ArisGlobal

# Exploring Enhanced Clinical Collaboration in Modern eTMF Systems

## How new standards can ease the technology burden for Clinical teams

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# Trial Master File Compliance Falls Short of Industry Goals

Managing trial master file (TMF) documents continues to frustrate people in clinical trial operations.

The most recent inspections report from the UK health authority reveals that the TMF essential documents cause the most findings within commercial sponsor organizations[1].

It wasn't supposed to be this way. For the past several years, technology vendors promised their electronic Trial Master File (eTMF) solutions would produce better results. Some of these systems used proprietary standards that blocked interoperation to limit risk. Others used common file sharing methods that failed make transfers fully compliant. No eTMF system had the right capabilities to meet the growing need for collaboration in research.

Meanwhile, clinical operations and technology leaders were juggling a greater number of research partners, broader regulatory burdens, and more nuanced approaches to fighting disease. The growth in research partnerships became a top priority as there is a direct link between high levels of collaboration and filing approval, a recent study shows[2].

# New Data Standard Facilitates Collaboration

Fortunately, a new industry standard holds significant promise for all stakeholders who contribute to the TMF. Known as the **eTMF Exchange Mechanism Standard (eTMF EMS)**, it bridges cross-platform gaps between clinical trial technology systems.

This paper explores the current state of eTMF technology and the new optimism for escaping the burden created by proprietary, dysfunctional file sharing methods. It describes industry perspectives on how the new data standard could enhance collaboration and improve TMF performance.

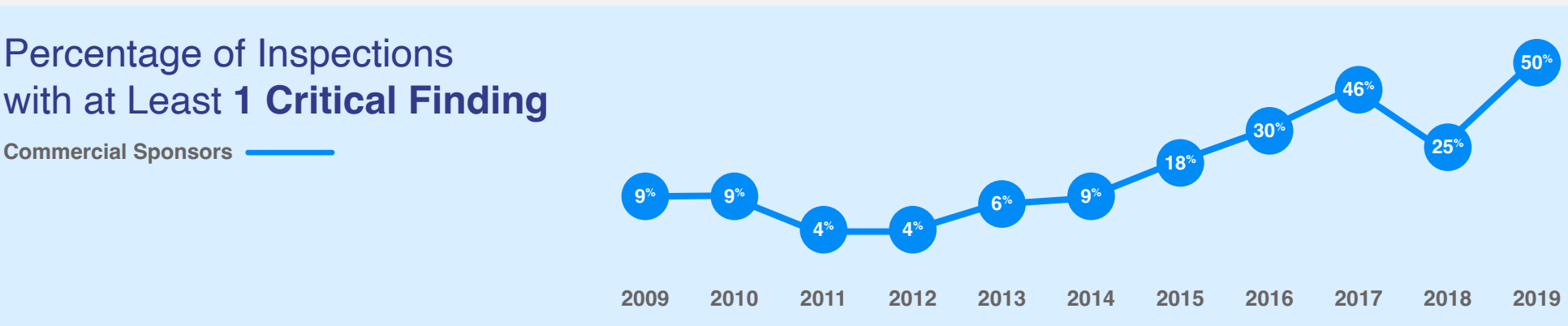
**eTMF Exchange Mechanism Standard** allows vendors to build a component that standardizes all TMF content and metadata for easy integration.

## eTMF adoption spreads yet GCP inspection findings increase

The new eTMF Exchange Mechanism Standard is ultimately designed to help clinical teams meet standards for Good Clinical Practices (GCPs). The trial master file should contain all information to ensure **"the integrity of clinical data on which product approvals are based and to help protect the rights, safety, and welfare of human subjects"[3].** Because the story of a clinical trial typically involves more collaborators today, the standard was needed to enhance cross-platform interoperation.

The urgency for interoperability has played out in regulatory findings year after year. The UK Medicines and Healthcare Products Regulatory Agency has been publishing results of its GCP inspections for over a decade. As referenced above, the latest version **shows the percentage of inspection findings with at least one critical finding for commercial sponsors increased from 4% in 2012 to 50% in 2019.** According to the report, "Recording and Keeping Essential Documents in the Trial Master File" is the number one source of major findings.

Besides the obvious compromise to trial integrity, TMF failures in timeliness, quality, or completeness create deeper issues. Findings can delay a trial or, in the worst-case scenario, stop it outright. Clinical staff must pause to answer the audit, research issues, and explain the findings. Much, if not all, of this process is manual, including updating documentation, amending processes, and retraining.



## Change Triggers Uncertainty and Optimism for Clinical Stakeholders

Traditionally, clinical sites have relied on sponsors or CROs to handle all TMF document management. Recent trends, however, point to sites adopting their own technology to streamline their efforts. Sites are becoming more tech-savvy with the adoption of electronic Investigator Site File systems, also known as e-regulatory binders. This is a positive development. But it can come with an unexpected workload when TMF teams must adopt proprietary standards and new processes to get aligned on a trial.

