



Investigator Site File Reference Model (ISF RM) User Guide for Clinical Research Sites

Version 1.0, Based on ISF RM v1.0 (Provisional)

Prepared by the CDISC Investigator Site File Reference Model
Training Team

Notes to Readers

This is the final Version 1.0 of the Investigator Site File Reference Model (ISF RM) User Guide for Clinical Research Sites.

Revision History

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See [Appendix C](#) for Representations and Warranties, Limitations of Liability, and Disclaimers.

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1 Introduction

1.1 Background

The Investigator Site File (ISF) represents the complete collection of records held and maintained by clinical trial sites to document and support the conduct of a clinical trial. These records are essential for demonstrating regulatory compliance and maintaining inspection readiness. A standardized approach to organizing and managing the ISF is therefore critical. Until now, no standard existed for the organization of clinical trial site records.

To address the need for an ISF standard, a CDISC ISF Reference Model (ISF RM) work group was established in 2024. The work group created the ISF RM to provide sites with guidance and recommendations for organizing ISF records using a consistent structure, clear filing expectations, and standardized terminology. This approach supports compliance with applicable regulations and guidelines; promotes inspection readiness; and improves communication across the clinical research industry, including sites, sponsors, and regulators.

The ISF RM is aligned with the [Trial Master File Reference Model](#) (TMF RM V3.3.1), which defines a standardized structure for sponsor-maintained trial records. This alignment helps ensure consistency between ISFs and TMFs, facilitating record exchange and a shared understanding of filing expectations.

1.2 Purpose

The purpose of this guide is to help clinical sites understand, navigate, and implement the CDISC ISF RM. This document provides an overview of the standardized CDISC ISF structure and offers practical steps to create and maintain an ISF. To best use this guide, readers should be familiar with the structure of the ISF RM and its associated terminology. Information and educational resources on the ISF RM are available at www.cdisc.org

Note that:

- This document does not replace or supersede the foundational CDISC standards and guides (available at <https://www.cdisc.org/standards>) and should not be used as a substitute for any other CDISC standard.
- As this document ages, parts of it may become outdated. Please bear in mind the release date when contrasting advice and/or modeling in this guide against that in other CDISC standards.
- The examples in this document use CDISC Controlled Terminology where possible. Some values that seem to be controlled terminology may still be under development at the time of publication or reflect "best-guess" placeholder values. The CDISC value set in the National Cancer Institute Thesaurus is the official source for controlled terminology (<http://www.cancer.gov/research/resources/terminology/cdisc>).

1.3 Audience

This guide is written primarily for clinical research site teams—investigators, coordinators, administrators, and other delegated site personnel—including those with little or no prior experience with CDISC or TMF/ISF standards. Sponsor personnel, CRO/service providers, auditors, and other stakeholders outside the site may also benefit from reviewing this guide.

1.4 What is an ISF?

The ISF has had many common names across the industry (e.g., “Site File,” “Regulatory Binder,” “Study Binder”). In a nutshell, the ISF is the organized set of records and data that shows what happened at a site during a clinical trial. It provides evidence of good practice and regulatory compliance. The CDISC ISF RM is a ready-made structure with common names that supports efficiently and consistently locating records.

1.5 ISF vs TMF: What's the Difference?

	ISF	TMF
Owner	Site/investigator	Sponsor
Purpose	Proves what happened at the site	Proves what happened across the whole study
Retention throughout lifecycle of archival period	Site responsible	Sponsor responsible

2 ISF Structure: How the ISF RM Is Organized

2.1 Organization and Zones

The ISF RM is an Excel spreadsheet that groups site research records into 14 zones, generally following the trial chronology. Each zone is grouped according to compliance domains aligning with ICH GCP expectations (https://database.ich.org/sites/default/files/Step4_FinalGuideline_2025_0106.pdf), the TMF RM, and CDISC guidance.



The following table summarizes the content of the 14 zones.

