APPENDIX J.
ESSENTIAL DOCUMENTS FOR THE CONDUCT OF A CLINICAL TRIAL

Essential documents are those documents that individually and collectively evaluate the conduct of a trial and the quality of the data produced. These documents demonstrate the compliance of the investigator and sponsor with the standards of Good Clinical Practice (GCP) and all applicable regulatory requirements. Note: The ICH Guidelines have been adopted by the FDA as guidances, not regulations.

The Office of Human Research Protection (OHRP) and Health and Human Services (HHS) regulations (45 CFR 46) and Good Clinical Practice recommendations apply for all trials that receive funding from a Health and Human Service agency. Trials with a Food and Drug Administration (FDA) Investigational Drug Application (IND) must additionally comply with 21CFR regulations.

Document	Purpose	File	Regulation/Reference
Assurance Number	The institution is responsible for obtaining and maintaining a current Health and Human Services (HHS) Assurance Number through the Office of Human Research Protection (OHRP) ■ The PI is responsible for ensuring that a current Assurance Number is in effect while conducting research on human subjects ■ All performance sites must maintain the Assurance Number on file and obtain renewal prior to expiration	In a regulatory binder at the site A copy of the Assurance Number must be on file with the sponsor	**45 CFR 46**
Auditing Reports	1. Document audit visits and findings of the auditor 2. Copies of all audit visit reports are filed at the site and sent to the sponsor	In the regulatory binder at the site	**ICH Guidance: E6 Good Clinical Practice: Section 5.19.3**
Case Report Form	1. Signed, dated, and completed Case Report Forms (CRFs): ■ Document that the investigator or authorized member of the investigator's staff confirms the observations recorded ■ Document all changes/additions or corrections made to CRF after initial data were recorded 2. Site retains copy 3. Originals retained by sponsor after study completion and/or site closure	In the patient's research record at the site	**21 CFR 312** **ICH Guidance: E6 Good Clinical Practice: Sections 8.3.14 8.3.15**
Communications	1. Document all relevant communications other than site visits, for example: ■ Letters ■ Meeting Notes ■ Notes of Telephone Calls ■ E-Mail Messages	In the appropriate regulatory binder or patient's	**ICH Guidance: E6 Good Clinical Practice: Section 8.3.11**

Document	Purpose	File	Regulation/Reference
Communications (continued)	2. Subject specific communications must be filed with source documents in the subject's research record 3. Document any agreements or significant discussions regarding trial administration, protocol violations, trial conduct, adverse event (AE) reporting, etc. 4. Save electronic media, originals, and/or certified copies	research record at the site	
Consent Form	1. Obtain signed informed consent forms in accordance with the protocol. They must be dated prior to participation of each subject in a trial 2. Save all versions submitted and approved by site's institutional review board (IRB) 3. Document revisions of the trial-related documents that take effect during the trial; save any revisions to: ▪ Informed Consent ▪ Any other written information provided to the subjects 4. Retain consents obtained for screening purposes even if the subject was not enrolled in the study 5. Non-English speaking subjects must be consented in a language they can understand Note: Annual Review and/or changes in consent forms due to AEs and/or Safety Memos are at the directive of the site's IRB	IRB approved copies in the regulatory binder at the site and signed consents in the patient's research record or in the regulatory binder at the site	**45 CFR 46** **21 CFR 50** **21 CFR 56** **ICH Guidance: E6 Good Clinical Practice: Sections 8.3.12 8.2.3 8. 3.2**
Curriculum Vitae	1. Document the qualifications and eligibility of the investigator(s) subinvestigator(s), and other key personnel to conduct a trial and/or to provide medical supervision of subjects 2. Available for all investigators, subinvestigators, any other person listed on FDA 1572 Form, and other key personnel at the site 3. Submit updated/revised investigator(s) and subinvestigator(s) CV to the PIO	In the regulatory binder at the site	**ICH Guidance: E6 Good Clinical Practice: Sections 8.2.10 8.3.5**
FDA 1572 Form	1. Document that the Investigator of Record (IoR) agrees to conduct the trial according to the obligations stated in the form 2. Update as study personnel and/or other data on the form changes 3. The original version and any updated forms must be retained as per regulatory requirements 4. The Investigator in box 1 of FDA 1572 Form is the individual who must sign and date the signature box 5. Only laboratories specified in the protocol need to be listed in Section 4	In the regulatory binder at the site	**21 CFR 312**