## eTMF Solution Closes the Clinical Data Gap

The eTMF Exchange Mechanism Standard eases this burden by bridging the gap between different platforms. It was developed by the DIA Document & Records Management Community, the same group

that created and maintains the **TMF Reference Model**. The eTMF exchange standard allows researchers to collaborate regardless of their individual technology solutions[4]. The standard facilitates an easy, open exchange of TMF content through a common data structure.

The standard uses an open API to transfer TMF content between different systems. Easy to adopt, the standard facilitates necessary integration, eliminating technology silos and bottlenecks, saving time and resources.

## Benefits of early eTMF EMS adoption

The eTMF Exchange Mechanism Standard (eTMF-EMS) is an essential addition to any eClinical system solution along with the TMF Reference Model. These industry standards not only increase collaboration but solve for the major friction points that Clinical teams face when conducting trials and sharing information.

### No added burden for clinical sites

With the open eTMF Exchange Standard, sites are not forced to onboard new technology in order to accept a study. They can use the simple standard with their existing technology. This means easy, real-time interaction with other stakeholders and more freedom to follow their own technical policies.

### Sponsors gain oversight and control

On the sponsor side, those with full outsourcing can be audit-ready, as the standard gives them their own system of record that is updated in real time. They can invite CROs into their eTMF while retaining control and gaining full transparency.

Sponsors using both outsourced and in-house resources can manage documents in real time, feed insights from clinical operations directly to data teams, and ensure that all systems interoperate, reducing IT headaches.

### Broader, stronger CRO service portfolios

For CROs, adopting the standard is a key differentiator. When CROs can tell clients they are ready to communicate seamlessly with client TMF systems with low interference and real-time information sharing, the competitive advantage is clear.

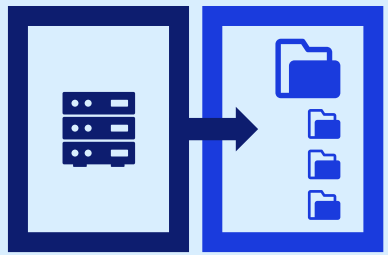
CROs are in a unique position to introduce new technologies faster than their sponsors. Providing partners with greater visibility, having enhanced capabilities, and increasing the CRO's own service offerings are critical advantagaes in a competitive landscape

ArisGlobal is not alone in its favorable assessment of the eTMF Exchange Mechanism Standard. The industry itself is embracing it, as shown by an April 2021 **survey conducted by the DIA standards group and referenced on page 8.**

# How the eTMF exchange mechanism standard works

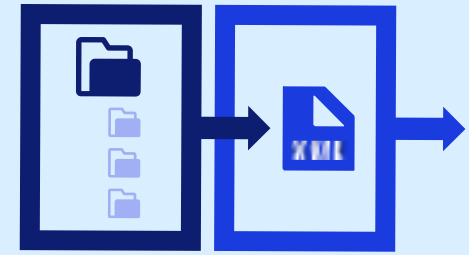
**1**

Exports eTMF artifacts to folder structure



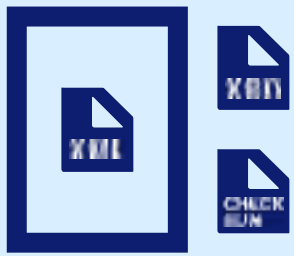
**2**

Adds XML Exchange File to enable transfer



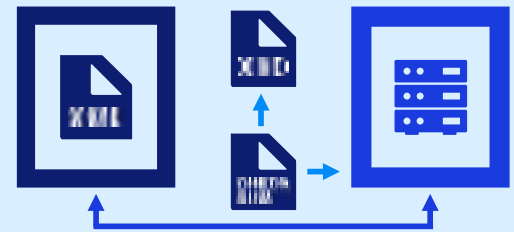

**3**

Validates transfer with Exchange XSD




**4**

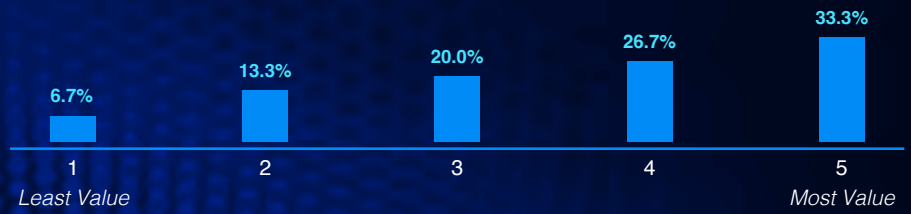
eTMF artifacts imported in real-time



# Change Triggers Uncertainty and Optimism for Clinical Stakeholders

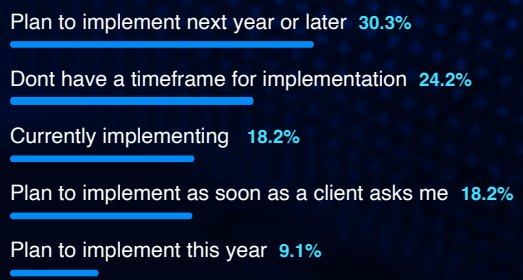
**Insights from the eTMF Exchange Mechanism Standard Survey**[5]

What would be the overall value to your organization if you were to use the eTMF-EMS to transfer interim TMF content?




