

Template Standard Operating Procedure:

Use of Florence for Electronic Records and Electronic Signatures

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# Purpose

* 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, customer to specify any relevant privacy laws (e.g. Health Insurance Portability and Accountability Act of 1996 (HIPAA) requirements, California Consumer Privacy Act (CCPA) or General Data Protection Regulation (GDPR)), and departmental procedures.
  2. At all times, study documents must be readily accessible for review and/or inspection by the regulatory agency (i.e., [Insert: US Food and Drug Administration (FDA) or any other applicable regulatory agencies you will be submitting to]), approving Institutional Review Board (IRB), and/or organizational personnel as appropriate.
  3. This Standard Operating Procedure (SOP) describes the identification and storage of regulatory Essential Documents for clinical research studies and trials in Florence [eTMF/eISF: Customer to Specify] and establishes the process by which roles and responsibilities are delegated to applicable personnel.

# Scope

* 1. This SOP applies to all electronic records for the clinical research studies and trials where Florence [eTMF/eISF: Customer to Specify] is utilized by [customer to specify organization].
  2. This SOP applies to personnel engaged in the collection, creation, retrieval, modification, maintenance, transmittal and/or storage of Essential Documents from the planning and study startup stage through study completion/archival. This SOP does not apply to legacy studies.
     1. Legacy studies are defined as studies [Customer to DEFINE: where the Clinical Trial Agreement (CTA) was signed prior to the go live date with Florence; or that were activated prior to the use of Florence.] Legacy documents will be: *select the appropriate option from below based on whether documents will be imported or not*
        1. Imported: Legacy documents will be maintained following the organization’s current Essential Documents SOP (reference: SOP-XYZ) until the time period when they can be imported, 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. **OR**
        2. Not imported: Legacy documents will be maintained following the organization’s current Essential Documents SOP [Insert: SOP ID].
  3. This SOP excludes the following Essential Documents which will be maintained following the organization's current SOP (reference: SOP-XYZ):
     1. [List applicable documents here – e.g., original wet-ink signed contracts]
  4. This SOP excludes the following records with Protected Health Information (PHI), which will be maintained following the organization's current SOP (reference: SOP-XYZ):
     1. [List applicable documents here – e.g., clinic EMR records, eConsent forms]

# Responsibilities

* 1. The [ Customer to specify the appropriate individual ] or designee is responsible for ensuring new Users (including any external auditors, monitors or inspectors) are trained on Florence [eTMF/eISF: Customer to Specify] prior to granting access to the system.
  2. The [ Customer to specify the appropriate individual ] or designee is responsible for assigning Role permissions based on designated study related tasks.
  3. The [ Customer to specify the appropriate individual ] or designee is responsible for the creation, modification, and termination of User accounts for all users (including any external auditors, monitors or inspectors) assigning Roles and managing access dates in Florence [eTMF/eISF: Customer to Specify].
     1. Upon a change in employment status for a User that discontinues the need for specific Team access and/or all Florence [eTMF/eISF: Customer to Specify] use, the [ Customer to specify the appropriate individual ] or designee is responsible for removing all permissions for the User and removing the User from each appropriate Team in Florence [eTMF/eISF: Customer to Specify].
     2. Temporarily inactive Users can have access dates turned OFF and Roles maintained without access. Examples of temporarily inactive Users include Users on a leave of absence, with plans to return.
  4. The [ Customer to specify the appropriate individual ] or designee is responsible for periodically reviewing all roles and permissions to ensure that all Users (including any external auditors, monitors or inspectors), are authorized to perform the available task(s).
  5. All users are responsible for maintaining a unique, secure, and private password.
     1. [To be deleted if not using SSO] 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.
  6. Each user’s identification code (e.g., email address or username) and password/PIN must be periodically checked, recalled, or revised.
  7. When granting external Sites with access to Florence, 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, maintained and/or signed in Florence, the [Customer to specify the appropriate individual ] or designee will ensure that an agreed-upon procedure is in place with each 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.).
  8. The [ Customer to specify the appropriate individual ] is responsible for facilitating the creation, approval, and termination of any new Team. The request will specify any requests for document management and archiving [based on any applicable organizational SOP’s]
  9. The [ Customer to specify the appropriate individual ] or designee is responsible for developing the Binder structure template for indexing the storage of electronic study documents.
  10. The [ Customer to specify the appropriate individual ] or designee is responsible for maintaining study documents in a timely and organized fashion.
  11. The [ Customer to specify the appropriate individual ] or designee is responsible for completing user acceptance testing to ensure the system is working as expected.

