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PhlexEarchive: The Right Solution for Electronic Archiving of TMF Content

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Introduction

Many sponsor organizations have already recognized the value of moving from paper to electronic Trial Master Files (eTMFs). But few sponsors have taken a more holistic approach to the TMF lifecycle and looked at the entire process from study start-up through archiving of the TMF in electronic format, also known as e-archiving. The recurring value of managing, tracking, maintaining and accessing electronic files should not stop at the point of archiving. All of the challenges of managing an active paper TMF carry through to a paper archive. All of the benefits of an electronic TMF also carry through to the electronic archive.

As companies look to move their compliance assets to secure, long-term storage, it is important to consider ongoing compliance requirements, security, accessibility, efficiency and costs of archiving TMF content in a digital format.

Traditional Approaches to TMF Archiving

Paper Archiving

Paper archiving is the most common of traditional approaches to archiving. Companies develop and implement controlled processes to manage the physical storage of paper, which is usually sent to an off-site storage facility. The paper files must be identified and tracked in a manner that supports quick access and retrieval by authorized personnel. This process is labor intensive and expensive to create, manage, track and maintain. It confines teams to serial processes and inhibits global collaboration. It slows down any type of content driven processes and does not support process optimization for archiving of TMF files. Because of these same attributes, paper also impairs compliance and archiving processes in a similar fashion. For all of these reasons, many companies are transitioning from legacy paper-based processes to electronic processes that include electronic archiving.

Online Archiving

Many organizations attempt to use their live on-line systems to archive their TMF content online. Though this approach alleviates the challenges of paper, it can be expensive and requires ongoing investments in costly servers and storage.

For companies with large amounts of archive data, this approach can also be challenging for routine system users because it clutters user interfaces with lists of files and choices that are rarely accessed in their daily activities. In addition, the large amounts of data can slow system performance. Online data also requires security controls to be in place so that access is managed according to archiving policies, and finally on-line information is open to accidental or deliberate change or even deletion. Archive information isn't frequently accessed but when it is needed, it usually needs to be made available quickly to support inspection activities.

Offline Electronic Archiving

The final and most cost effective approach is to store the archived electronic TMF files offline. By leveraging the benefits of electronic files in an offline model, users can archive their TMF content, ensure its protection and rely on quick retrieval to support compliance. This approach maintains all of the benefits of using electronic files in the archive while removing the challenges and costs of online storage.

Benefits of an Electronic TMF Archive

Compliance

The primary reason for creating a TMF is to support compliance requirements. This main purpose does not change as the TMF moves through its lifecycle. A digital archive helps sponsors to ensure continued compliance while also protecting their previous investment in the quality and accuracy of the TMF content by applying rules-based controls and enabling global access. Electronic files also position sponsors to support compliance activities such as inspection audits with quicker responses. Prompt and accurate responses to inspector inquiries position the sponsor to move through inspections with relative ease. Relying on paper doesn't necessarily support this vision since paper can only be stored and accessed in one location at any given time. Scanning or duplication and transport of paper files add time and costs as well as opportunities for error in reproduction and delivery of compliance information.

In addition, regulatory authorities now accept the use of electronic media for archiving and provide guidance on issues that should be considered: UK S.I. 2006 No. 1928, §31A Trial master file and archiving; EU Rules governing medicinal products, Vol. 10, Ch. 5 Recommendation on the content of the TMF and archiving and the principles as defined by the FDA for Electronic records and Electronic signatures (21 CFR Part 11).

Security

Profile driven access continues throughout the archive retention period ensuring controlled access and protection of compliance assets. In addition, reliable electronic archiving facilities maintain redundant electronic systems where copies of documents are stored in multiple locations to safeguard against destruction or damage of the TMF content while also enabling rapid restoration of electronic files in the event of a catastrophe. Security access controls can be designed to support various activities throughout the assigned retention period. In addition, industry standard electronic archiving formats protect against software obsolescence and ensure accessibility well into the future.

Offline electronic archiving also reduces the risk that archived information would be modified or changed in any way during routine TMF maintenance activities. If the data is online, there is a greater chance of authorized users inadvertently changing the information and potentially impacting compliance. Offline storage requires the user to specifically request electronically archived content to be loaded for review.

Global Accessibility

Online and offline electronic archives support access to archived content that can be made available upon request, around the globe. Electronic archives enable rapid remote access that may be required to support regulatory authority inquiries and inspection activities. Requesters and reviewers of information can have the content come to them instead of having to travel to review paper files. This saves time and resources but also helps the sponsor to quickly and efficiently demonstrate compliance with content that can be retrieved using simple searching techniques. This proactive approach to compliance across the entire TMF lifecycle is important in the development of open and honest discussions with health authority officials.