ISF Zone	Zone Name	Description
ISF_01	Planning & Procedures	Plans, guidelines, manuals, and foundational documents required to conduct the trial (e.g., ISF Index, operational manuals, data entry guidelines)
ISF_02	Study Library	Core trial documents (e.g., protocol, investigator's brochure, trial team information)
ISF_03	Participant Materials	Subject-facing documentation such as informed consent forms (ICFs), questionnaires, diaries, and participant logs
ISF_04	Regulatory Submissions	Records supporting submissions to and approvals by health authorities, when maintained at the site
ISF_05	IRB / IEC	Documentation related to ethics committee submissions, approvals, and communications
ISF_06	Other Committees	Records for submissions to and approvals by non-IRB/IEC committees, as applicable (e.g., biosafety, radiation safety)
ISF_07	Site Documentation	Site management records not otherwise categorized (e.g., agreements, CVs, licenses, training evidence)
ISF_08	IP or Device Documentation	Records related to investigational product or medical device management, accountability, storage, labeling, and recall
ISF_09	Trial Supply Documentation	Documentation for non-IP clinical trial supplies including shipment, storage, and returns
ISF_10	Testing Facility Documentation	Records for laboratories and other testing facilities, including certifications, normal ranges, sample handling, and results
ISF_11	Monitoring Logs & Reports	Monitoring visit logs, reports, correspondence, and related oversight documentation
ISF_12	Safety Events, Logs & Reports	Study and site level safety documentation (e.g., SAEs, SUSARs, safety reports, safety communications)
ISF_13	Study and/or Participant Data & Logs	Data management records including deviations, data corrections, system access logs, and unblinding documentation
ISF_14	Correspondence & Notes to File	Trial-related correspondence and notes to file not included elsewhere in the ISF structure.

These 14 zones represent top-level categories. Within each zone, there are standardized sections (see figure). The sections (i.e., Artifacts) represent mid-level divider tabs within categories (e.g., ICF). The Artifact is the standard location for a specific study record, the Subartifact (e.g., Main ICF, Screening ICF, ICF addendum). As updates occur throughout the trial, their respective records can be filed in the Subartifact.



2.2 Metadata

The ISF RM Excel document is organized into 12 columns, each providing descriptive metadata to support the consistent identification, classification, and filing of records within the ISF. Column-level filters allow users to efficiently search, sort, and locate specific artifacts within the ISF RM.

Column	Column Name	Description
A	ISF Zone Combined #/Name	Automatically generated combination of the ISF zone number and name
B	ISF Zone Number	Unique numeric identifier assigned to the zone
C	ISF Zone Name	Descriptive name representing the overall contents of the zone
D	ISF Section Combined #/Name	Automatically generated combination of the ISF section number and name
E	ISF Section Number	Unique numeric identifier assigned to the section
F	ISF Section Name	Descriptive name representing the overall contents of the section
G	ISF Artifact Combined #/Name	Automatically generated combination of the artifact number and name
H	ISF Artifact Number	Unique numeric identifier assigned to the artifact
I	ISF Artifact Type	Classification of the artifact type
J	ISF Subartifact Name	Sub-artifacts within each artifact/artifact type
K	TMF Artifact Group	Corresponding TMF Reference Model (v3.3.1) artifact
L ^a	ISF Inclusion	Indication of whether the artifact/subartifact is a Core or Recommended artifact

^aCore means “file it if it exists and applies”; Recommended means “file it if you create it or receive it.” These determinations may or may not pertain to decisions made in a specific ISF index.

3 Implementation of the ISF RM

To effectively implement the ISF RM requires developing an ISF plan for the study to drive its creation and maintenance, and an ISF index for organizational reference. Development of the ISF plan and the ISF Index will occur simultaneously as co-effecting decisions are made.

Note: For questions or additional guidance on how to use the ISF RM v1.0 (Provisional) or the ISF Plan template, please email tmf-isf@lists.cdisc.org

3.1 The ISF Plan

The ISF plan (see Appendix C) defines how the ISF will be created, maintained, quality controlled, and stored throughout the trial lifecycle to ensure completeness and inspection readiness.

