Medical College of Wisconsin (MCW) Standard Operating Procedure: Use of Florence eBinders™ for Electronic Records and Electronic Signatures

Version 1: 07/01/2021

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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.US Food and Drug Administration (FDA), US Department of Health and Human Services (DHHS), study sponsor/designee, approving Institutional Review Board (IRB), other regulatory authorities 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 which an MCW Principal Investigator (PI) or their designee delegates study-related responsibilities 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. Documents with more than one purpose or that are applicable to more than one study e.g., investigator and staff professional licenses, curriculum vitae, training certifications, site facility information, laboratory normal ranges, site Standard Operating Procedures, IRB rosters, etc.) may be stored centrally, in a non-study specific location.

2.2. 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 7/1/2021.

2.3. Legacy studies are defined as studies that were activated prior to the use of Florence. Legacy documents may be:

2.3.1. Scanned: Legacy documents will be maintained following the organization's current corporate policies regarding the collection and security of research data (RS.GN.050) and ownership, access, and integrity of research data (RS.GN.070) and HRPP policy for Research Consent Storage: Electronic Copies; until the time period when they can be scanned, verified for completeness and signed as certified copies. As time permits, legacy documents can be uploaded into Florence at which point it will comply with this SOP.

2.3.2. Not scanned: Legacy documents will be maintained following the department's current Essential Documents SOP.

2.4. This SOP includes Essential Documents which will be maintained following Good Clinical Practice (GCP) and regulatory requirements, including but not limited to:

- Signed Protocol and Amendments, if applicable (all versions)
- Investigator's Brochure (all versions)
- FDA 1572 Statement of Investigator Form

- FDA 3454/3455 Certification & Disclosure of Financial Interests
- FDA 3674 Certification of Compliance with ClinicalTrials.gov (If applicable)
- Informed Consent Form & information given to subjects
- IRB approvals & correspondence
- Safety committee approval(s), if applicable
- IRB rosters
- Laboratory certification/accreditation
- Operations Manuals (all versions)
- Information for Use (all versions)
- Monitoring reports/correspondence with sponsor
- Investigator/staff curriculum vitae, licensure, training certifications, etc.
- Subject screening and enrollment logs
- Delegation of Authority Log
- Approved Recruitment & Retention materials Fully executed Clinical Trial Agreement (CTA)
- Laboratory normal ranges
- Study financial records
- Any updates to any of the above documentation during the course of the study

2.5. This SOP includes the following records with Protected Health Information (PHI), which will be maintained following the organization's current corporate policy regarding the collection and security of research data (RS.GN.050) and HRPP policy for Research Consent Storage: Electronic Copies):

2.5.1. Documents with PHI may Include, but are not limited to, EMR records and eConsent/scanned Informed Consent forms.

3. Definitions

3.1. **Certified Copy**: A certified copy is a copy of original information that has been verified, as indicated by a dated signature, as an exact copy having all of the same attributes and information as the original.

3.2. **Electronic Signature**: An electronic sound, symbol or process that is attached to or logically associated with a record and executed or adopted by a person with the intent to sign the record.

3.3. **Regulatory/Essential Documents**: Those documents which individually and collectively permit evaluation of the conduct of a trial and the quality of the data produced. These documents serve to demonstrate the compliance of the investigator, sponsor and monitor with the standards of Good Clinical Practice and with all applicable regulatory requirements.

4. Responsibilities

4.1. All MCW investigators or their designee(s) engaging in research at the trial site, or at external participating sites (when MCW is the Coordinating site) are responsible for maintaining study documents in a timely and organized fashion.

4.2. The Principal Investigator (PI) or designee conducting an industry-sponsored study (ISS) activated after 7/1/2021 is responsible for incorporating the one-time institutional Florence fee into the study budget. This one-time fee permits sponsor with secure remote access to essential documents and study records in Florence for study oversight monitoring. Federally funded research, research funded by non-profit entities, Investigator-initiated trials (IITs), and/or consortium-led studies are not subject to the institutional Florence fee.

4.3. Organizational Administrators in the MCW Office of Research with the Team Set Up Role or their designee develops the eBinder structure template for indexing the storage of electronic study documents. Those with the Team Set-Up role will have the capability to access all records in the system. All document views are automatically recorded in the audit trail, which is not alterable.

4.4. The Principal Investigator (PI) or their designee 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.

4.5. For Sponsor-Investigator studies that grant external Sites with access to Florence:

4.5.1. **Site Users have sole control of their site records**. To ensure sole control of a site's electronic records and protect the availability of the site's records that are created, modified, and/or signed in Florence, the Principal Investigator (PI) or designee will ensure that an agreed-upon procedure is in place with each participating site if and when the site no longer has access to Florence (e.g., sites retain ongoing access to view and download and/or sites are trained to export/download records at study closeout/completion/closure, etc.).

