FAQs About eTMF Archiving

The Trial Master File (TMF) plays a pivotal role in regulatory compliance and trial integrity by serving as a cornerstone of documentation. Comprehensive TMF compliance entails the maintenance and storage of critical documentation, even after the conclusion of a trial. Retaining this documentation after study close-out is referred to as electronic archiving, or eArchiving. This is a key step in meeting the regulatory standards set by the Food and Drug Administration (FDA) and the European Medicines Agency (EMA). A good archival workflow safeguards data integrity and streamlines the audit process.

The following FAQs explore the basic facts about the archival process. It is important to consider each of the following points when establishing an archival plan or considering the adoption of an archive solution.

1. What is archiving?

Archiving in the context of clinical trials refers to the organized, secure collection and storage of essential trial documents and data that occurs after a study concludes. Also called the electronic Trial Master File, this practice safeguards the consistency and reliability of trial information, ensuring it is accessible for inspection and review by regulatory authorities, such as the FDA in the United States and the EMA in Europe. This process also confirms compliance with regulation, data integrity, accuracy, long-term storage, and preservation, and generally represents the legal and ethical responsibility and obligation of the trial sponsor to all trial participants and the scientific community.

2. Is archiving a study expensive?

The eArchival of a clinical study does not need to be expensive and can be cost-effective with the right strategies. Efficient document management throughout the study, utilizing affordable digital storage solutions, and choosing long-term formats resistant to obsolescence help keep costs down. Ensuring regulatory compliance from the outset avoids expensive retrofits. Automated processes and scalable storage also contribute to cost efficiency, ensuring that expenses align with the actual needs for data preservation and accessibility for audits and regulatory reviews.

3. What are the main goals of an eArchive?

The main goals of an eArchive in the context of clinical trials revolve around ensuring data integrity, maintaining regulatory compliance, facilitating audit readiness, and mitigating risks. Data integrity is paramount; eArchiving preserves the accuracy, completeness, and reliability of trial data, ensuring that it remains unaltered for reliable use in regulatory submissions and audits. Regulatory compliance is achieved by adhering to the stringent guidelines set by bodies such as the FDA and EMA, maintaining all trial documents and data in accordance with regulation and guidance.

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Audit readiness is another key objective. An active eArchive is structured to allow for efficient review and verification by regulatory agencies or internal auditors. Lastly, risk mitigation is addressed through eArchiving by establishing secure storage strategies that protect against data loss, corruption, and obsolescence. This safeguards the electronic Trial Master File's integrity, ensuring that essential trial documents remain accessible at all times, which is crucial for the continuity and credibility of the trial. In summary, an eArchive serves as a foundation for a trustworthy and compliant clinical trial process.

4. What are the benefits of long-term storage via eArchive?

Certain regulations, such as those from the FDA and EMA, require clinical trial documentation to be retained for a specific timeframe post-marketing approval, so the eTMF must stay inspection-ready until the agency inspection period is complete. Long-term storage via eArchive ensures regulatory compliance by preserving clinical trial documents for this required period in accessible, secure formats like CSV for metadata and PDF/A for documents. These open formats are designed for longevity and are widely accepted by regulatory bodies like the FDA and EMA. Additionally, eArchiving provides enhanced data protection with encryption, safeguarding sensitive information against unauthorized access and thereby maintaining data integrity and confidentiality long-term.

5. Should I keep multiple copies of my eTMF?

Yes, maintaining multiple copies of the eTMF is a best practice for data redundancy and security. It ensures that if one copy is lost or corrupted, others remain intact. This redundancy is critical for disaster recovery and maintaining compliance with regulatory requirements. It's advisable to store copies in different locations, with at least one off-site, to mitigate risks such as natural disasters or system failures. Additionally, regular backups and version control should be implemented to preserve the integrity and history of the eTMF documents.

6. Why is an eArchive important for inspection readiness?

An eArchive is vital for inspection readiness as it ensures that clinical trial data and documents are stored in a way that meets the regulatory standards of eTMF readiness at all times. This is especially pertinent before and after a product's marketing authorization when scrutiny is most intense. An eArchive facilitates efficient document retrieval, which is crucial during regulatory inspections, allowing for quick and precise access to necessary information. It also assures the integrity, accuracy, and reliability of the stored data by demonstrating that trial documents have remained unaltered. Moreover, eArchival systems come equipped with robust access controls, ensuring that sensitive trial information is accessed only by authorized personnel. This not only enhances the security of the eArchive but also instills confidence in regulatory bodies that the data is protected from unauthorized access and manipulation. The implementation of a well-structured eArchive, therefore, is integral to maintaining continuous readiness for regulatory inspections and audits, reinforcing the credibility and compliance of the clinical trial process.