Considerations for ISF plan contents include:

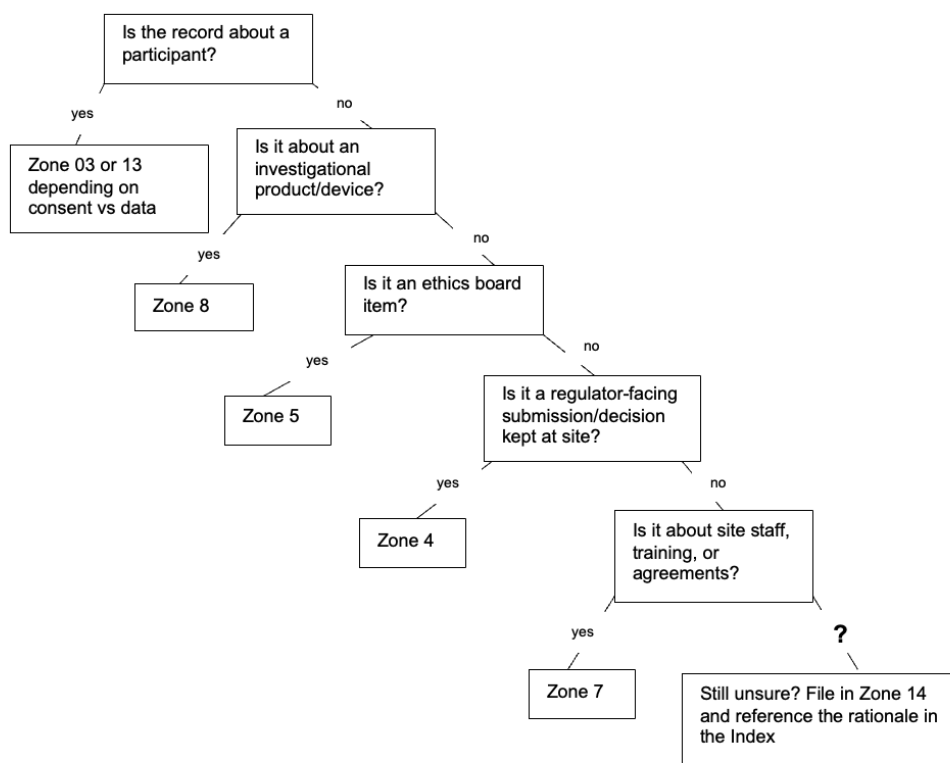
- Scope: Study covered, paper/electronic, alternative storage locations (e.g., CVs maintained by HR, study agreements, SOP)
- Roles and responsibilities: Who develops/approves ISF plan and index, who files, who reviews, how oversight of the ISF is done
- Filing rules: Naming conventions (e.g., StudyID_SiteID_Zone_Artifact_Subartifact_Version_Date), version maintenance/control, relevant correspondence, translations
- Quality checks: Frequency, what to check (e.g., ALCOA+, metadata), how to fix gaps (e.g., monthly ISF self-check using the index to identify what is missing/outdated/expired)
- Access and privacy: Who can see what (site personnel vs. monitors, auditors or inspectors), how access is managed, PHI safeguards
- Close-out and record retention: How to reconcile the index, address missing items, prepare records for retention (per regulations and contracts), and record storage locations
- Definitions/abbreviations: Reference for ISF plan and site- or study-specific terminology
- References: Relevant SOPs, guidelines, regulations

Note: If any of the ISF management information noted in this list is contained within an SOP, the SOP can be referenced instead of repeating the information.

3.2 The ISF Index

The ISF Index maps out what records belong in the ISF for the study. Use the ISF RM Spreadsheet as a starting point for the Index. Considerations for ISF Index contents include:

- Capture any local naming conventions your site uses so staff recognize them.
- Note who is delegated or responsible for filing and checking each item (e.g., coordinator, pharmacist).
- Instruct where to file “hybrid” items that could live in more than one place. These instructions may be presented as a decision tree. For example:



3.3 Getting Started

For low-resourced sites, a well-structured paper binder or electronic tool may be acceptable depending on the regulatory oversight of the study. If using electronic tools, ensure basic controls: access permissions, version control, and an audit trail (even if manual via a change log).

