TRIAL INTERACTIVE

The 15 Must-Have Features for Modern eTMF

THE ESSENTIAL CAPABILITIES ALL MODERN ETMF SHOULD HAVE

YOUR KEY TAKEAWAYS

As the requirements and complexities of clinical trials grow, so does the need for a more sophisticated Electronic Trial Master File (eTMF). In this guide for clinical leaders, we will review the top 15 features that you should expect from a modern eTMF. Each of these features works together to help your organization maintain quality control, inspection readiness, effective collaboration, and predictable timelines for your studies.

Included in this Checklist:

- The evolution of eTMF
- 15 must-have features of a modern eTMF
- The value of a modern eTMF

THE EVOLUTION OF ETMF

In the 1990s and early 2000s, clinical trial processes were predominantly paper-based, posing numerous challenges such as physical storage limitations, retrieval difficulties, potential human errors, and inconsistencies. These challenges prompted the need for innovative solutions to enhance operational speed, ensure compliance, and reduce costs associated with administration and paper-driven processes.

The concept of the Electronic Trial Master File (eTMF) emerged in 2010 as a significant advancement in the management of critical trial documentation. The evolution of eTMF can be traced back to key milestones and regulatory guidelines that influenced its development:

1. **1996: ICH-GCP Guidelines Help Create the TMF Standard:** The International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH) published the Good Clinical Practice (GCP) guidelines. These guidelines established requirements for clinical trial documentation and laid the foundation for the creation of the Trial Master File (TMF) standard.
2. **1997: FDA Outlines Electronic Signatures and Records Criteria:** The U.S. Food and Drug Administration (FDA) introduced CFR 21 Part 11, which provided support for the use of electronic records and digital signatures in clinical trials. This regulation opened doors for leveraging technology and paved the way for the development of the eTMF.
3. **2013: EMA Approves Electronic Records:** The European Medicines Agency (EMA) approved the use of electronic records and digital signatures in 2013. This approval by the EMA further solidified the acceptance and adoption of electronic documentation in clinical trials.

As a response to these regulatory developments, the eTMF rapidly evolved, capitalizing on the opportunities presented by electronic records and digital signatures. By replacing manual, paper-based TMFs, eTMF applications gained prominence as game-changers in the clinical trial landscape.

Today, modern eTMFs offer a wide range of sophisticated features that streamline document handling, ensure regulatory compliance, and facilitate real-time communication among key stakeholders. These advanced eTMF systems have revolutionized trial documentation management, mitigating many of the challenges associated with traditional paper-based approaches.

HOW A MODERN ETMF SUPPORTS YOUR STAKEHOLDERS

Your employees depend on a smoothly functioning eTMF in order to achieve peak productivity, maintain inspection readiness, achieve real-time visibility into study data, and gain the necessary insight to make smart decisions. Here are a few ways that different stakeholders typically rely on modern eTMF.

Study Managers

An eTMF helps study managers track TMF completeness in real time, hold teams accountable and view robust reporting dashboards.

Business Leaders

An eTMF provides comprehensive, real-time reporting and analytics, to help business leaders facilitate data-driven decision making.

CRAs

An eTMF supports CRAs in reducing manual processes, viewing fewer sites in person, identifying missing documents, and overseeing the TMF from mobile or desktop.

IT Teams

An eTMF reduces the burden on in-house IT teams by simplifying and speeding implementation. Due to the inherent complexity in every study, TMF expertise and technical support should be readily available from the eTMF vendor.

Quality & Auditing Teams

An eTMF allows quality teams and auditors to perform TMF periodic reviews and audits in the eTMF system. There is no need for manual trackers and spreadsheets when a review can be scoped, performed, and reported within the system.

For more ways to empower inspection ready teams, explore our resources:

- Establishing a Culture of Inspection Readiness
- 15 Ways to Avoid Inspection Findings
- Ultimate TMF Resource Pack
- Top 5 Skills for a Successful TMF Team
- The CDISC Trial Master File Reference Model as Industry Standard

TOP 15 ETMF FEATURES

- Index and Review Two-Step QC Workflow
- Required Document Lists and Placeholders based on the TMF Reference Model
- Quality Review Audit and Inspection Module
- Milestone and Event Manager with TMF Health Management
- Query Management with Email Notifications and Response Handling
- Automatic Classification and Metadata Extraction Using Machine Learning
- Compliance-Focused, Contemporaneous Capabilities
- Duplicate Document Detection and Comparison
- Interoperability with a Platform That Includes Optional Site Portal, Content Authoring, Study Start-Up, and CTMS Applications
- Email and Study Correspondence Inbox with Relevance Checks
- Document Redaction, Manipulation, and Certification
- Out-of-the-Box TMF Reference Model with Best Practices Oversight
- Bulk Upload and Migration
- Mobile App for CRAs to Capture and Reconcile Site Documentation
- Portfolio Dashboard with KPI Metrics and Comprehensive Platform Reporting