Efficiency

Electronic archives provide an excellent mechanism for accessing TMF content quickly. Searching through an entire study file using key attributes is far quicker than combing through boxes of paper. Imagine the following scenario: You are participating in an inspection audit and need to retrieve 25 documents. In the paper world, 10 minutes per file would be a conservative estimate for locating the specific files within the physical archive, retrieving the documents, making copies and presenting the copies to an inspector. That equates to 250 minutes or over 4 resource hours to retrieve the documents. From a electronic archive, these same documents could be retrieved in a matter of seconds using simple keyword searches and indexing information (metadata). In addition, documents can be viewed on-line instantly and don't require time for copying, collation, etc. The resource savings are significant but the real value lies in the ability to respond to inspector inquiries quickly and thoroughly.

Costs

The costs of electronic archiving are minimal compared to paper storage. However, whether you choose to archive online or offline can impact this line item. Online storage is more expensive and can slow production system performance over time. Though the users can reap the benefits of electronic archives, the costs of maintaining the documents online (IT support, hardware, back-up and recovery processes for production systems) can be reduced by moving to offline storage, given the limited frequency of access required for archived files. Offline electronic storage is substantially less expensive and still provides compliance, security, accessibility and efficiency.

Archiving Requirement	Rationale (why it is important)
Compliance	Non-compliance may result in regulatory action by a health authority and may raise questions about other aspects of this or other studies. In addition to these risks, there are also costs associated with non-compliance and remediation.
Security	Insufficient security (physical and/or logical) raises questions about the TMF integrity, accuracy and compliance.
Global Accessibility	Inadequate accessibility slows inspection activities of health authorities around the world and raises concerns about continued compliance.
Efficiency	Inefficient approaches waste a sponsor's investment in TMF quality and their ability to respond quickly to health authority queries. Inefficiencies are also reflected in costs.
Costs	The costs of storing paper are high. The cost of storing documents online is cheaper but still higher than offline storage. The cost of offline electronic archiving is the least expensive and the savings over time can be considerable.

PhlexEarchive Solution

The PhlexEarchive Solution is a cost effective, offline archiving model that protects the sponsor's investment in an electronic TMF while enabling the organization to continue to realize all of the benefits of electronic archiving within the TMF lifecycle.
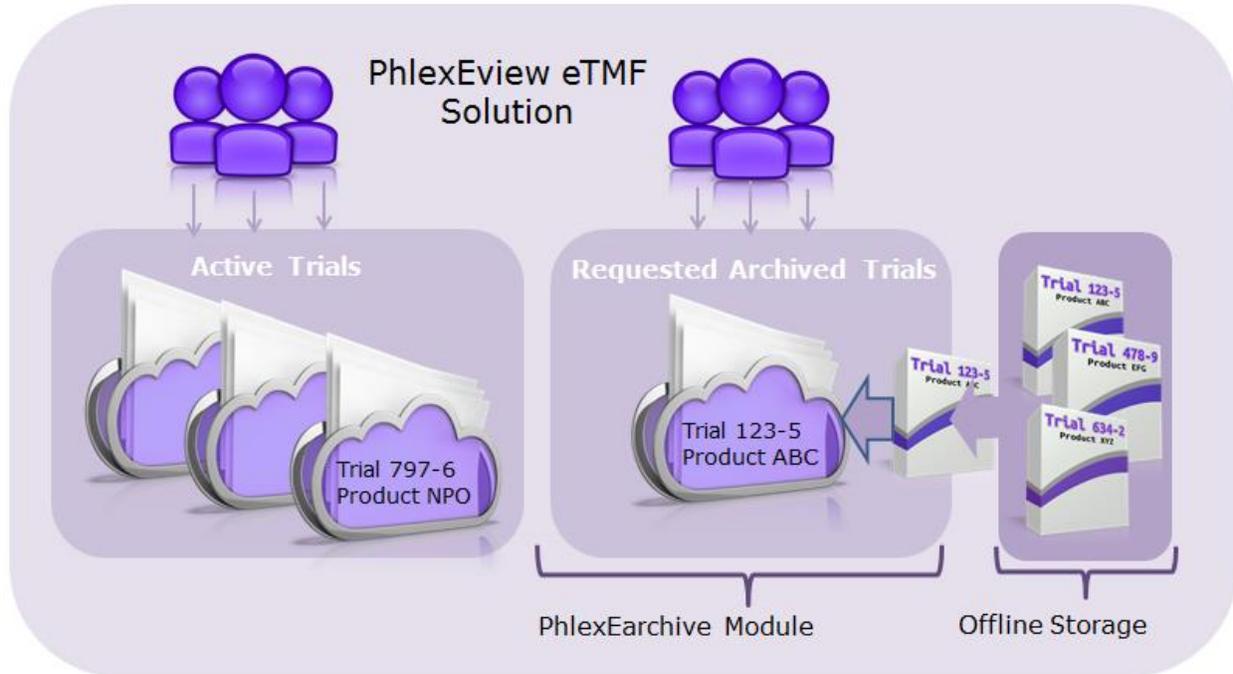

