ACRO

Clinical Trial Record-Keeping Obligations:

ACRO Best Practice Recommendations

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Introduction

Clinical trial record-keeping is a core part of the International Council for Harmonization (ICH) E6(R3) Guideline for Good Clinical Practice (GCP or ICH E6(R3)). It supports participant protection, data integrity, trial reconstructability, regulatory review and inspection readiness. In practice, these obligations are fulfilled primarily through the trial master file (TMF) framework: the TMF plan, TMF index, filing model, system-of-record decisions and archiving process.

This framework is important because not every record created during the administration of a clinical trial is a TMF record or an essential record. The key tasks are to identify which records are required to evidence trial conduct, GCP/regulatory compliance, and data reliability; where those records are held; who controls them; how they can be retrieved; and how they will be preserved for the required retention period.

The central concept is the "essential record." Under ICH E6(R3), essential records are documents, data, and relevant metadata, in any format, that facilitate trial management and allow evaluation of its methods, the factors affecting the trial, and the actions taken to determine the reliability of the results and verify compliance with GCP and applicable regulatory requirements. Identifying whether a record is essential is therefore the gateway decision that drives responsibility, system of record, retention period, and inspection exposure.

This paper is intended to provide a practical, plain-language overview for sponsors, clinical research organizations (CROs), clinical technology companies (CTOs), investigators, institutions, and others, with a primary focus on the sponsor perspective. Throughout this paper, we utilize the term "service provider" to generally include CROs, CTOs, and others performing comparable sponsor-delegated trial record-keeping activities.[1] This paper addresses TMF and essential records required under GCP and applicable clinical trial requirements in the US and EU. While this paper focuses on US and EU regulatory frameworks, the core ICH GCP principles discussed herein apply across all ICH member jurisdictions, although their implementation may vary under applicable national or regional requirements. This paper is not intended to address every data point, operational record, or document incidentally created in connection with the administration of a clinical trial.

SCOPE AND OBJECTIVES

This paper provides a principles-based overview of clinical trial record keeping, intended to establish a common conceptual foundation for sponsor-service provider discussions. It addresses the distinction between essential records and the broader universe of project and operational records, particularly where discussions about retaining "all trial records" may otherwise obscure which records must be retained, where they are held and controlled, and how responsibilities are allocated through the TMF framework. The paper therefore focuses on identifying the essential record set, determining the relevant systems of record and control, and ensuring that those records remain complete and retrievable for the applicable retention period. Its regulatory analysis is grounded in the principal applicable US and EU legal and regulatory frameworks.

[1] This usage of "service provider" aligns well with the glossary in ICH E6(R3) Guideline for Good Clinical Practice, which takes a broad approach to defining "service provider" as "a person or organization (commercial, academic or other) providing a service used by either the sponsor or the investigator to fulfil trial-related activities."

The paper is deliberately introductory and does not seek to provide detailed operational or jurisdiction-specific guidance on every aspect of clinical trial retention and archiving. Accordingly, outside its current scope are detailed analyses of numerous topics, including, but not limited to:

- jurisdiction-specific retention requirements.
- computerized-system archiving, exports, migration, close-out, and decommissioning.
- preservation of metadata, audit trails, and functionality when system-native records are exported or transferred.
- control and continuing access to source records maintained in sponsor-, service provider-, or vendor-provided systems.
- allocation and retention of system-validation and study-specific configuration records.
- qualification evidence for technology and platform personnel.
- detailed TMF oversight, lifecycle management, and archive destruction or return.
- emerging record types and technologies, including audio/video records and AI-enabled systems.

We encourage stakeholders to consider exploring these more granular topics through suitably focused companion essays that build on the foundations of this paper.

Core Principles



Essential Records are the starting point. The most important question is whether a record is needed to evaluate trial conduct in relation to the reliability of its data and compliance with GCP and regulatory requirements. Under-identification creates obvious GCP risk because genuinely required records may be missing. Over-identification also creates risk because non-essential material may be drawn into long-term regulatory retention and treated as part of the evidentiary record for audit or inspection. It may also result in the unnecessary retention of personal data or commercially sensitive information, increasing exposure in the event of a security incident.



The TMF is both a repository and a map. The trial master file should identify, control, and make retrievable the essential record set. Many static, standalone records can be filed directly in the sponsor-controlled TMF, the investigator/institution-controlled TMF, or another agreed authoritative repository, where practical. Other records, especially system-native data, relevant metadata, audit trails and source records, may be maintained in validated source systems or controlled repositories, provided the TMF plan or index clearly identifies where they are held, how they can be accessed, and how they will be made available upon regulatory request. Dynamic records may therefore be signposted in the TMF plan during the trial, with a final version, export, or transfer filed or made available at the appropriate point.