FEATURE 1: Index and Review Two-Step QC Workflow

The top feature of a modern eTMF is the index and review two-step workflow, which is powered by artificial intelligence and machine learning. This feature allows all incoming documents to be indexed and reviewed for TMF archival. Within the first step of the workflow, the AI/ML technology, released in 2019, should categorize and organize documents within the eTMF to ensure that documents can be quickly and easily located within the eTMF. Then, the second step verifies that the documents have been correctly categorized and that all documents have been included in the eTMF.

Why This Feature is Critical for a Modern eTMF:

Serving as the basis for all eTMF quality checks, the two-step index and review workflows allow clinical document specialists to ensure that all documents in the TMF meet archival standards for quality and completion.

Trial Interactive released this feature in 2008.

FEATURE 2: Required Document Lists and Placeholders Based on the TMF Reference Model

Required document lists and placeholders based on the TMF Reference Model allow you to configure rules for your document processes to ensure compliance to your standards. They also allow you to set up document placeholders for all of your required documents so you can easily determine the completeness of your TMF. Placeholders and required document lists ensure that all expected and essential documents are captured in your final TMF.

Why This Feature is Critical for a Modern eTMF:

A fundamental part of ensuring eTMF health and completion, these lists ensure that all essential documents are ultimately received in the clinical trial archive.

Trial Interactive released this feature in 2010.

FEATURE 3: Quality Review Audit and Inspection Module

Any modern eTMF should have an audit and inspection module for quality review, which allows auditors to perform timely quality audits throughout the study and keep the TMF healthy. Auditors should be able to audit parts or portions of the archive using flexible selection criteria, respond to problems, open queries to handle document issues, and measure the overall quality of the audited documents.

Why This Feature is Critical for a Modern eTMF:

Audit and inspection modules allow for a standard measurement of the quality of an eTMF, a more flexible, risk-based means of quality review, as well as improved sponsor oversight, a record of compliance, and an interface for agency inspections.

Trial Interactive released this feature in 2011.

FEATURE 4: Milestone and Event Manager with TMF Health Management

A milestone and event manager with TMF health management makes it possible to create placeholders and required documents in the eTMF as changes occur during the trial. The feature also allows for the ability to configure the eTMF with events on your study timeline such as investigator meetings, site visits, study amendments, last subject last visits, and database locks, and more etc.

Why This Feature is Critical for a Modern eTMF:

Milestones and events support better eTMF Health by ensuring all clinical trial events, milestones, and their associated required document lists are captured in a timely fashion, thus enabling the TMF to stay fully current and contemporaneous.

Trial Interactive released this feature in 2014.

FEATURE 5: Query Management with Email Notifications and Response Handling

Query management with email notifications and response handling allows queries to be raised about specific documents in the TMF. Replacement documents may be sent from the site or CRA, questions may be answered, and status is tracked. Additionally, advanced eTMF allows you to respond to the queries via email, without logging into the eTMF.

Why This Feature is Critical for a Modern eTMF:

Documents in the TMF are aggregated from many different sources. It is essential that queries may be raised about documents coming in and answered by users at the sponsor, CRO partners, CRA's and sites. This essential part of sponsor oversight allows the correct version of a document to be easily captured, and also allows eTMF users to request missing documents from a variety of sources.

Trial Interactive released this feature in 2015.

FEATURE 6: Automatic Classification and Metadata Extraction Using Machine Learning

Automatic classification and metadata extraction automatically classifies documents that are collected in the eTMF and captures their metadata, assigning them to the correct country, site, and user.

Why This Feature is Critical for a Modern eTMF:

While the proper review and quality check of eTMF documents is always essential, the use of AI-assisted technology to classify and extract information from documents is a time saver for your team.

Trial Interactive released this feature in 2020.

FEATURE 7: Compliance-Focused, Contemporaneous Capabilities

Compliance-focused, contemporaneous capabilities enforce compliance and result in an active, accumulative eTMF. These can include internal requests for documents, sharing of content from a content management system, document due dates, upcoming requirements, overdue documents, reminders, and responsible parties.

Why This Feature is Critical for a Modern eTMF:

Without built-in assistance, enforcing compliance across internal teams that owe documents to the eTMF is unnecessarily complex. Tying together sharing, authoring, and translation features simplifies team communication and document submission. This is essential for ensuring TMF completeness.

Trial Interactive released this feature in 2019.

FEATURE 8: Duplicate Document Detection and Comparison

Duplicate document detection and comparison verifies that a document is unique and does not have a duplicate in the eTMF archive, either based on identical metadata, or an exact copy or duplicate scan.