Document	Purpose	File	Regulation/Reference
FDA 1572 Form (continued)	6. Section 6 must list any individual: ▪ Responsible for conducting/ performing study visits ▪ Authorized to prescribe study medication This may include but is not limited to the following: ▪ MDs ▪ Pharmacist of Record ▪ Nurse Practitioner ▪ Physician's Assistant ▪ Study Coordinator ▪ Research Nurse If there are no individuals that need to be listed, then write "NONE"		
Final Close Out Monitoring Report	Final report by investigator is sent to the IRB where required and, where applicable, to the regulatory authorities, to document completion of the trial. Included is the following information: ▪ Disposition of the subjects ▪ Location of the research records ▪ Disposition of the specimens ▪ Disposition of the study drugs ▪ Other information as required by the institution or local IRB (e.g., number of patients screened, number enrolled, serious adverse experiences)	In the regulatory binder at the site	**ICH Guidance: E6 Good Clinical Practice: Sections 4.13 8.4.5 8.4.7**
Financial Disclosure	1. Document the financial aspects of the trial and the financial agreement between the investigator/institution and the sponsor for the trial 2. Certification or disclosure statement to: ▪ Certify that there is no financial interest or ▪ Disclose specific financial interests of Investigators and subinvestigators listed on FDA Form 1572, as well as their spouses and dependent children 3. Local institution/IRB and/or Group SOPs may have additional requirements	In the regulatory binder at the site	**ICH Guidance: E6 Good Clinical Practice: Section 8.2.4**
Investigational Drug Brochures (IDBs) and Safety Package Inserts	1. Document that relevant and current scientific information about the investigational product has been provided to the investigator 2. Include updates to document that investigator is informed in a timely manner of relevant information as it becomes available 3. Keep a copy on file for EACH study medication used within the protocol 4. Include the following: ▪ The most recent version ▪ Addendum to IDBs ▪ Safety letters 5. Some IDBs must be shredded per protocol/sponsor. Some studies require that a historical trail of IDBs and their individual IRB letters of acknowledgement be retained	In the regulatory binder at the site and in the pharmacy	**ICH Guidance: E6 Good Clinical Practice: Sections 8.2.1 8.3.1**

Document	Purpose	File	Regulation/Reference
Investigational Product/Study Drug Accountability	1. The Pharmacist of Record must keep records to account for the disposition of investigational products/study drugs by documenting the following: ▪ Shipment dates ▪ Batch number 2. Document tracking of: ▪ Product batch ▪ Review of shipping conditions ▪ Accountability 3. Document that the investigational products have been used according to the protocol 4. Document the final accounting of investigational products: ▪ Received at the site ▪ Dispensed to subjects ▪ Returned by the subjects ▪ Returned to the sponsor ▪ Destroyed by the site	In the pharmacy records at the site	**ICH Guidance: E6 Good Clinical Practice: Sections 8.2.15 8.3.8 8.3.23 8.4.1**
IRB Correspondence	1. Copies of all materials submitted to the IRB with dated proof of submission and IRB approval (when appropriate) for the following: ▪ Advertisements: document that recruitment measures are appropriate and not coercive ▪ All versions of consent forms ▪ All protocols and amendments ▪ Annual reports to the IRB ▪ IND safety reports/Adverse Event Report ▪ Initial protocol submission ▪ Investigational drug brochure or safety package inserts ▪ Protocol specific education material ▪ Subject compensation ▪ Any other documents receiving IRB approval or their favorable opinion ▪ Any other written information to be provided to subjects will be given appropriate written information (content and wording) to support their ability to give fully informed consent ▪ Any other pertinent communications with the IRB	In the regulatory binder at the site	**45 CFR 46 21 CFR 50 21 CFR 56** **ICH Guidance: E6 Good Clinical Practice: Sections 3.1.4 4.10 5.17.3 8.2.3 8.2.7 8.3.2 8.3.3 8.3.19**

