Baystate Health Florence Electronic Regulatory Binder Policy and Procedure

1. Purpose

1.1. Federal regulations require documentation of all study-related activities. Investigators are responsible for maintaining study documents in accordance with applicable federal regulations, International Conference on Harmonization (ICH) Good Clinical Practice (GCP) Guidelines, Health Insurance Portability and Accountability Act of 1996 (HIPAA) requirements, and departmental procedures.

1.2. At all times, study documents must be readily accessible for review and/or inspection by the regulatory agency (i.e., the Food and Drug Administration and health authorities such as the Joint Commission, organizations that accredit hospitals and research programs, study monitors, and companies that sponsor the study and companies that work for the sponsor), approving Institutional Review Board (IRB), and/or organizational personnel as appropriate.

1.3. This Standard Operating Procedure (SOP) describes the identification and storage of regulatory Essential Documents for clinical research studies and trials in Florence eBinders™ and to establish the process by study-related responsibilities are delegated to applicable personnel and by which necessary information about each team member's involvement in the study is maintained.

2. Scope

2.1. This SOP applies to all electronic records for the clinical research studies and trials where Florence eBinders™ is utilized by this organization.

2.2. Documents with more than one purpose or that are applicable to more than one study (e.g., investigator professional licenses, site facility information, laboratory normal ranges, Curriculum Vitae, etc.) may be stored centrally, in a non-study specific location.

2.3. This SOP applies to personnel engaged in the collection, creation, completion, maintenance, and/or storage of Essential Documents from the planning and study startup stage through study completion/archival, effective with studies starting on or after March 1, 2021.

2.4. Legacy studies are defined as studies where the Clinical Trial Agreement (CTA) was signed prior to the date the contract was signed with Florence; or that were activated prior to the use of Florence. Legacy projects and their associated documents may be uploaded to the eBinder system at the discretion of the Office of Research leadership and Project PIs.

2.4.1. Scanned: Legacy documents will be maintained following the organization's current institutional SOPs until the time period when they can be scanned, verified for completeness and signed as certified copies. As time permits, legacy documents will be uploaded into Florence at which point it will comply with this SOP.

2.4.2. Not scanned: Legacy documents will be maintained following the organization's current practices in conjunction with Good Clinical Practice guidelines.

2.5. This SOP includes, but is not limited to, the Essential study Documents which will be maintained following the organization's current Human Research Protection Program, Clinical Trial Office and Institutional SOPs and policies as applicable. Essential documents that are not stored in Florence due to a sponsors or regulatory body request for original wet ink signature will be maintained following the organization's current procedures.

3. Responsibilities

3.1. Baystate authorized individual with appropriate system permissions, designated by the Baystate Approved Roles and Permissions Document, is responsible for maintaining study documents in a timely and organized fashion.

3.2. Baystate authorized individual with appropriate system permissions, designated by the Baystate Approved Roles and Permissions Document binder structure template for indexing the storage of electronic study documents.

3.3. The Baystate authorized individual with appropriate system permissions, designated by the Baystate Approved Roles and Permissions Document, is responsible for ensuring that the appropriate Users (including external monitors and auditors), have the necessary access and permissions to conduct document management, completion, review, and archiving as detailed in the Team Access Control section below.

3.4. For Sponsor-Investigator studies with an eTMF:

3.4.1. To protect PII/PHI visibility from the Sponsor-Investigator, the individual with the initial Team Setup Role is to ensure that this Role's access dates are configured to protect PII/PHI document visibility.

Authorized Individual: The list of authorized individuals and the associated Florence Roles and Responsibilities is described in the Baystate Approved Roles and Permissions Document.

4. Policies and Procedures – Team Creation and Access Control

4.1. The process of maintenance of Team Accounts, User Accounts, User Roles, and User access in the Florence eBinders™ system, including how to create or delete a Team Account as well as how to create, modify, or revoke a User Account.

4.2. Baystate authorized individual with appropriate system permissions, designated by the Baystate Approved Roles and Permissions Document, will approve the creation and

termination of all new Teams and delegate which Users will be the Team Administrator(s).

4.3. The Baystate authorized individual with appropriate system permissions, designated by the Baystate Approved Roles and Permissions Document, will determine Role permissions based on designated study related tasks.

4.4. The Baystate authorized individual with appropriate system permissions, designated by the Baystate Approved Roles and Permissions Document, will create, modify, and terminate User accounts, assign Roles, manage access dates, and conduct periodic reviews to verify the status of all Users.

4.5. The Baystate authorized individual with appropriate system permissions, designated by the Baystate Approved Roles and Permissions Document, may submit a written request to Florence Support to assist with creating new User accounts.