Why This Feature is Critical for a Modern eTMF:

Duplication is commonplace because documents enter into the eTMF from a wide variety of sources, teams, and locations. Sometimes the duplicates are legitimate because the same document is shared to multiple clinical sites, but many times they are simply duplicate scans or repeated information.

Trial Interactive released this feature in 2012.

FEATURE 9: Interoperability with Site Portal, Content Authoring, Study Start-Up, and CTMS Application

eClinical platform interoperability provides a seamless connection and flow of data between the eTMF and other critical applications such as a site portal, eISF and site binders, content management, document authoring, study start-up, and clinical trial management systems.

Why This Feature is Critical for a Modern eTMF:

Interoperability enables a seamless connection and flow of data between various eClinical applications. This means that information can be easily shared and exchanged between different systems automatically and archived in the eTMF in accordance with best practices. It reduces the risk of errors, improves data integrity, speeds decision making, and saves time and resources.

Trial Interactive released this feature in 2012.

FEATURE 10: Email and Study Correspondence Inbox with Relevance Checks

Email and study correspondence inbox with relevance checks captures all email correspondence for each study. Once a correspondence email is sent in, it is rendered to PDF and may be selected for inclusion in a separate interface by study staff. Attachments are checked for duplicates and are linked back to the original email. Emailing documents and site correspondences securely into the eTMF ensures GCP compliance.

Why This Feature is Critical for a Modern eTMF:

Secure email and email correspondence management remains a consistent and reliable method for sending documents and data to the eTMF archive, particularly from clinical sites. In addition, a dedicated email and correspondence inbox increases compliance.

Trial Interactive released this feature in 2014.

FEATURE 11: Document Redaction, Manipulation, and Certification

Document redaction, manipulation, and certification allows selected team members to remove personal information to meet data privacy requirements as well as to repair, split, and merge documents. Additionally, it allows you to certify documents to ensure proper paper disposal.

Why This Feature is Critical for a Modern eTMF:

As GCP, HIPAA, and other privacy regulations become more common and restrictive, and health information more highly regulated, it is essential that a modern eTMF platform include ways to correctly detect, remove and redact PII and PHI, and ensure that this information is never included as part of the eTMF archive.

Trial Interactive released this feature in 2015.

FEATURE 12: Out-of-the-Box Configuration According to TMF Reference Model or Flexible Configuration

Modern eTMF should use a standard out-of-the-box configuration that aligns with the TMF Reference Model or the Clinical Data Interchange Standards Consortium (CDISC). The standard configuration has built-in best practices and supports many different clinical studies, phases, therapeutic areas, and situations. There should also be an option to configure your eTMF to custom structure requirements and keep it aligned with the most current standards should you need to add additional fields or metadata.

Why This Feature is Critical for a Modern eTMF:

Both TMF Reference Model and CDISC standards provide best practices for eTMF configuration. By aligning your eTMF with the most up-to-date standards, you further improve TMF quality, completeness, and timeliness. In addition, with flexible configuration options, you accommodate for the many different requirements that may be necessary, depending on the type of clinical trial. It is important that the eTMF is flexible enough to support a wide variety of unique trial situations.

Trial Interactive released this feature in 2010.

FEATURE 13: Bulk Upload and Migration

Bulk upload and migration provides the ability to easily migrate documents and their metadata into the eTMF with high quality. With preconfigured bulk upload and migration processes, moving documents and data into (or out of) your eTMF is easier.

Why This Feature is Critical for a Modern eTMF:

Modern trials have many different business situations that can occur, requiring collected documents to be easily and quickly loaded into the eTMF format, ready for an inspection in a short period of time. Preconfigured bulk upload also supports TMF completeness by minimizing the likelihood of human error when uploading documents.

Trial Interactive released this feature in 2010.

FEATURE 14: Mobile App for CRAs to Capture and Reconcile Site Documentation

A mobile app for CRAs to capture and reconcile site documentation makes it possible to reconcile site binder documents against collected site documents in the eTMF and generate a reconciliation report, from any device. The modern eTMF will provide a user-friendly experience for CRAs through a mobile app as a standard web interface.

Why This Feature is Critical for a Modern eTMF:

CRAs must generate a site reconciliation report during their site visit. Having a mobile app capable of capturing documents directly and reconciling them against the eTMF saves both time and effort during each site visit. Providing CRAs with intuitive experiences on any device saves time at the site, increasing complete data capture and ensuring that site visits run smoothly.

Trial Interactive released this feature in 2018.