# Site Personnel Training

* 1. All users must have the appropriate training, education, experience, and access (e.g., roles and permissions) to perform their assigned tasks.
  2. Upon completion of the training, the new User shall submit acknowledgement of completed training to the [ Customer to specify the appropriate individual ] or designee to receive access to the system. *Note: The Florence Training Attestation form serves as additional evidence that a user’s specific electronic signature is the legally binding equivalent of the signer's handwritten signature.*
  3. [Customer to expand - add any additional information to this section to make this your own SOP.]

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# Policies & Procedures –Electronic Document Management

* 1. Requirements for documentation, record keeping, and record retention apply to electronic records as they do for paper systems.
  2. Key study documents will be managed, stored, and presented electronically. [Customer to add one of the following]
     1. [For eTMF customers] Sites that are subject to this SOP should be notified of this prior to study initiation.
     2. [For eISF customers] ​​Sponsors and auditors should be notified of this policy prior to study initiation and before any audits or inspections.
  3. Documentation of Florence’s electronic security controls, secure backup schedule, and routine vulnerability testing are available and maintained by Florence Healthcare, Inc in the Florence Compliance Team.
  4. Retention and/or destruction of electronic documents in Florence [eTMF/eISF: Customer to Specify] 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. [Customer to Specify how records will be archived upon study completion ( ex. within the Florence system or downloaded from Florence and maintained per site SOP’s)].
  6. Electronic certified copies
     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.
     2. Only the User who possesses the original copy may create the Electronic Certified Copy.
     3. The User who possesses the original copy of the Document will upload an electronic copy of the Document into Florence [eTMF/eISF: Customer to Specify], review and verify the uploaded Document for completeness and readability and then sign the Document as a Certified Copy.
     4. The audit trail will track and record the timestamp, reason, and author for authenticity and responsibility.
  7. Central Documents and General Files
     1. Documents that will be used across studies can be maintained centrally.
     2. Document duplications or shortcuts may be utilized allowing Users to access central documents as appropriate based on the User’s access controls assigned. When Florence’s “duplicate” feature is used, a version-specific copy is created. When Florence’s “shortcuts” feature is used, a new document is created that always reflects the current-version of the document.
     3. Central documents may include, but are not limited to CVs, medical licenses, CAP/CLIA, lab normal, SOPs, and training.
  8. Document Version Control
     1. Version tracking within Florence [eTMF/eISF: Customer to Specify] can be utilized for draft documents, completed forms, logs, redacted documents, etc.
     2. Designated “Archive” folders can be used for version tracking of approved documents such as IRB approved Informed Consents, Protocol Versions, etc.
     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.
  9. Documents with more than one purpose or that are applicable to more than one study (List applicable documents here – e.g., investigator professional licenses, site facility information, laboratory normal ranges, etc.) may be stored centrally, in a non-study specific location.
  10. Florence import via email function may be used to ensure all relevant study- and trial-related correspondence (email and related attachments) with subjects, sponsors, sites, and study team members are retained in appropriate locations within Florence [eTMF/eISF: Customer to Specify].
  11. [Customer to determine if they are using this functionality] Applicable electronic Records may be marked as PHI 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:
      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) and the roles and permissions related to documents with or without PHI.
  12. [Customer to determine if they are using this functionality]Florene eLogs may be utilized to create and maintain traditionally paper logs within Florence. [Customer to add additional details on which logs they will be maintaining as eLogs, ex. DOA, Training, Screening and Enrollment, etc]
      1. Users must have the required permissions to create, manage, annotate/sign, and update eLogs.
  13. [Customer to determine if they are using specific integrations and outline processes for this functionality]

# Policies & Procedures – Electronic Signatures

* 1. All users utilizing electronic signatures shall ensure the following:
     1. Credentials are unique, secure, and remain confidential (i.e., not reused by, not reassigned to, and not shared with other individuals).
     2. Their user profile is complete to assure their signature manifestation includes all components required per applicable governing regulatory bodies.
     3. Signatures are performed only by the authenticated user.
  2. For clinical trials regulated by the US FDA, the [Customer to specify the appropriate individual] or designee 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.
  3. [Customer to specify one of the following]:

This SOP serves as documentation to hold individuals accountable and responsible for actions initiated under their electronic signatures, in order to deter record and signature falsification. **OR**

Additional testimony exists to hold individuals accountable and responsible for actions initiated under their electronic signatures, in order to deter record and signature falsification. {Customer to name their related SOP here if applicable}.