1. Draft the study-specific ISF plan
 - a. Review the considerations mentioned previously in this guidance.
 - b. Download the ISF RM Excel document and keep it open during setup.
2. Draft the study-specific ISF index
 - a. Within the ISF RM Excel document, filter by Zone to work in small chunks.
 - b. Mark each Artifact/Subartifact as Applicable, Not Applicable, or Provided by Sponsor.
3. Maintain the study-specific ISF
 - a. Start filing immediately — don't wait until the first participant.
 - b. Filing in real time and according to the ISF plan/index keeps the ISF up to date, healthy, and complete (i.e., audit/inspection ready).
4. Update the ISF plan and index as needed during the study if ISF content or organization of records changes.

4 Appendices

Appendix A: Glossary and Abbreviations

The following abbreviations and terms are used in this document.

Term / Acronym	Definition
Artifact	TMF/ISF term referring to a logical grouping of records
CDISC	Clinical Data Interchange Standards Consortium
Core (designation)	Indicates that if the record exists and is applicable to the study, it must be filed in the ISF
CRO	Contract research organization
CTA	Clinical trial agreement
DOA	Delegation of authority (log)
eISF	Electronic Investigator Site File
GCP	Good Clinical Practice; an international ethical and scientific quality standard for designing, conducting, recording, and reporting clinical trials
ICH	International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use
IEC	Independent ethics committee
IP	Investigational product; pharmaceutical products, biologics, or medical devices under investigation
IRB	Institutional review board
IRT	Interactive response technology
ISF	Investigator Site File; the complete collection of essential documents maintained by the clinical trial site
ISF Index	A study-specific index derived from the ISF Reference Model that identifies applicable record groups and record types for a trial
ISF Plan	A document describing how the ISF will be created, maintained, quality-controlled, and archived throughout the trial life cycle
ISF RM	Investigator Site File Reference Model
KPI	Key performance indicator
PSF	Pharmacy site file
QC	Quality control
Recommended (designation)	Indicates that the record is not required to be produced; however, if created or collected, it should be filed in the ISF
SAE	Serious adverse event
Section (ISF)	A structural subdivision within an ISF Zone used to further organize Record Groups
SOP	Standard operating procedure
Subartifact	TMF/ISF term referring to a specific record within an Artifact
SUSAR	Suspected unexpected serious adverse reaction
TMF	Trial Master File; the collection of essential documents maintained by the sponsor (or CRO on behalf of the sponsor)
TMF SM v1	Trial Master File Standard Model, Version 1
Zone (ISF)	A high-level organizational category within the ISF RM that groups records by trial function or lifecycle stage

Appendix B: ISF Plan Template Instructions

The Investigator Site File Plan is a per-study governance record describing how the ISF will be created, maintained, reviewed, closed, and archived. It is distinct from the ISF Index (the study-specific contents list derived from the ISF Reference Model); the Plan describes the “how,” and the Index describes the “what.”

- The intent of the template is to share the collective experience of the CDISC ISF RM Working Group, a wholly volunteer consortium. The content does not reflect regulatory requirements; rather, it shares the real-life knowledge of the consortium and is meant to be adapted to the appropriate scenario.
- The template may be adopted by clinical research sites of any size. Sites may also adapt the template into a network-wide or institutional ISF Plan that applies across multiple studies.
- The template is aligned with ICH GCP E6(R3) terminology. Where E6(R3) uses "investigator/institution," "essential records," "participant," and "service provider," this template generally follows that usage.
- Each site may use its own practices; however, any SOPs or plans referenced in the ISF Plan should be accessible.
- *Blue bold and italicized* text is where expected content should be completed.
- After adjusting the template, you may need to update the table of contents so that the page numbers are accurate (in Word: right-click the TOC and select Update Field).

Note: For questions or additional guidance on how to use the ISF RM v1.0 (Provisional) or the ISF Plan template, please email tmf-isf@lists.cdisc.org

Overview Page

Complete with as much detail as possible, including the site name, protocol number or other study identifier, and the date and version number of the ISF Plan.

Table of Contents

After the record is finalized, right-click the table of contents and choose “Update Field” to refresh page numbers.