Responsibilities follow control and role. Sponsors are responsible for maintaining the sponsor-controlled TMF and may do so directly or by delegating to a service provider. Investigators and institutions are responsible for maintaining investigator-controlled essential records and source records (in the Investigator Site File or ISF), including records that may contain participant-identifying information. Service providers often generate, collect, review, file, or transfer records as part of delegated activities, but any long-term role for service providers in archiving the TMF depends on the written delegation, study processes, and any expressly scoped archiving arrangement.[2]

[2] The written-agreement standard applies to whichever party performs the archiving/hosting role under contract. Where migration, export, hosting or archiving is expected to continue beyond the term of the principal services agreement, the parties should expressly document the applicable responsibilities, duration, format, access arrangements and associated costs.

Retention should be proportionate. Regulatory retention requirements apply to the relevant TMF content and other required essential records. They do not automatically apply to every record generated, received, or handled by a sponsor, investigator, or service provider. Other records may still need to be retained for operational, quality, legal, evidentiary, or contractual reasons, but they should be managed under the appropriate pathway rather than automatically treated as essential records.

Regulatory Framework

ICH E6(R3) is the key international reference point. ICH E6(R3) Appendix C recognizes that many records are generated during a trial, that the nature and extent of essential records depends on trial design and risk-proportionate approaches, and that essential records may be maintained in, or referred to from, repositories held by the sponsor and by the investigator/institution. It also requires that the parties maintain a record of where essential records, including source records, are located, and that storage systems support identification, version history, search, and retrieval.

In the EU, the Clinical Trials Regulation requires the sponsor and investigator to archive the content of the clinical trial master file for at least 25 years after the end of the clinical trial. European Medicines Agency (EMA) TMF guidance reinforces the need for organized, contemporaneous, secure and inspection-ready TMF management, including appropriate controls for electronic TMFs.

In the US, Food and Drug Administration (FDA) regulations require sponsors and investigators to retain specified clinical investigation records for the applicable FDA period, generally two years after marketing approval or discontinuation of the investigation.

FDA regulations recognize that a sponsor may transfer obligations to a service provider by written agreement. EMA guidance similarly expects service provider responsibilities for TMF activities to be expressly delegated and defined in writing. To the extent obligations are expressly transferred or delegated, the service provider may be responsible for those obligations.

As a reminder, different jurisdictions will also have applicable regulations, such as the UK Clinical Trial Regulations, 2025, and the Clinical Trials Ordinance in Switzerland.

How This Works Operationally

The study-level TMF plan and TMF index are the practical tools for turning the regulatory concept of essential records into operational expectations. They should identify which record types are expected for the trial, where they are held, and who is responsible for them. They should address which essential records – such as protocols, approvals, signed plans, required curricula vitae (CVs) or similar files – will be filed centrally in the core TMF system with the view to best supporting contemporaneous filing, version control, search, retrieval, reconciliation, and inspection readiness. Records that are inherently system-based, dynamic or investigator-controlled may be better maintained in their authoritative system or repository, provided they remain accessible, readable, secure and complete for the required retention period and are clearly mapped in the TMF.

Source records are essential records. Those relating to the investigator's/institution's responsibilities should remain under their control, including where they are maintained in a sponsor or service provider system. The system arrangements should preserve the investigator/institution's continuing access to, and ability to maintain and retain, the complete source records and relevant metadata. This is especially important where records contain participant-identifying information, such as medical notes, signed consent forms, or subject identification code lists. Sponsors and service providers should not ordinarily receive participant-identifying site records unless there is a clear and appropriate basis within the study model, consent materials, contracts, data-protection framework, and applicable law.

Where multiple service providers may be involved, the TMF plan should identify where relevant essential records are maintained, including any study-specific system configuration or validation records needed to evidence trial conduct or data reliability, and how those records can be accessed and retrieved. Other system-development and validation records may remain with the relevant technology company or service provider under the applicable quality and retention arrangements.