Do you plan on (partially or fully) implementing the eTMF-EMS?


If you have not implemented the EMS, what is your timeframe for implementation?




Input from sponsors, CROs, sites, vendors, and integrators show widespread enthusiasm for the standard. Notably**, just 3.2% of respondents answered, "We already have a mechanism for exchanging content that works fine." The need is clear.**

DIA Document & Records Management Community conducted a survey of TMF stakeholders in 2021 to evaluate interest in the new eTMF Exchange Mechanism Standard.

The survey found a cautious approach to the new technology, as might be expected among clinical professionals. Slightly more than half of the respondents said they did not know of plans to implement the standard. Yet responses also pointed to optimism about the new exchange standard. Two thirds of them expected to gain high levels of value when using it to transfer interim TMF content.

The survey also revealed the top use cases that are of greatest interest to respondents. Approximately 65% saw the standard's value in transferring a final TMF file from a CRO to a sponsor, and more than half of respondents were interested in the standard's ability to ease archiving TMF content and metadata. On the transfer of interim TMF content, **80% of respondents noted that it would "improve quality/compliance," and 66.7% indicated it would "save time." An overwhelming 93.3% noted that clinical operations would gain business value with this use.**

Because of these benefits and others, nearly 56% of respondents planned on fully or partially implementing the eTMF Exchange Mechanism Standard, and 10.9% have already done so. By offering software that supports the standard, ArisGlobal is supporting industry preferences for making collaboration easy and more compliant.

## The Promise of End-to-End Clinical Collaboration

eTMF systems using  the standard can exchange TMF content in real time. This includes digital content archiving, security and access control, change controls, audit trails, and system validation per federal regulations and guidelines in the U.S. and the U.K.

On a practical level, eTMF facilitates real-time file sharing that improves inspection outcomes and compliance. Legacy eTMF systems have not delivered on promised compliance efficiency. In fact, they are getting in the way of needed collaboration. Industry consensus shows a strong desire for fully connected, real-time eTMF.

When ecosystem partners use the exchange standard to connect disparate technologies, meaningful connections and improved outcomes are possible.

There's clearly an evolution occurring, as eTMF systems change in function and scope to facilitate broader ecosystem integration. As the industry moves from scanning paper at one end of the maturity spectrum to real-time connectivity, a unified clinical platform is key. Integrating with a true end-to-end clinical solution that supports the eTMF exchange standard enables Clinical teams to manage data seamlessly, reduces the burden on clinical sites, and facilitates partnership between sponsors and CROs with real-time data access — all of which are crucial business advantages in a competitive market.

New efficiency and collaboration make all the difference in successful trials. This is particularly important when battling rare diseases and other complex conditions in which a broad range of partners bring their focus areas together to solve clinical puzzles.

# The Forefront of Industry Transformation

Supporting the emerging industry standard breaks down barriers, improves compliance, reduces compliance risks and findings, and reduces site burden. When these benefits are realized, site-friendly operations and patient-friendly outcomes result. As the first platform in the industry to support both EMS and eTMF, ArisGlobal's **LifeSphere eTMF** solution is at the forefront of this movement, helping to drive this important transformation for increased inspection-readiness. The entire clinical trial ecosystem will certainly be better served by this new era of collaboration and success.

Ready to view clinical collaboration and eTMF in action?

**Schedule a demo today**



## REFERENCES


1 **GCP Inspections Metrics Report**, GCP Inspectorate, Medicines and Healthcare Products Regulatory Authority, 12 February 2021, Accessed 9 July 2021.

2 Gary Lin, **Examining association between cohesion and diversity in collaboration networks of pharmaceutical clinical trials**, Journal of the American Medical Informatics Association, 2020.

3 **Digital R&D: Transforming the Future of Clinical Development**, Deloitte, 14 February 2018, Accessed 9 July 2021.

4 **Regulations: Good Clinical Practice and Clinical Trials**, U.S. Food and Drug Administration, 21 January 2021, Accessed 9 July 2021.

5 **eTMF Exchange Mechanism Standard Survey**,TMF Reference Model Exchange Mechanism Group, Published 11-April 2021.

## ABOUT ARISGLOBAL

ArisGlobal transforms the way today's most successful Life Sciences companies develop breakthroughs and bring new products to market. The end-to-end drug development technology platform, LifeSphere®, integrates our proprietary cognitive computing engine to automate all core functions of the drug development lifecycle. Designed with deep industry expertise and a long-term perspective that spans more than 30 years, LifeSphere® is a unified platform that boosts efficiency, ensures compliance, delivers actionable insights, and lowers total cost of ownership through multi-tenant SaaS architecture. In 2021, Frost & Sullivan recognized ArisGlobal with the Customer Value Leadership Award for Clinical Development and Pharmacovigilance Software.

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