Section 1: Approvals

Approval and form of approval are at the discretion of the site. At a minimum, consider including the principal investigator and the individual responsible for ISF management (e.g., regulatory coordinator, lead study coordinator, site director, quality manager).

The table may be replaced by a simple approval statement, depending on site practices.

Section 2: Record Version History

Enter the version of the ISF Plan that is being changed and a summary of the changes; if this is the initial version, note that in the Summary of Changes.

Section 3: Definitions and Abbreviations

These terms are aligned with ICH GCP E6(R3) (January 2025), the CDISC ISF Reference Model v1.0 (Provisional), and the ISF RM User Guide. Add or remove definitions and abbreviations as appropriate for the site. Site-specific terminology may differ; update accordingly.

Section 4: Introduction

The Plan should not duplicate or repeat information covered in SOPs, standard processes, or work instructions maintained elsewhere; instead, reference those records in Section 5.

Section 5: Applicable SOPs

List the applicable site SOPs, policies, or work instructions that govern ISF activities. Examples are provided in blue text; replace with record titles used at the site. This table is optional; you may instead reference your site's SOP register and remove this table.

Section 6: ISF Training

Describe how training will be handled for site personnel and for any external users (e.g., sponsor or service provider monitors with eISF access, inspectors, auditors). Append, embed, or reference training plans or other records as appropriate.

Document for each role:

- Provider: site, sponsor, or service provider, depending on who maintains the ISF and is responsible for training the end users
- Method: how training is delivered (e.g., instructor led, eLearning module, read-and-acknowledge, on-the-job training)
- Filing: where training records will be filed (e.g., ISF, site training file, eLearning system as authoritative source).

Section 7: ISF Oversight and Access Arrangements

7.1 Responsibilities

Complete the table as appropriate for the site. This table may be maintained as a separate record and appended, embedded, or referenced here. Indicate the function or role responsible for each of the activities. Where activities are also documented in the sponsor's TMF Plan or in the clinical trial agreement, assignments here should be consistent with those source records.

7.2 Access Arrangements

Describe how access to the ISF (paper or electronic) is granted, modified, and removed when no longer required. Reference applicable system SOPs and the site's user-access review procedure. Per ICH GCP E6(R3) Section 2.12.10, access controls form part of the data governance expectations for site-deployed computerized systems.

7.3 Service Providers

Complete this section if any service providers are involved in ISF activities (e.g., a third-party eISF vendor, a records storage vendor, a CRO supporting site-level documentation). If the ISF is maintained entirely on site-owned systems or on paper, mark this section "Not Applicable" and proceed to Section 7.4. Per ICH GCP E6(R3), "service provider" is the umbrella term for organizations providing services to the investigator/institution or sponsor; this replaces and broadens the earlier CRO/vendor framing.

7.4 Inspections

Modify the text to align with site SOPs and procedures or replace it with a reference to a site-specific inspection management SOP. Per ICH GCP E6(R3) Section 2.12.14, upon request of the monitor, auditor, IRB/IEC, or regulatory authority, the investigator/institution will make available for direct access all requested trial-related records. For eISFs, this includes providing inspectors with brief navigation training as needed.

Section 8: ISF Content

8.1 ISF Format, Structure, and Index

State the index/structure used for this study, either the CDISC ISF Reference Model v1.0 (Provisional) or a site-specific index. The ISF Index should be a study-specific derivation that identifies which artifacts apply to this trial. ICH GCP E6(R3) Appendix C.1.1 makes clear that "the nature and extent of the records generated and maintained are dependent on the trial design, its conduct, application of risk-proportionate approaches and the importance and relevance of that record to the trial." The ISF Index is the site-level expression of this risk-proportionate determination.

You may include the current version of the ISF Index inline here, append it as an appendix, embed it as an object, or reference its location. Avoid hyperlinks that may break and consider the ultimate file size of the Plan.

Data integrity and confidentiality should be considered to ensure that ISF records comply with applicable regulations and site or sponsor standards. Per ICH GCP E6(R3) Appendix C.2.1, essential records should be identifiable; version controlled; and, where appropriate, include details of authors, reviewers, and approvers.