At close-out, the sponsor's system of record should be complete. In the ordinary model, sponsor essential records managed by a service provider are filed in, or transferred into, the sponsor's system of record so that the sponsor can meet its archiving obligations under GCP and regulatory requirements. A service provider should be treated as taking on long-term retention or archiving of sponsor essential records only where that responsibility is expressly agreed in writing and operationally scoped, including archive content, access, inspection readiness, retention period, cost model, storage location, quality assurance measures, security controls, data-protection roles, and return or destruction process per applicable regulatory guidelines.

Electronic Systems, Metadata and Audit Trails

Modern trials rely on electronic systems such as Electronic Data Capture (EDC), Electronic Clinical Outcome Assessment (eCOA)/ Electronic Patient-Reported Outcome (ePRO), Electronic Consent (eConsent), imaging, central laboratory, Interactive Response Technology (IRT), Clinical Trial Management System (CTMS), and Electronic Trial Master (eTMF) Platforms. These systems generate documents, data, metadata, and audit trails. The important question is not whether the information exists in an electronic system, but whether it is needed to evaluate trial conduct in relation to GCP and regulatory compliance or the reliability of trial data.

Trial data, relevant metadata, and audit trails may be essential records. An audit trail showing initial entry and changes to data values, who entered or changed a data value, when and why, may be integral to the reliability of the underlying data. It should not be lost through a flattened export, system decommissioning or end of a hosting contract. If the live system will not be maintained for the required period, the parties should implement a validated migration, certified export or archive solution that preserves the data, relevant metadata and audit trail in a readable and inspection-ready form.

Not all system-generated material is an essential record. Infrastructure logs, enterprise security logs, back-up logs, disaster-recovery records and general performance data may support system operation and

security rather than trial reconstruction. Where they are not needed to evidence trial conduct, data reliability, system validation, or delegated responsibilities, they should be managed as operational or quality records under the relevant party's own retention schedule.

Frequently Asked Questions

Under ICH GCP, do long-term clinical trial record-retention requirements apply to every project record handled by a sponsor or service provider?

No. Long-term GCP regulatory retention requirements apply to the relevant TMF content and other required essential records, not automatically to every record generated, received, or handled by a sponsor or service provider. Other sponsor/service provider-held records – such as operational records, quality records, system logs, working files, correspondence, copies, and back-ups – should be managed under the applicable retention pathway unless they constitute essential records.

Are all essential records physically stored in a single centralized TMF system?

No. The TMF should identify, control, and make retrievable the essential record set, but every essential record does not have to be copied into one eTMF as a standalone file. A practical rule of thumb is: file static, document-like essential records in the TMF where practical; cross-reference dynamic, system-native or investigator-controlled records where that is the better authoritative source; and always ensure the TMF identifies where each essential record is and how it can be retrieved.

Are all research personnel CVs and training records essential records?

No. The question is whether the individual performed significant trial-related activities and whether the record is needed to evidence qualification or trial-specific training for those activities. For investigator/institution site personnel, this is usually reflected through the delegation log and associated qualification/training records. For sponsor and service provider personnel, the relevant roles should be identified through the TMF index, TMF plan, and related processes. Where CVs or training records are required, the focus should be on the relevant qualification evidence and trial-specific training, rather than every CV update or general corporate/system training record. Treating every operational team member's CV or training record as essential can create unnecessary long-term retention, privacy and inspection burden.

What if post-studycompletion a site asks a service provider whether archived records can be destroyed or transferred?

Investigator/institution controlled essential records, including source records and participant-identifying information, should remain under the investigator/institution's control, including where they are maintained in a sponsor or service provider system. The arrangements should preserve the investigator/institution's continuing access to, and ability to maintain and retain, those records for the applicable retention period. In accordance with ICH E6(R3) and regulatory requirements, destruction or transfer should be managed through the site's own institutional archive process and applicable regulatory, ethics, consent, and local legal requirements. Sponsors and service providers may help confirm study-specific information where available but should not ordinarily take custody of participant-identifying site records or decide whether those records may be destroyed. Where the relevant study information cannot be confirmed, the records should generally remain subject to the site's own archive governance process.

How should broad service provider contractual retention clauses be applied?

Clauses requiring retention of trial records for long periods should be interpreted alongside ICH E6(R3), regulatory requirements and the underlying record-keeping framework. Essential records should be captured in the appropriate part of the TMF and archived for the applicable period. Source records should remain with the investigator/institution. Service provider operational records, working files, logs, back-ups and correspondence should not automatically be converted into sponsor essential records. Relevant regulatory guidance should also be considered, including section 3.2 of the EMA "Guideline on the content, management and archiving of the clinical trial master file", which addresses service providers. In practice, these issues are best resolved during clinical trial start- up through the TMF plan, TMF index, filing model, role allocation, system-of-record decisions, and close-out/archiving process.