7. What capabilities are important to enable during an agency inspection?

It is important that the eArchive format be flexible enough to enable inspection readiness at all times. When inspectors look at the eTMF, they expect document retrieval and viewing through powerful search and indexing features and a meticulously organized index of documents with metadata and version control, allowing authorized personnel to efficiently locate and present documents to auditors. Safeguarding data integrity is paramount, as archived documents remain unaltered and shielded from unauthorized changes. Through access controls, encryption, and robust audit trails will assist in enhancing both security and accessibility. This will allow the archive to meet the stringent ALCOA principle (attributable, legible, contemporaneous, original, and accurate). Moreover, the archived eTMF serves as a historical record of the trial, aiding auditors in assessing regulatory compliance at each stage.

8. How long should I keep an eTMF archive?

While most audits happen within the first few years after a clinical trial ends, European regulatory bodies require an available eTMF archive for 25 years. There is also the possibility of new discoveries making the trial research more relevant and data more important. For more information on how long you should keep an eTMF archive, you can access the EMA guidelines (EMA/INS/GCP/112288/2023) as well as the current standards body, CDISC, here.

9. Are you using the CDISC TMF Reference Model?

Sustaining an eTMF is an active state that provides users with the flexibility to make edits, introduce new documents, and remove existing files. While this flexibility is advantageous for ongoing trial management and document updates, it concurrently introduces a potential risk to the overarching integrity of the database. The dynamic nature of an active eTMF environment opens avenues for errors, version control challenges, and the inadvertent loss of critical information. Striking the right balance between a dynamic eTMF for operational efficiency and the need for a stable, auditable record is crucial to mitigate risks and ensure the integrity of the trial data throughout its lifecycle.

10. Should I use a paper archive?

The decision to use a paper or electronic archive depends on factors like familiarity, accessibility needs, and regulatory requirements. Paper archives offer tradition and accessibility but face challenges in terms of limited access, risk of loss, and storage space. Electronic archives provide efficiency, advanced search capabilities, and security measures but may involve initial implementation costs and technology dependence. Consider your specific requirements and resources to determine the most suitable approach.

11. How should documents that are no longer needed be disposed of?

Establishing a comprehensive data retention plan is not only advisable but also integral to adhering to regulatory guidelines and ensuring the responsible management and archival of TMF documents. When maintaining documents in electronic formats, it is essential to align with regulatory standards such as those outlined by the EMA. The EMA guidance on the content, management, and archival of the TMF emphasizes the importance of retaining original documents in their authentic formats unless they have been replaced by certified copies. If original documents are destroyed, the guideline states that a record of the destruction must be kept along with the certified copy.

A well-crafted data retention plan not only harmonizes with regulatory guidance but is also a proactive strategy for optimizing storage, minimizing redundancy, and aligning with evolving industry practices. The adherence to guidelines, such as those set forth by the EMA, ensures that the electronic management and archival of TMF documents are conducted in a manner that is compliant and transparent, safeguarding the integrity and accessibility of trial-related information throughout its life cycle.

12. How do I know if my eArchive has integrity?

Users can help establish eArchive integrity by implementing the following:

- Clear policies: Clearly define document management, outlining processes for creation, storage, and retrieval.
- Version control: Implement a robust version control system to keep track of document changes and ensure accessibility to the latest versions.
- Regular audits and integrity checks: Conduct routine internal audits and checksums to assess the integrity of the eArchive, examining access logs and document versions.

Additionally, a cryptographic hash function or similar encryption approach can be leveraged to verify that the archived content has not been altered.

13. Who should manage my eArchive?

- Internal archivist: Having an in-house archivist who can perform the general functions of setting up purge dates and managing audits will be ideal for keeping regulatory bodies up to date in the quickest way possible.
- eArchive Partner: Having an eArchive managed by experts who perform yearly integrity checks and can retrieve the documents from long-term storage, when necessary, will typically improve efficiencies over just having an in-house archivist alone.

eArchiving is not just about document storage—it is a cornerstone of regulatory compliance, data integrity, and inspection readiness in the realm of clinical trials. It is therefore important for organizations to consider approaches to long-term document storage, including the advantages of electronic over paper archives. Successful organizations have robust systems in place to ensure that clinical data is safeguarded in a retrievable way both during and after the conclusion of trial conduct.

To learn more about other best practices for archiving your eTMF, reach out to us at info@trialinteractive.com.