Timeliness expectations for filing records are dependent on internal processes; specify them here if not covered elsewhere. A common site practice is to file records in the ISF within 5 business days of finalization or receipt; sites should confirm this against any sponsor or service provider expectations and against the clinical trial agreement.

The ISF Index should also list the authoritative source location of each artifact group during the trial. Authoritative sources are physical or cloud-based locations of records and should be access controlled, secure, validated where required, and capable of maintaining records throughout the retention period.

8.1.1 Pharmacy Site File

If the site maintains a separate pharmacy site file (PSF) for IP-related records held by the clinical trials pharmacist, describe here how the PSF relates to the ISF, where each record type is held during the active phase of the trial, and any plans for merging the PSF into the ISF at archival. If a PSF is not used at this site, mark “No.”

8.1.2 ISF Content Generated by External Parties

List sponsors, service providers (e.g., CROs, central labs, imaging vendors, IP distribution centers, IRT providers, home nursing, eISF vendors) that generate records expected to be filed in the ISF, along with how and when content will be transferred to the site.

8.2 Records Handling: Originals, Certified Copies, E-Signatures, and Personal Data

This subsection addresses how originals, certified copies, e-signatures, wet inks, raised seals, and records containing participant personal data are handled at the site. Per ICH GCP E6(R3) Appendix C, essential records may exist in any medium (paper, electronic, or both), and the original record should generally be retained by the party who generated it (Appendix C.2.7). E6(R3) is media-neutral; the goal is integrity, accessibility, and traceability rather than a particular format.

8.2.1 Originals and Certified Copies

Address the following:

- How originals will be handled (whether the original is the paper signed page, the electronic record, or a hybrid)
- How originals are generated (e.g., source records created at the site, electronic copies provided by the sponsor)
- How originals are stored (e.g., investigator source records remain at the site; certified copies are provided to the sponsor)
- Process for creating and certifying copies (whether certified by wet ink signature, raised seal, or a validated electronic certified-copy workflow)

Per E6(R3) Appendix C.2.5, where certified copies replace original records, the certification process should be documented.

8.2.2 E-Signatures

Define whether your site uses e-signatures that are compliant with [FDA 21 CFR Part 11](#) and [EU Annex 11](#) and how e-signed records are handled. If a site SOP exists, reference it.

Per ICH GCP E6(R3), consideration should be given to which signatures need to form part of the ISF, including:

- Protocol and any amendments (signed protocol signature page)
- Contracts and agreements
- Signed ICFs

- Signature sheet/delegation of authority (DOA) log (per E6(R3) Section 2.3.3, the investigator should ensure a record is maintained of the persons/parties to whom investigator activities have been delegated)
- Source records and data acquisition tool entries

8.2.3 Records Containing Participant Personal Data

Per ICH GCP E6(R3) Section 2.12.7, the investigator/institution should implement appropriate measures to protect the privacy and confidentiality of personal information of trial participants in accordance with applicable regulatory requirements on personal data protection. Per E6(R3) Appendix C.2.11, careful consideration should be given to the sharing of records when there are blinding considerations and when the records are subject to applicable data protection legislation.

This subsection should describe:

- Which artifacts in the ISF typically contain identifiable participant personal data (e.g., signed ICFs, screening logs, enrollment logs, source records linking participant identifiers to study IDs)
- Where these records are stored during the active phase of the trial (e.g., a separate restricted-access folder in the eISF, a locked filing cabinet, the ISF rather than the sponsor's TMF)
- Whether and how identifiable records are redacted before being shared with the sponsor or service providers (and reference to the site's redaction SOP)
- How access to identifiable records is restricted (e.g., role-based access, separate folder permissions in the eISF)
- How the site complies with applicable data protection regulations (e.g., HIPAA in the US, GDPR in the EU, local data protection laws)

8.3 Relevant Correspondence

Define what the site considers to be "relevant correspondence"—typically, any communication that documents a decision affecting the conduct of the trial, the safety of participants, or the integrity of data. State who is responsible, how it should be filed (e.g., by topic, by sender), and in what format (e.g., PDF). If covered by an SOP, reference that instead.