* 1. This section applies to all documents and clinical research studies and trials where Florence [eTMF/eISF: Customer to Specify] is utilized by [customer to specify this organization] and where electronic signatures and handwritten signatures executed to electronic documents are intended to be equivalent to paper records and handwritten signatures.
  2. Users are responsible for reviewing their accounts for pending signature requests on a regular basis.
  3. Electronic signatures may be used for all documents stored in Florence [eTMF/eISF: Customer to Specify], except:
     1. (List applicable documents here – e.g., original wet-ink signed contracts))
  4. 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.
  5. Documents can be signed in Florence through use of stamp or Addendum signatures. 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. Signature requests can be made by individuals with the appropriate permission and access to do so within Florence [eTMF/eISF: Customer to Specify].
  7. Signing Documents
     1. The individual signing the document reviews the document and the requested reason for their signature in Florence [eTMF/eISF: Customer to Specify].
     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.
     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.

# Policies & Procedures – Signature Logs

* 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 [eTMF/eISF: Customer to Specify] documents.
     1. The purpose of the Signature Log is to have a record of the handwriting sample of every individual involved in study-related activity.
     2. An individual Signature Log should be maintained for each team member who participates on a study or trial that uses wet-ink handwriting.
     3. The Signature Log will include [customer to update as necessary per their template]:
        1. Printed name
        2. Signature
        3. Initials
        4. Numbers 0-9
        5. Date when the signature log was completed
     4. The [ Customer to specify the appropriate individual ] or designee will initiate the Signature Log with each new user.
     5. Each Team member should provide a complete handwritten copy of the Signature Log to the [ Customer to specify the appropriate individual ] or designee.
        1. Each completed Signature Log will be uploaded and stored in Florence [eTMF/eISF: Customer to Specify] by the [ Customer to specify the appropriate individual ] or designee
        2. In case of a name change for a Team member, a new Signature Log must be created and uploaded to Florence [eTMF/eISF: Customer to Specify].

# References

* 1. Florence Compliance Team Key Training Resources: FDA (Part 11 Predicate Rules) ICH, GCP EU/UK GDPRand More!

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

* 1. US FDA 21 CFR Part 11 Electronic Records; Electronic Signatures ([here](https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CFRSearch.cfm?CFRPart=11))
     1. General Principles of Software Validation; Final Guidance for Industry and FDA Staff ([here](https://www.fda.gov/media/73141/download))
     2. Part 11, Electronic Records; Electronic Signatures – Scope and Application ([here](https://www.fda.gov/regulatory-information/search-fda-guidance-documents/part-11-electronic-records-electronic-signatures-scope-and-application))
  2. US FDA 21 CFR Part 312.62(c) – Investigational New Drugs – Drugs for Human Use ([here](https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CFRSearch.cfm?fr=312.62))
  3. US FDA 21 CFR Part 812 – Investigational Device Exemption ([here](https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CFRSearch.cfm?CFRPart=812))
  4. US FDA Industry Guidelines ([here](https://www.fda.gov/regulatory-information/search-fda-guidance-documents/clinical-trials-guidance-documents))
  5. FDA Compliance Policy Guidance Programs ([here](https://www.fda.gov/regulatory-information/search-fda-guidance-documents))
  6. E6(R2) Good Clinical Practice, Guidance for Industry ([here](https://www.fda.gov/regulatory-information/search-fda-guidance-documents/e6r2-good-clinical-practice-integrated-addendum-ich-e6r1))

1. Related Resources:
   1. Customer to specify [Organizational – Essential Documents SOP for Legacy Studies] and any other related resources; or state Not Applicable.