TRIAL MASTER FILE
TMF
REFERENCE MODEL

Implementation Guide

Version 2

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This document is freely distributable and is based on the opinions of the TMF Reference Model User Guide and Implementation Subgroup.

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Version History

Version	Steering Committee Approval Date	Changes
1.0	14-Mar-2018	Original version
2.0	02-Nov-2020	Updated to include TMF Reference Model Version 3.2 changes

Contents

1 Purpose of the Implementation Guide

The Trial Master File Reference Model (TMF RM) Implementation Guide provides a framework for implementing the TMF RM in your organization. The information presented in this guide was created by industry volunteers responsible for designing, implementing, managing, maintaining, evolving, and otherwise working with Trial Master Files and the TMF RM.

This guide assumes knowledge of Trial Master Files and the TMF RM, including the organization and filing structure of the TMF RM. For more information on the use of the TMF RM, please refer to the TMF User Guide.

Both documents can be downloaded at https://tmfrefmodel.com/

2 Scope

This guide presents an organized overall process for an implementation approach which can be adjusted based on your Organization's specific needs.

This guide is intended to bring perspective to those involved such that knowledgeable decisions, those that leverage the benefits of the TMF RM, can be made. The intended audience for the TMF RM includes biopharmaceutical and device companies, CROs, academic institutions, and other vendors, all of whom are involved with managing study-specific TMFs. It also is applicable to investigators managing their Investigator Site Files and conducting Investigator Initiated Studies.

3 Laying the Groundwork

Any clinical trial Organization, be it as a commercial or non-commercial sponsor, a contract research organization, an academic research organization, or a clinical site, needs to have a robust way to manage the documentation created before, during, and at the closing of their trials.

Since its inception, Trial Master File Reference Model has become a broadly adopted global standard filing structure for the management of trial documentation.

Before implementing the Model, it is critical to have a thorough knowledge of your Organization's current TMF filing structure, Standard Operating Procedures (SOPs), and practices. It is important for those involved in the effort to come to agreement on the goal(s) and/or benefits of implementing the TMF RM.

Benefits of adopting the model include:

- avoids use of company-specific content and structure - regulatory requirements and inspection expectations are not company-specific;
- simplifies engagement with contract research organizations and other partners e.g. during acquisitions or co-development activities;
- simplifies consolidation of TMF content from different sources (internal and/or external) into a single TMF in real-time, at defined intervals and/or at the end of the trial;

- using a structure that is familiar across industry and regulatory agencies, thereby not putting your organization at a competitive disadvantage.

Critical to success is ensuring acceptance and readiness for change taking into consideration your Organization's culture. Individuals and functions within an Organization can become very tied to a particular method and structure of filing that is difficult to change. Planning activities should consider the potential obstacles which can include the number and size of Artifacts in the TMF, length of trials, inspection readiness, integration requirements, and accessibility of individual documents/Artifacts.

Implementing the TMF RM may expose deficiencies in good content management and stewardship, awareness of TMF management responsibilities, and gaps in inspection readiness of the TMF on an ongoing basis. Resistance to change may be encountered due to a perception that:

- The workload or resource demands will increase;
- Implementing the TMF RM will result boundary breaches; and
- Implementing the TMF RM will impact on current development timelines.

To successfully evaluate and adapt or adopt the TMF RM, your organization must:

- be committed to change;
- agree on the value of making the change;
- have effective senior management support for the change across all business functions/units that generate TMF content;
- ensure global input during the project; and
- be willing to work through several iterations of detailed TMF content listing analysis.

Finally, as a result of using the TMF RM, it may become evident that changes to existing processes or the development of new processes, which may include a review and/or modification of existing organizational roles and responsibilities, are required.