Practical Operating Model

- Define the study-level TMF plan and TMF index at start-up, including what is required, not required, or not applicable.
- Distinguish sponsor-controlled TMF records, investigator/institution records, source records, service-provider operational records, system data, metadata, copies, and express archive arrangements.
- File static, document-like essential records centrally where practical.
- Use controlled cross-references for system-native or investigator-controlled records, with clear location and access information.

- Confirm at close-out that required records, data, metadata, and audit trails are complete, readable, secure, retrievable, and linked to the relevant data elements.
- Transfer sponsor essential records into the sponsor's system of record unless a long-term service provider archive role is expressly agreed and scoped.
- Apply separate retention schedules to non-essential operational, quality, legal, HR and system records.
- Document judgement calls, especially where records are borderline, risk-based, or intentionally excluded from the TMF.
- Consider appropriate continuity and exit arrangements for systems holding Essential Records, including any necessary export, migration, or decommissioning arrangements.

Conclusion

Clinical trial record keeping works best when it is disciplined, proportionate, and lifecycle-based. Required essential records must be identified, controlled, retained, and retrievable. At the same time, not every record associated with a trial should automatically be treated as an essential record or retained for the longest regulatory period. The defensible approach is to make a documented study-level judgment, connect each record to its purpose and system of record, and ensure that the retained record set remains complete, secure, readable, and inspection-ready for the required period.

References and Source Materials

This paper draws on the principal GCP, EU/EMA, and FDA materials listed below. These references identify the main regulatory and guidance sources underpinning the discussion and are not intended to be an exhaustive statement of all potentially applicable clinical trial, data protection, contractual, ethics, health-record, or local-law requirements.

- **ICH E6(R3) Good Clinical Practice.** ICH Harmonised Guideline, Guideline for Good Clinical Practice E6(R3), final version adopted 6 January 2025, including Appendix C on Essential Records.
- **FDA E6(R3) Good Clinical Practice Guidance.** Final (Level 1) FDA Guidance for Industry, E6(R3) Good Clinical Practice, issued September 2025.
- **EU Clinical Trials Regulation.** Regulation (EU) No 536/2014, including Article 57 on the clinical trial master file and Article 58 on archiving of the clinical trial master file.
- **EMA TMF Guideline.** EMA, Guideline on the content, management and archiving of the clinical trial master file (paper and/or electronic), EMA/INS/GCP/856758/2018, adopted 6 December 2018.
- **EMA Computerised Systems Guideline.** EMA, Guideline on computerised systems and electronic data in clinical trials, EMA/INS/GCP/112288/2023, adopted 9 March 2023.
- **EMA GCP inspection guidance.** EMA guidance for the conduct of Good Clinical Practice inspections, including Annex I for investigator sites and Annex IV for sponsors and service providers.
- **EMA Q&A on Good Clinical Practice.** EMA Q&A materials addressing GCP responsibilities, delegation, contracts and related inspection expectations.
- **FDA IND regulations.** 21 C.F.R. Part 312, including21 C.F.R. §§ 312.52, 312.57and312.62 on transfer of sponsor obligations, sponsor recordkeeping and investigator recordkeeping.

- **FDA Electronic Records and Source Data Guidance.** FDA guidance on electronic systems, electronic records, and electronic signatures in clinical investigations; FDA guidance on electronic source data in clinical investigations; and Electronic Systems, Electronic Records, and Electronic Signatures in Clinical Investigations: Questions and Answers; Guidance for Industry. Final FDA Guidance, issued October 2024; Electronic Source Data in Clinical Investigations; Guidance for Industry. Final FDA Guidance, issued September 2013
- **FDA Investigator Responsibilities Guidance.** FDA Guidance for Industry, Investigator Responsibilities – Protecting the Rights, Safety, and Welfare of Study Subjects, October 2009.
- **UK Clinical Trials Regulations.** The Medicines for Human Use (Clinical Trials) Regulations 2004, as amended by The Medicines for Human Use (Clinical Trials) (Amendment) Regulations 2025, UK Statutory Instrument 2025 No. 538, fully effective from 28 April 2026.
- **Swiss Clinical Trials Ordinance.** Ordinance of 20 September 2013 on Clinical Trials with the exception of Clinical Trials of Medical Devices (Clinical Trials Ordinance, ClinO), SR 810.305, including Article 45 on archiving.