If a sponsor is already using PhlexEview, archiving TMF content into PhlexEarchive ensures that the quality investment that they have already made in their eTMF is protected as the content is moved to an electronic archive. It also provides cost savings for long-term storage compared to online storage options.

The process for archiving and requesting access to this information is described below.

1. TMF content is archived in PDF/A format with an associated xml backbone file
2. Users request a retrieval of an archived study
3. A digital copy of the study TMF content (documents and meta-data) is made available online via PhlexEarchive within 24 hours of the request
4. Permissioned users/Inspectors can then search and review the content online within the PhlexEarchive module

5. When review is complete, the information is deleted from the module but remains in secure offline storage.
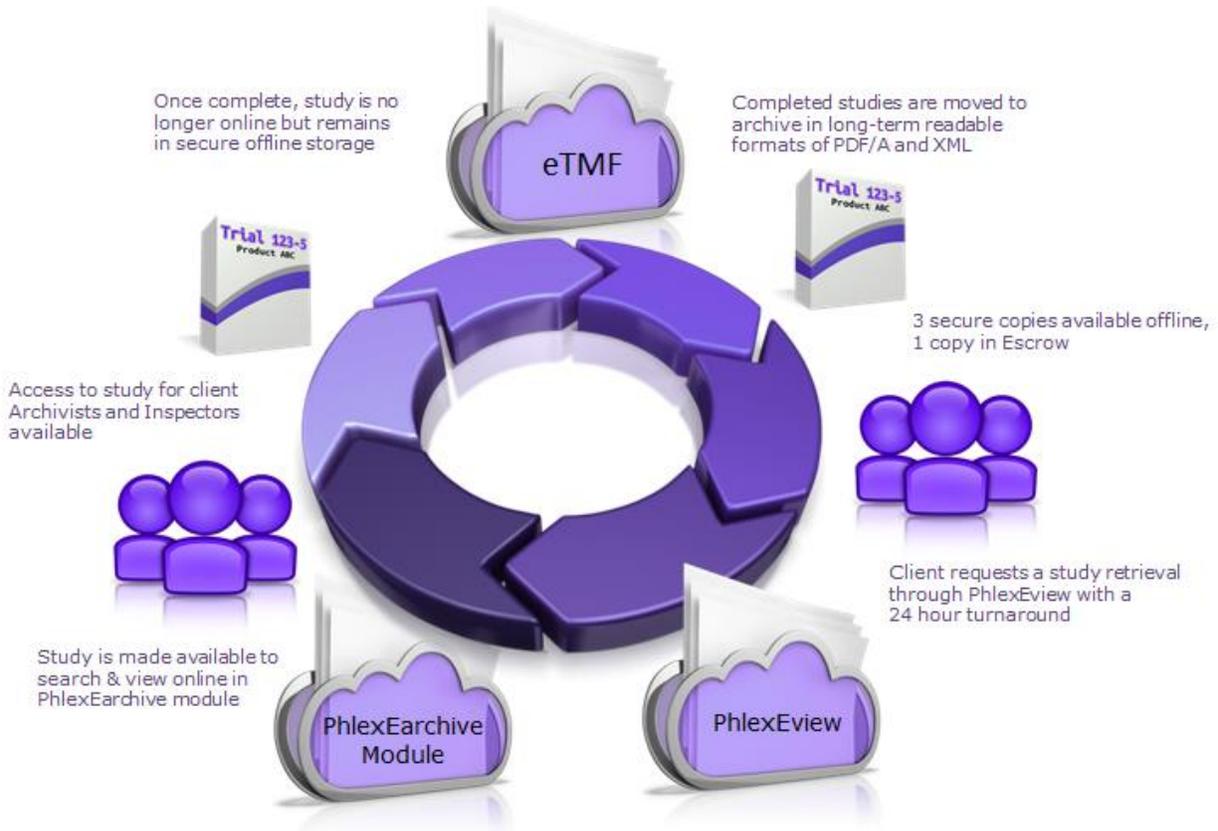
If a company is not currently using PhlexEview to manage their TMF, Phlexglobal offers services to import the documents and data into PhlexEarchive.