4.6. End users or supervisors should notify the study team and/or PI about any change of employment status, including holds (e.g., termination of employment or leave of absence).

4.7. All end users should maintain a unique, secure, and private password. For users using Single Sign-On (SSO) for authentication, Florence signing personal identification numbers (PINs) are used to sign documents. Passwords and signing PINs are to be periodically checked, recalled, and revised as necessary. Florence Password and PIN reset policies are configured at the Team level.

4.8. Written requests for new Team Accounts in Florence eBinders™ may be submitted to Florence Support by any registered organization User. Florence Support will forward the Team creation request to the Baystate Systems Administrator(s) for approval and documentation of the delegated study team member prior to the creation of any new Team.

4.9. <u>User Account Creation:</u>

4.9.1. The User provides the following information to the Authorized Individual when requesting a new account:

4.9.1.1. First Name

4.9.1.2. Last Name

4.9.1.3. Study Team Affiliation

4.9.1.4. Authorized Organization Email Address

4.9.2. The Baystate authorized individual with appropriate system permissions, designated by the Baystate Approved Roles and Permissions Document, will arrange for the new User to be trained on Florence eBinders™.

4.9.3. Upon completion of the training, the new User shall submit acknowledgment of completed training to the Authorized Individual with appropriate permissions to receive access to Florence eBinders.

4.10. User Account Initiation:

4.10.1. The Baystate authorized individual with appropriate system permissions, designated by the Baystate Approved Roles and Permissions Document, will initiate the new User's account.

4.10.2. The User's unique authorized organization email address is added, an appropriate Role is assigned based on the organization's approved Roles, and access dates are assigned to the new User. This will grant the User the permissions to perform delegated functions.

4.10.3. Florence Support may assist in creating new Roles based on documented permission requests from the Baystate System Administrator or designee however they may not assign Roles or access dates to specific Users. All assignments must be completed by the delegated the Baystate System Administrator or study team member with appropriate permissions.

4.10.4. For new Users not using Single Sign-On (SSO) authentication, the new User will receive an email notification from Florence with a link to the Florence eBinders™ URL to complete the User registration process.

4.11. User Account Modification:

4.11.1. Upon a change in status impacting the use of Florence eBinders™ for a User, The Baystate authorized individual with appropriate system permissions, designated by the Baystate Approved Roles and Permissions Document, modifies the User's Role(s) and Permissions and notifies the User of the change(s).

4.11.2. Florence Support may assist in modifying existing Roles based on documented requests from the Baystate System Administrator or designee. Written requests must include a list of all impacted Users as well as the modifications requested. Florence Support will complete the request and provide a confirmation to the Baystate System Administrator or designee. The Baystate System Administrator(s) or designee are responsible for verifying that Roles created and/or modified by Florence Support are appropriate.

4.11.3. The Baystate System Administrator(s) or designee must conduct periodic reviews of all Users in Florence eBinders™ to ensure that all Users have the correct permissions and are still active.

4.12. User Account Holds and Revocation:

4.12.1. Temporarily inactive Users can have access dates turned OFF and Roles maintained without access. Examples of temporarily inactive Users includes Users on a leave of absence, with plans to return.

4.12.2. Upon a change in employment status for a User that discontinues the need for specific Team access and/or all Florence eBinders™ use, Baystate System Administrator or designee removes all permissions for the User and removes the User from each appropriate Team in Florence eBinders™.

4.13. Team Termination:

4.13.1. The Baystate System Administrator or designee, submits a written request to Florence Support to terminate an existing Team. The request will specify any requests for document management and archiving based on the organization's established SOP.

5. Policies & Procedures –Electronic Document Management

5.1. Requirements for documentation, record keeping, and record retention apply to electronic records as they do for paper systems.

5.2. Key study documents will be managed, stored, and presented electronically. Sponsors and auditors should be notified of this policy prior to study initiation and before any audits or inspections.

5.3. User access control to electronic documents is described in the Team Creation and User Access Control section above.

5.4. Electronic security controls, secure backup schedule, and routine vulnerability testing are described in the Florence eBinders™ Security Overview provided and the Florence Healthcare Disaster Recovery Plan, both provided and maintained by Florence Healthcare, Inc.

5.5. Retention and/or destruction of electronic documents in Florence eBinders™ at the conclusion of the study is performed in accordance with local institution/IRB/IEC policies and procedures as established in U.S. Federal regulations.

5.6. Electronic certified copies

5.6.1. Electronic documents may include a blend of original and certified copies. Electronic certified copies are defined as copies that have been created and verified against the original and tracked with a dated signature. Electronic signatures with an audit trail demonstrate evidence of authenticity. Per ICH E6(R2), the data is to include the context, content, and structure, as the original. For studies regulated by the US FDA, the copy is to have all of the same attributes and information as the original.