4.5.2. To prevent certain users (e.g., Sponsor) from any unintended/accidental visibility of records containing protected health information (PHI) that the Florence system identifies as not containing PHI:

4.5.2.1. Users who upload PHI are to be trained on the use of Florence, including appropriate masking procedures and available functionality (e.g., Florence redaction tool and/or flag record as containing PHI).

4.5.2.2. Users who are prohibited from viewing PHI (e.g., select Sponsor/CRO users) with the team-level permission to "View Documents Without PHI" (including the individual with the Team Setup Role, if applicable) will ensure access to this Role (and/or permission) is turned off before PHI records are uploaded to the Team (e.g., remove the Role or configure access dates to "OFF").

5. Policies and Procedures – Team Creation and Access Control

5.1. 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.

5.2. Organizational Administrators in the MCW Office of Research will approve the creation and termination of all new Teams and delegate which User(s) will be the individual with the Team Set Up Role.

5.3. The Principal Investigator (PI) or their designee will determine Role permissions based on designated study related tasks.

5.4. The Principal Investigator (PI) or their designee and/or Department Superuser Admin will create, modify, and terminate User accounts, assign Roles, manage access dates, and conduct periodic reviews to verify the status of all Users.

5.5. The Principal Investigator (PI) or their designee may submit a written request to the Organizational Administrators in the MCW Office of Research, or as directed to Florence Support to assist with creating new User accounts.

5.6. End users or supervisors should notify the Organizational Administrators in the MCW Office of Research or designee about any change of employment status, including holds (e.g., termination of employment or leave of absence).

5.7. All end users should maintain a unique, secure, and private password. MCW will utilize Single Sign-On (SSO) for authentication, and 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 and will require reset every 180 days.

5.8. 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 Organizational Administrators for approval and documentation prior to the creation of any new Team.

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

5.9.1. The User provides the following information to their Department Superuser Admin or the Organizational Administrator to request initiation of his/her account:

- First Name
- Last Name
- Study Team Affiliation
- Authorized Organization Email Address

5.9.2. The Individual with the Team Set Up Role, the Department Superuser Admin or designee will arrange for the new User to be trained on Florence eBinders™.

5.9.3. Upon completion of the training, the new User shall submit acknowledgment of completed training using the Florence Training Attestation Form to the Organizational Administrators or designee as outlined in the organization's policy to receive access to Florence eBinders™. The new user will also use the Florence Training Attestation form to confirm that their specific electronic signature is the

legally binding equivalent of the signer's handwritten signature and confirm that they will follow appropriate masking procedures uploading PHI.

5.10. User Account Initiation:

5.10.1. The Department Superuser Admin or the Team Admin in the MCW Office of Research or designee will initiate the new User's account.

5.10.2. 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.

5.10.3. Florence Support may assist in creating new Roles based on documented permission requests from the Organizational Administrators in the MCW Office of Research however they may not assign Roles or access dates to specific Users. All assignments must be completed by the delegated Individual with the Team Set Up Role or designee.

5.10.4. 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.

5.11. User Account Modification:

5.11.1. Upon a change in status impacting the use of Florence eBinders™ for a User, the Department Superuser Admin or the Organizational Team Admin modifies the User's Role(s) and Permissions and notifies the User of the change(s).

5.11.2. Florence Support may assist in modifying existing Roles based on documented requests from the Team Admin in the MCW Office of Research. 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 Organizational Team Admin in the MCW Office of Research or designee. The Team Admin in the MCW Office of Research or designee are responsible for verifying that Roles created and/or modified by Florence Support are appropriate.

5.11.3. The Department Superuser Admin or the Organizational Team Admin must conduct periodic reviews of all Users in Florence eBinders™ to ensure that all Users have the correct permissions and are still active.

5.11.4. User is responsible for notification of Organizational Admin in the MCW Office of Research when they change departments within MCW. This will ensure that User has correct permissions and is active in their new department.

5.12. User Account Holds and Revocation:

5.12.1. 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.

5.12.2. Upon a change in employment status for a User that discontinues the need for specific Team access and/or all Florence eBinders™ use, the Department Superuser Admin or the Team Admin in the MCW Office of Research removes all permissions for the User and removes the User from each appropriate Team in Florence eBinders™.

