed by:** SOP Committee (8/24/15; 4/8/16)
**Approved by:** Tracy Butryn, Director of Clinical Trials and Research (8/26/15; 11/11/15; 6/24/16)

| Effective Date(s): | Revision Date(s): |
|---|---|
| 9/26/15 | 11/11/15; 4/8/16 |