5.6.2. Only the User who possesses the original copy may create the Electronic Certified Copy.

5.6.3. The User who possesses the original copy of the Document will upload a electronic copy of the Document into Florence eBinders™, review and verify the uploaded

Document for completeness and readability and then sign the Document as a Certified Copy.

5.6.4. The audit trail will track and record the timestamp, reason, and author for authenticity and responsibility.

5.7. Central Documents and General Files

5.7.1. Documents that will be used across studies can be maintained centrally.

5.7.2. Links, or shortcuts, will allow Users to access central documents as appropriate based on the User's access controls assigned. Shortcuts are to be used for viewing purposes and not as part of the official study records needed for archiving.

5.7.3. Central documents may include, but are not limited to CVs, medical licenses, CAP/CLIA, lab normal, SOPs, and training.

5.8. Monitor, Auditor, and Inspector Access

5.8.1. Monitors, auditors, and inspectors will be given access to Florence eBinders™ by following the guidelines described in the Team Creation and User Access Control section above.

5.8.2. All access is monitored via the audit trail.

5.9. Document Version Control

5.9.1. Version tracking within Florence eBinders™ can be utilized for draft documents, completed forms, logs, redacted documents, etc.

5.9.2. Designated "Archive" folders can be used for version tracking of approved documents such as IRB approved Informed Consents, Protocol Versions, etc.

5.9.3. The version tracking tool maintains each version of the document and the audit trail logs, the action of modification by authorized Users, date of modification, as well as the time stamp of modification to verify compliance with GCP.

6. Policies & Procedures – Electronic Signatures

6.1. This section applies to all documents and clinical research studies and trials where Florence eBinders™ is utilized by this organization and where electronic signatures and handwritten signatures executed to electronic documents are intended to be equivalent to paper records and handwritten signatures.

6.2. For clinical trials regulated by the US FDA, the Baystate Research Compliance Officer, or other delegated individual, will complete and submit a non-repudiation letter to the FDA prior to the use of electronic signatures on any clinical trial document attesting to the fact that their electronic signatures are legally binding equivalents of their traditional hand-written signatures.

6.3. All Florence eBinders™ Users will be responsible for maintaining secure passwords and updating them at the interval specified by their governing organization.

6.4. Users are responsible for reviewing their accounts for pending signature requests on a regular basis.

6.5. The Team Administrator(s) or designee will verify the identity of each Florence eBinders™ User per the Team Creation and User Access Control section and if applicable, via the email-based User registration process for non-SSO Users. The Team Administrator(s) or designee is also responsible for ensuring that the appropriate individuals have the necessary User permissions and access to request signatures and/or sign documents in Florence eBinders™.

6.6. Electronic signatures may be used for all documents stored in Florence eBinders™, unless Sponsor contract or Baystate policy state otherwise.

6.7. Each electronic signature shall be unique, using the individual's organization email address as the unique identifier in Florence eBinders™.

6.8. When a document is signed in Florence (via Addendum or Stamp), the details of each electronic signature is listed on the signature addendum page, which can be included when the document is downloaded. If the Stamp signature option is used, the signature is also visible on the document itself.

6.9. Signatures only apply to the version of the document signed. Any updates to a version of the document do not carry over signatures from the previous version. Any updates which require review, acknowledgment, and/or approval must be signed by the appropriate Users.

6.10. Use of the Addendum (invisible) signature option and the Stamp (visible) signature option are seen as equivalent and can be utilized on all electronic documents interchangeably as both signature types maintain the details required by US FDA 21 CFR Part 11.

6.11. <u>Signature Requests</u>

6.11.1. Signature requests can be made by individuals with the appropriate permission and access to do so within Florence eBinders™.

6.11.2. The individual requesting an electronic signature is required to specify:

6.11.2.1. Document that requires the electronic signature(s)

6.11.2.2. User(s) who need to sign the document

6.11.2.3. Reason/meaning of the signature (Approval, Acknowledgment, Authorship, Certified Copy, Responsibility, or Review)

6.11.2.4. Optional Signature Type, either Addendum (invisible on the document) or Stamp (visible on the document.

6.11.2.5. Optional Sign by Date to specify the date by which the document must be signed.

6.12. Signing Documents

6.12.1. The individual signing the document reviews the document and the requested reason for their signature in Florence eBinders™.

6.12.2. If the user agrees, the username (authorized organization email address) and password (or signing PIN) are entered, and the system confirms that they match the User's verified secure credentials.

6.12.3. The signature addendum page and audit trail for the document are updated to reflect the new electronic signature, its reason/meaning, and the date and time of execution.