Document	Purpose	File	Regulation/Reference
IRB Membership List	1. Document that composition of IRB/independent ethics committee (IEC) is in agreement with Good Clinical Practice (GCP) 2. Update when members change and as required by local institution/IRB policy 3. Investigator needs current IRB composition on files: ■ Titles ■ Affiliation ■ Names are not necessary	In the regulatory binder at the site	**45 CFR 46** **21 CFR 50** **21 CFR 56** **ICH Guidance: E6 Good Clinical Practice: Section 8.2.8**
Laboratory	1. Document competence of facility to perform required tests, and support reliability of results of medical/laboratory/technical procedures/tests: ■ Certification or Accreditation ■ Update when certifications expire or laboratory changes to document that tests remain adequate throughout the trial period ■ Established quality control and/or external quality assessment 2. Document normal values/ranges for medical/laboratory/technical procedures/tests included in the protocol 3. Update documentation of normal values/ranges when they are revised during the trial 4. The reference ranges and certifications must be on file for the following listings: ■ Local or central laboratories that analyze specimens for the study ■ Any group central laboratory	In the regulatory binder at the site	**ICH Guidance: E6 Good Clinical Practice: Sections 8.2.11 8.2.12 8.3.6 8.3.7**
Screening and Enrollment Randomization Logs	1. Document identification of subjects who entered pretrial screening 2. Document chronological enrollment of subjects by number 3. Screening and enrollment/ randomization logs may be separate or combined 4. Include the following information: ■ Initials of all patients screened for each study ■ PID number ■ Date screened ■ Date randomized ■ If not randomized, indicate reason	In the screening files or protocol files at the site	**ICH Guidance: E6 Good Clinical Practice: Sections 8.3.21 8.4.3**
Subject Identification Code List	1. Document that the investigator keeps a confidential list of names of all subjects allocated to trial numbers upon enrolling in a trial 2. Allows investigator/institution to permit identification of all subjects enrolled in the trial in case follow up is required 3. List needs to be kept in a confidential manner and for agreed upon time	In the protocol file at site	**ICH Guidance: E6 Good Clinical Practice: Sections 8.3.21 8.4.3**
Serious Adverse Events (SAE)	1. Notification by originating investigator to sponsor of serious adverse events, related reports, and other safety information 2. Notification by sponsor to investigators of safety information	In regulatory file at site	**45 CFR 46** **21 CFR 50** **21 CFR 56**

Document	Purpose	File	Regulation/Reference
Serious Adverse Events (SAE) (continued)	3. Notification by sponsor and/or investigator, where applicable, to regulatory authorities and IRB of unexpected serious adverse drug reactions and of other safety information		**21 CFR 312** **ICH Guidance: E6 Good Clinical Practice: Sections 4.11 5.16.2 5.17 8.3.16 8.3.17 8.3.18**
Signature Log	1. Document signatures and initials of all persons authorized to make entries and/or corrections on CRFs. Include all site staff working on a study, such as: ■ Clinicians ■ Physicians ■ Pharmacists ■ Data Personnel 2. Include on the log: ■ Initials ■ Legal signature, including first and last name ■ Printed signature ■ Credentials (if appropriate)	In the regulatory file at the site	**ICH Guidance: E6 Good Clinical Practice: Section 8.3.24**
Source Documents	1. Document the existence of the subject and substantiate integrity of trial data collected 2. Original documents and/or certified copies of documents related to the trial, medical treatment, and history of the subject 3. Must be signed and dated	As per requirements of local institutions	**21 CFR 11** **21 CFR 312** **ICH Guidance: E6 Good Clinical Practice: Section 8.3.13**
Unblinding	1. Decoding procedures for blinded trials to document how, in case of an emergency, identity of blinded investigational product can be revealed without breaking the blind for the remaining subjects' treatments 2. Document any decoding that may have occurred at the site during the trial	In the protocol files at the site or in the pharmacy files and in the patient record	**ICH Guidance: E6 Good Clinical Practice: Sections 8.2.17 8.4.6**