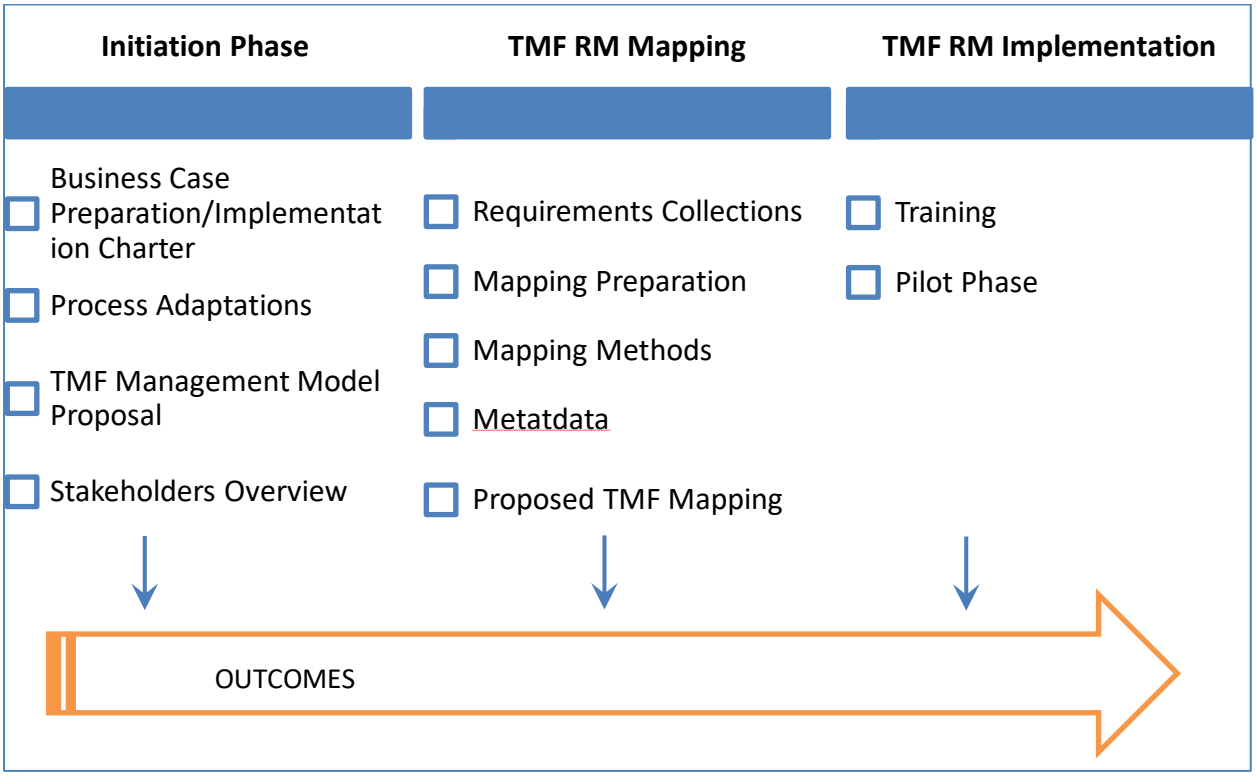
As the benefit to proceed with such extensive changes to implement an external model may not appear clearly to all impacted stakeholders, it may be preferable to prepare a business case to the attention of all.

4 TMF RM Implementation Process Overview

There are typically four phases of the TMF RM implementation process (see diagram below):

- Initial Phase to set-up appropriate Change Management Procedures and initiation the Business Case (Plan)
- TMF RM Mapping Phase to set-up the TMF RM specification/mapping and implementation plan: stakeholders' engagements, requirements collection, implementation resources, timelines, and budgeting (Do)
- TMF RM Implementation Phase to execute this implementation (Check)
- Monitoring & Control Phase to the TMF RM Maintenance and continuous improvement (Act-Adjustments)

These processes for TMF RM Implementation could be described as a 'Plan-Do-Check-Act/Adjustment' cycle.



5 Detailed Process

The following section will describe a proposed process to implement the TMF RM in your organization.

5.1 Initial Phase

5.1.1 Business Case Preparation

If you are required to present a business case for implementing the TMF RM it may include, but not be limited to, defining:

- The Implementation Team which may include the clinical documentation manager, Business Unit managers; Project Team members from the project to which the TMF RM is being mapped; individual(s) responsible for your Organization's TMFs, representation from Quality Assurance and/or Auditing, among others
- The purpose for implementing the TMF RM should be clearly defined
- Clear explanation of the problem that you expect to solve by implementing the TMF RM. Example – incomplete listing of the TMF, difficulty realizing "inspection readiness" due to incomplete listing, etc.
- Alignment with your organization's goals or responses to a health authority inspection finding
- Potential obstacles and mitigation strategies – for example infrastructure constraints, organizational change, etc.
- Expected resourcing costs for the project

- Timeline

If not already done so, you should identify the Project Owner as well as all of the Stakeholders, which may include representatives from QA, Regulatory, SOP Administration, SMEs from each of the 11 TMF RM Zones, and any other group that creates content in support of a trial. A stakeholder should be identified for each part of the TMF (called Zones in the TMF RM). (Note – A stakeholder could very well be responsible for multiple zones) see 5.1.4 for more information.