8.4 Unblinded Records

Different organizations refer to either "blinded" or "unblinded" records for the same purpose. Refer to site SOPs for consistency and update the heading to match your site's terminology. Ensure alignment with the sponsor and any service providers. Per ICH GCP E6(R3) Appendix C.2.11, careful consideration should be given to the sharing of records when there are blinding considerations.

Provide:

- The location where records that contain unblinding information are maintained until formal unblinding
- When such documentation is filed in the ISF and by whom
- How security within the system is configured to maintain the blind (e.g., restricted folders, separate login)

8.5 Living/Fluid Records

Describe how living/fluid records (e.g., DOA log, screening logs, enrollment logs, training logs, monitoring visit logs, temperature logs) are managed and when they are uploaded or refiled in the ISF.

Section 9: Conducting ISF Reviews

ICH GCP E6(R3) establishes quality by design and a risk-proportionate approach as principles of GCP. Per E6(R3) Appendix C.1.1, the nature and extent of records generated and maintained should be dependent on the trial design, its conduct, and the importance and relevance of each record to the trial. The same principle applies to ISF reviews: the scope, frequency, and depth of reviews should be calibrated to the criticality of the records under review and to the risks they mitigate (e.g., participant safety, data reliability, regulatory compliance).

Comprehensive reviews of ISF content should be performed based on the study design, the status of the study, decisions made, events that have occurred, and the SOPs and standards that apply. Describe a risk-proportionate approach to reviewing the ISF to ensure overall quality.

Some questions to ask when completing an ISF content review:

- Is the ISF Index up to date and does it reflect all expected records? If not, what is missing?
- Are all versions of expected records available (including superseded versions, where applicable)? Per E6(R3) Appendix C.2.1, essential records should be identifiable and version controlled.
- Is all relevant correspondence and email related to the study filed?
- Are there any duplicate records that should be removed or reconciled?
- Are all records complete, legible, and, where appropriate, signed and dated?
- Where records contain participant personal data, are access controls and any required redactions in place (see Section 8.2)?

Reference any list of process standards/SOPs and/or work instructions and guidance records to be followed for the ISF content review in Section 5, Applicable SOPs.

9.1 ISF Review Plan

General considerations: The following may be managed in a separate SOP or appended as an appendix to these instructions.

- The site documents when ISF reviews are performed based on study duration, phase, and/or business criticality. Reviews are recommended at study milestones and at the time of major events (e.g., protocol amendment, change in principal investigator, addition of a new staff member to the delegation of authority log, addition or change of service provider).
- For long-duration studies, define a frequency of review (e.g., quarterly, every 6 months). Best practice is to conduct periodic reviews on at least a quarterly basis.
- Completeness checks and cross-checks among related records (e.g., DOA log vs. training records vs. CV/licensure) are expected during ISF content review.
- Enter in the table all reviews that are planned to be performed, including any additional reviews performed by the site to validate reviews performed by a service provider.
- Consider including the table as a separate record appended or embedded as version 1 (the current version) and stating where subsequent versions will be located, to avoid constant updates to the Plan.
- Include completeness, quality, and timeliness as ISF KPIs and describe how they will be measured.
- Describe quality expectations for the different types of reviews: primary vs. secondary QC, periodic QC, etc.
- Evidence of ISF health (e.g., review reports, KPI dashboards) should be filed in the ISF along with evidence of the reviews themselves.

Examples are listed in blue text; each site should define its own QC types.

9.2 ISF Review Documentation

Describe the records that will be generated and maintained to support ISF reviews performed during the study, including how and where they will be filed and how findings will be tracked to resolution. If this information exists in procedural documentation, refer to Section 5, Applicable SOPs.

Section 10: Close-out, Record Retention, and ISF Disposition

10.1 ISF Close-out

This section covers ISF close-out, retention, archival, legal hold, and destruction. Where the site has an institutional records management program with a defined retention schedule, that program may be referenced rather than restated

here. Per ICH GCP E6(R3) Section 2.12.11, the investigator/institution should have control of all essential records generated by the investigator/institution before, during, and after the trial.