7. Policies & Procedures – Email Correspondence

7.1. As set forth in organizational and sponsor guidelines, all relevant study- and trial-related correspondence with subjects, sponsors, sites, and study team members should be retained for review.

7.2. A User can forward an email and related attachments to the appropriate location within Florence eBinders™ using the 'Import via email' function if they are granted the appropriate permissions to do so.

7.3. Once emails are received in Florence eBinders™, renaming of the emails for organizational purposes is permitted by a User with permissions to do so.

8. Policies & Procedures – Signature and Delegation of Authority Logs

8.1. This process includes the completion and maintenance of the Signature Log for any clinical research studies and/or trials that include wet-ink handwriting for eISF documents as well as the Delegation of Authority Log (DOAL).

8.2. Signature Log

8.2.1. The purpose of the Signature Log is to have a record of the handwriting sample of every individual involved in study-related activity.

8.2.2. An individual Signature Log should be maintained for each team member who participates on a study or trial that uses wet-ink handwriting.

8.2.3. At a minimum, the Signature Log will include:

8.2.3.1. Printed name

8.2.3.2. Signature

8.2.3.3. Initials

8.2.3.4. Numbers 0-9

8.2.3.5. Date when the signature log was completed

8.2.4. The Authorized Individual will initiate the Signature Log with each new user.

8.2.5. Each Team member should provide a complete handwritten copy of the Signature Log to the Authorized Individual.

8.2.5.1. Each completed Signature Log will be uploaded and stored in Florence eBinders™.

8.2.5.2. In case of case of a name change for a Team member, a new Signature Log must be created and uploaded to Florence eBinders™.

8.3. Delegation of Authority Log

8.3.1. The purposes of the study-specific DOAL include:

8.3.1.1. Documentation of the roles and responsibilities of those on the study team

8.3.1.2. Evidence of agreement between the PI and study team member

8.3.1.3. Notification to study team members of their responsibilities

8.3.1.4. Record of duration of study involvement

8.3.2. A DOAL must be maintained for all non-exempt human subject research. There must be a separate DOAL per study.

8.3.3. Prior to initiation and for the duration of the study, the PI is responsible for reviewing study requirements and determining assigned duties in the DOAL.

8.3.4. The PI is responsible for ensuring all applicable federal and state regulations, institutional policies, and any protocol-specific requirements are followed when delegating study-related duties.

8.3.5. All members of the study team should be listed on the DOAL. If an investigator does not wish to participate in the study, they must inform the study regulatory specialist (RS), clinical research coordinator (CRC) and/or project manager so that the investigator can be removed from the application, FDA 1572, and financial disclosure statements.

8.3.6. Initiation of the DOAL:

8.3.6.1. Study Team Member with appropriate system permissions, will initiate the DOAL.

8.3.6.2. The appropriate columns for each team member should be completed at the initiation of the DOAL and uploaded to Florence eBinders™.

8.3.6.3. Study Team Member with appropriate system permissions, will request an electronic signature from each study team member listed on the DOAL for acknowledgment of their assigned duties.

8.3.6.4. Study Team Member with appropriate system permissions, requests an electronic signature from the PI responsible for study oversight for approval of assigned duties, indicating its effective date.

8.3.6.5. No study related duties may be performed until BOTH the PI and the study team member have signed the DOAL.

8.3.7. The DOAL must be updated each time a new member joins the study team, when a delegated individual's role in the research changes, when an individual's employment status changes, if the individual will no longer be a member of the research team and/or the study closes.

9. References

9.1. Florence eBinders™ V2 User Guide

9.2. US FDA 21 CFR Part 11 Electronic Records; Electronic Signatures (here)

9.2.1. General Principles of Software Validation; Final Guidance for Industry and FDA Staff (here)

9.2.2. Part 11, Electronic Records; Electronic Signatures – Scope and Application (here)

9.2.3. Use of Electronic Records and Electronic Signatures in Clinical Investigations Under 21 CFR Part 11 - Questions & Answers (here)

9.3. US FDA 21 CFR Part 312.62(c) – Investigational New Drugs – Drugs for Human Use (here)

9.4. US FDA 21 CFR Part 812 – Investigational Device Exemption (here)

9.5. US FDA Industry Guidelines and Information Sheets (here)

9.6. FDA Compliance Policy Guidance Programs (here)

9.7. E6(R2) Good Clinical Practice: Integrated Addendum to ICH E6(R1), Guidance for Industry (here)

10. Related Resources:

10.1. Human Research Protection Program SOPs

10.2. BH-HRPP-1.11 Certified Copies

11. SOP History

Version	Changes/Reason	Approval Date	Effective Date
1.0	N/A – Initial Version	**February 26, 2021**	**March 1, 2021**