5.13. Team Termination:

5.13.1. The Team Admin in the MCW Office of Research 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.

6. Policies & Procedures –Electronic Document Management

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

6.2. Key study documents will be managed, stored, and presented electronically. Sponsors and auditors and the Institutional Review Board (IRB) should be notified of this policy prior to study initiation and before any audits or inspections.

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

6.4. Electronic security controls, secure backup schedule, and routine vulnerability testing are described in QMS-002 Florence Healthcare, Inc. Security Overview and the QMS-006 Florence Healthcare Disaster Recovery Plan (DRP), both provided and maintained by Florence Healthcare, Inc.

6.5. 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.

6.6. Electronic certified copies

6.6.1. 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.

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

6.6.3. The User who possesses the original copy of the Document will upload an 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.

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

6.7. Central Documents and General Files

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

6.7.2. 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. This will require use of Archiving folders, as all versions during the life of a trial should be in the protocol e-Binder for storage and as part of the trial activity

documentation. Note: Shortcuts reflect the document's current version and are updated with each new version.

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

6.8. Monitor, Auditor, and Inspector Access

6.8.1. 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.

6.8.2. All access is monitored via the audit trail.

6.9. Document Version Control

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

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

6.9.3. 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.

7. Policies & Procedures – Electronic Signatures

7.1. 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.

7.2. For clinical trials regulated by the US FDA, MCW has submitted 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.

7.3. All Florence eBinders™ Users will be responsible for maintaining secure passwords and updating them at the interval specified by their governing organization (every 180 days).

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

7.5. The PI 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 Department Superuser Admin 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™.

7.6. Electronic signatures may be used for all documents stored in Florence eBinders™, except clinical trial agreements (CTA) or contracts processed through MCW Grants & Contracts Office (MCW GCO). MCW GCO will maintain their standard e-signature workflows via DocuSign or via wet-in signature, when required by sponsor. Each

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

7.7. 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.

7.8. 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.

7.9. 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.

7.10. Signature Requests

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

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

7.10.2.1. Document that requires the electronic signature(s)

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

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

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

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

7.11. Signing Documents

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

7.11.2. If s/he 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.

7.11.3. 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.

8. Policies & Procedures – Email Correspondence

8.1. 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.

8.2. 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.

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

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

9.1. 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 Electronic Investigative Site Files (eISF) documents as well as the Delegation of Authority Log (DOAL).

9.2. Signature Log

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

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

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

9.2.3.1. Printed name

9.2.3.2. Signature

9.2.3.3. Initials

9.2.3.4. Numbers 0-9

9.2.3.5. Date when the signature log was completed

9.2.4. The Department Superuser Admin or the Team Admin in the MCW Office of Research will initiate the Signature Log with each new user.

9.2.5. Each Team member should provide a complete handwritten copy of the Signature Log to the Department Superuser Admin or the Team Admin in the MCW Office of Research.

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

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

9.3. Delegation of Authority Log (DOAL)

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

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

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

9.3.1.3. Notification to study team members of their responsibilities

9.3.1.4. Record of duration of study involvement

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

9.3.3. 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.

9.3.4. The PI is responsible for ensuring that s/he follows applicable federal and state regulations, institutional policies, and any protocol-specific requirements when delegating study-related duties.

9.3.5. 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 PI and clinical research coordinator (CRC) so that the investigator can be removed from the application, FDA 1572, and financial disclosure statements.

9.3.6. Initiation of the DOAL:

9.3.6.1. The Clinical Research Coordinator or designee for each study will initiate the DOAL, as directed by the PI.

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

9.3.6.3. The Clinical Research Coordinator or designee will request an electronic signature from each study team member listed on the DOAL for acknowledgment of their assigned duties.

9.3.6.4. The Clinical Research Coordinator or designee requests an electronic signature from the PI responsible for study oversight for approval of assigned duties, indicating its effective date.

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

9.3.7. 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.

10. References

10.1. Florence Compliance Team Key Training Resources: FDA (Part 11 Predicate Rules) ICH, GCP EU/UK GDPR, TMF and More!

https://florencehealthcare.zendesk.com/hc/en-us/articles/360048969714

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

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

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

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

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

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

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

10.6. FDA Compliance Policy Guidance Programs (here)

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

11. Related Resources:

11.1. RS.GN.050 Collection and Security of Research Data

11.2. MCW Office of Research SOP "Research Consent Storage: Electronic Copies of Paper Informed Consent Forms" Version 2.0, 9/30/2016

12. SOP History

Version	Changes/Reason	Approval Date	Effective Date
1.0	N/A – Initial Version	**7/1/2021**	**7/1/2021**