FEATURE 15: Portfolio Dashboard with KPI Metrics and Comprehensive Platform Reporting

Portfolio dashboard with KPI metrics and comprehensive platform reporting provides critical business insight for appropriate team members. In a modern eTMF, it is easy to keep track of KPI metrics such as real-time completeness, timeliness, quality, open issues, queries, and overall eTMF health. These active and configurable options increase accountability and awareness of eTMF health. Study managers and authorized team members can also view reports and receive reminders about eTMF-related activities, such as internal requests for documents, sharing of content, document due dates, upcoming requirements, and overdue documents.

Why This Feature is Critical for a Modern eTMF:

To ensure TMF health, it is essential that key performance indicators are readily available to authorized team members. In the fast-paced world of clinical trials, features that provide enhanced visibility and TMF health reporting and reminders help keep study timelines and compliance on track.

Trial Interactive released this feature in 2019.

THERE'S A BETTER WAY TO AVOID INSPECTION FINDINGS AND GAIN REAL-TIME OVERSIGHT OF YOUR TRIAL MASTER FILE.

Trial Interactive emerged as an early influencer and leader in digitizing clinical operations. Trial Interactive's modern eTMF is a practical, modern, and compliant single access point for TMF documentation. TI eTMF supports all essential document processes and reduces clinical trial delays, costs, and compliance risks.

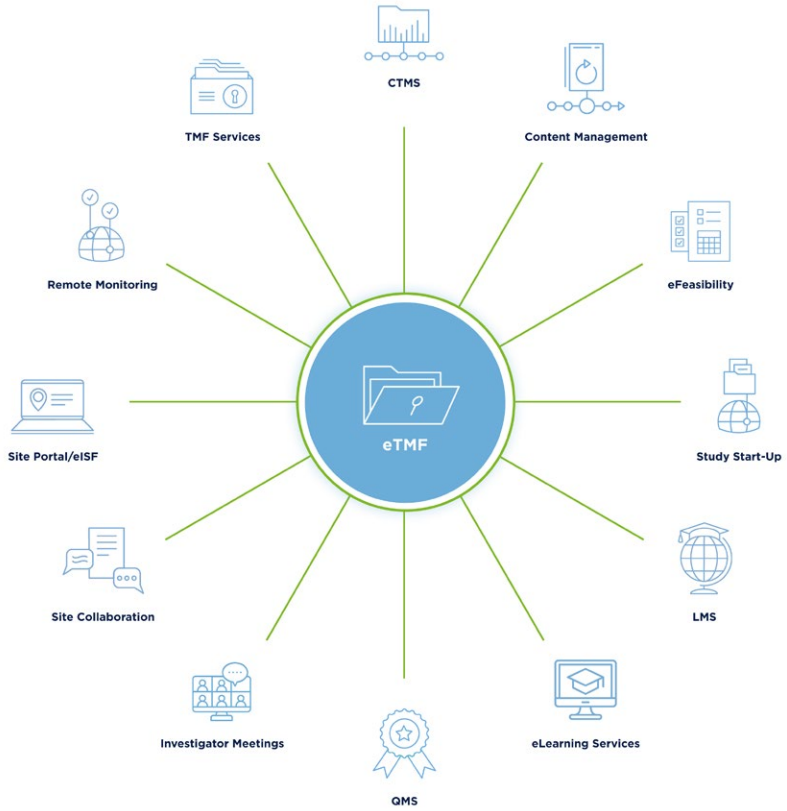
With Trial Interactive eTMF, you can:

- Automate metadata and indexing workflows with machine learning to make inspection readiness easier than ever with 98% accuracy.
- Launch faster with painless implementation that takes weeks, not months and 24/7 support.
- Streamline TMF document processing and quality control in a single source of truth for your inspection readiness and decentralized collaboration.
- Manage your eTMF anytime, anywhere with a mobile application that allows CRAs to perform critical TMF tasks and oversight on the go.
- Maintain TMF completeness and health with real-time document processes and audit trails.
- Speed timelines with proactive oversight of dashboards, analytics, and mobile insights.

Trial Interactive's eTMF seamlessly connects to our 21 CFR Part 11 compliant eClinical platform.

As we celebrate 15 years of serving biotechnology and pharmaceutical companies, Trial Interactive is the only platform that provides a comprehensive solution that enables clinical trial efficiency from site identification to study closeout. We ensure customer success through enterprise technology paired with comprehensive support services. Our platform grows with you, whether you're seeking a complete platform experience, or looking to phase in seamlessly connected solutions like CTMS, eTMF, eISF, Remote Monitoring, Study Start-Up, QMS, and LMS as needed.

Choose the platform that over 250 sponsors use to reduce 75% of their TMF inspection findings, speed up site activation by 50%, and save an average of $3.2M for a 50 site study. Learn more at trialinteractive.com.



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