Compliance

The PhlexEarchive Solution was designed to maintain compliance while also providing a safe and efficient archiving approach for TMF content. PDF/A technology ensures page fidelity, XML backbone assists in searching and maintains the original structure (TMF Reference Model) and the use of file level checksums confirm the individual file integrity over time.

Security

The PhlexEarchive module is only accessible to authorized users with proper permissions. An inspector role can be configured to support inspection reviews by regulatory authorities. Controls can be configured so that the inspector only has access to specified studies and permissions can be removed once the inspection is complete.

Global Accessibility

The PhlexEarchive module and the retrieved archive content can be accessed by any user with proper authority, from anywhere in the world via the internet. This removes the need for users to travel to a central file location or to request duplication or scanning of archived TMF content.

Efficiency

The PhlexEarchive module supports quick retrieval of archived TMF content. Once loaded into the PhlexEarchive module, the TMF content can be reviewed quickly using searches, full page views and navigation based on the TMF Reference Model. This allows sponsors to promptly respond to inspection queries.

Costs

The PhlexEarchive offline archiving model offers significant costs benefits in addition to the compliance, security, accessibility and efficiency benefits previously described. Phlexglobal estimates that long-term storage costs for one paper file are 36 times higher than those for storing the equivalent digital file offline. This offline storage estimate illustrates a cost savings over online storage as well. Phlexglobal estimates that long-term, offline file storage is approximately 20% of typical online storage costs[1].

These tangible costs can be significant and are compounded as more studies are conducted over time. Yet there are even greater costs that must be considered when looking across the TMF lifecycle. The cost of non-compliance should be the greatest real cost driver in developing an archiving approach.

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[1] Paper storage cost estimates based on current market pricing for offsite, paper archives. Online and offline estimates compare hosted system storage with offsite, electronic archiving prices.

Sponsors that have implemented successful TMF strategies cannot afford to waste the investment with a less-than-ideal archiving strategy. Archiving should be considered in the context of the TMF lifecycle rather than as a separate function. As TMF content moves through the lifecycle to the final archiving stage, it is important to remember that health authorities frequently inspect completed studies that have already been archived. Quick and accurate retrieval of the study information is important. Content that takes a long time to retrieve will raise questions from the inspector. This is true while the TMF is active and continues to be true when the TMF content moves to archive. The cost of non-compliance can be great but a sound eTMF archiving strategy can alleviate this risk.

Conclusion

The PhlexEarchive solution connects disjointed components of the TMF lifecycle to ensure continued regulatory compliance. PhlexEarchive offers offline digital archiving that supports compliance objectives while providing a quick and efficient way to access archived TMF content in a timely manner. PhlexEview and the PhlexEarchive module enable sponsors to take a systematic approach to TMF management from cradle to grave while also reaping the benefits of electronic files across the lifecycle. PhlexEarchive was designed to address the compliance, security, global accessibility, efficiency and cost requirements that are key elements of any trial master file strategy.

Archiving Requirement	Rationale (why it is important)
Compliance	Non-compliance may result in regulatory action by a health authority and may raise questions about other aspects of this or other studies. In addition to these risks, there are also costs associated with non-compliance and remediation.
Global Accessibility	Inadequate accessibility slows inspection activities of health authorities around the world and raises concerns about continued compliance.
Efficiency	Inefficient approaches waste a sponsor's investment in TMF quality and their ability to respond quickly to health authority queries. Inefficiencies are also reflected in costs.
Costs	The costs of storing paper are high. The cost of storing documents online is cheaper but still higher than offline storage. The cost of offline electronic archiving is the least expensive and the savings over time can be considerable.

The PhlexEarchive Solution addresses the challenges of TMF archiving by providing the following benefits:

- A secure and efficient alternative to paper archiving that reduces the inhibitors that paper naturally imposes on content processes.
- A cost effective alternative to online archiving that enables companies to continue to reap benefits from electronic processes in the archiving stage.
- A proven technology and associated processes for managing the transition of TMF content from an active to an archived state.
- A straightforward solution that offers compliance and control while reducing TMF archiving costs.
- An effective solution that supports rapid retrieval of archived content while reducing the resources required to support these critical activities.

To learn more about Phlexglobal's flagship product, PhlexEview, and the PhlexEarchive module, please visit our website at www.phlexglobal.com.