10.2 Archiving

This section assumes the site has an ISF management process that includes archiving. If not, provide a short paragraph describing the site's archival approach. The intent of this section is not to list all locations of all records, but to identify where the archived ISF will reside and where archival information is recorded (for some studies, this may be defined in the clinical trial agreement). Per ICH GCP E6(R3) Appendix C.2.6, essential records should be retained in a way that ensures they remain complete, readable, and readily available, and are directly accessible upon request by regulatory authorities, monitors, and auditors. Alteration to essential records should be traceable.

10.3 Person Responsible for Essential Records During Retention

Per ICH GCP E6(R3) Section 2.12.13, the investigator/institution should keep the sponsor informed of the name of the person responsible for maintaining essential records during the retention period (e.g., when the investigator site closes or an investigator leaves the site). This is a substantive change from E6(R2) and should be operationalized at the site.

10.4 Record Retention

Per ICH GCP E6(R3) Section 2.12.12, the investigator/institution should retain the essential records for the required retention period in accordance with applicable regulatory requirements, or until the sponsor informs the investigator/institution that the records are no longer needed, whichever is the longest. E6(R3) removed the fixed retention period from the prior R2 text; sites should rely on applicable regulations and on written sponsor notification rather than a default duration. Per E6(R3) Section 3.16.3(b), the sponsor is responsible for informing the investigator/institution in writing of the need for essential records retention and for notifying the investigator/institution in writing when the records are no longer needed.

Record retention timeframes should adhere to applicable regulations (e.g., FDA 21 CFR Part 312 for IND trials; EU CTR Regulation (EU) 536/2014 - 25 years; local laws), the clinical trial agreement, IRB/IEC requirements, and any institutional policies. The longest applicable retention period should be applied.

10.5 Legal Hold/Preservation Notice

This section captures information about the preservation notice or legal hold process. Site legal counsel should agree with this section before implementation. This section may be deleted if not applicable or if covered by another SOP.

10.6 Destruction of Records

Describe the destruction process. Per ICH GCP E6(R3) Section 3.16.3(b), the sponsor should notify the investigator/institution in writing when trial-related records are no longer needed; per Section 2.12.12, the investigator/institution retains records for the longer of the applicable regulatory requirement or until the sponsor provides such notification. Confirm that no destruction occurs while a legal hold is in place.

Section 11: Transfer and Archiving of ISF

This section describes how ISF records may be transferred between organizations or systems (e.g., from a contracted eISF service provider back to the site at study close, between site systems during a system migration, to a long-term archival service provider). Follow site-specific SOPs and work instructions for data transfer or migration. Where the transfer involves a change of ownership of essential records, note that per ICH GCP E6(R3) Section 3.16.3(c), the sponsor is responsible for reporting any transfer of ownership of essential records to the appropriate regulatory authorities.

Transfers of ISF records should be documented in an ISF transfer agreement that captures:

- What is being transferred and when the transfer will occur
- Which organizations are the issuer and the recipient
- Format and method of transfer (e.g., sFTP, encrypted USB, hard drive, paper)
- Method to verify successful transfer (e.g., file count and checksum reconciliation, sign-off)
- Whether the transfer is of certified copies or the authoritative source

A copy of the transfer agreement(s) should be approved and retained as an annex to the ISF Plan. If multiple transfers are expected, multiple agreements may be drawn up. Include details of where the ISF will be stored for the duration of the retention period and how the integrity of records, metadata, and audit trail will be maintained.

Section 11: Appendix

List, append, embed, or state the location of any other records that would be beneficial to include in or alongside the ISF Plan. This may include (and is not limited to):

- The study-specific ISF Index (current version)
- ISF processing workflows or process maps
- ISF transfer agreement(s) (see Section 11)
- Site-specific QC checklists for ISF reviews (see Section 9)
- Reference to or copy of relevant site SOPs not embedded in Section 5

Any embedded files should be retrievable/accessible when the Plan is finalized.

Appendix C: Representations and Warranties, Limitations of Liability, and Disclaimers

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http://www.cdisc.org/system/files/all/article/application/pdf/cdisc_20ip_20policy_final.pdf