5.1.2 Process Adaptations

The transition to the TMF RM may require changes or additions to existing processes. Some considerations may be the following:

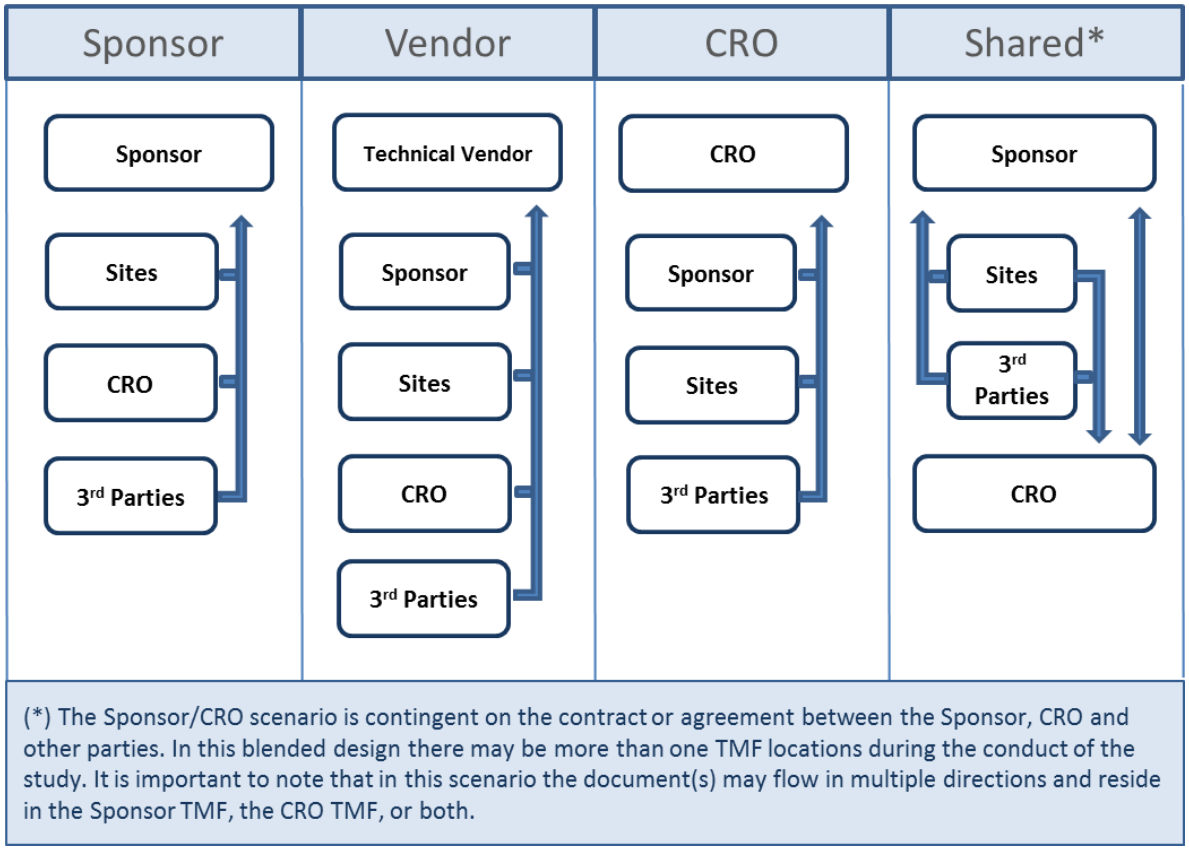
- Identify new or modified business roles and responsibilities based on the TMF Reference Model and develop appropriate communications to ensure that those roles and responsibilities are clearly defined and understood
- Evaluate your existing SOPs. If necessary, develop or modify the SOPs. Example your SOPs should address the process for developing, capturing and managing TMF Artifacts
- Current training should be evaluated to determine if additional or revised training is required based on new or modified roles and responsibilities. SOPs for capturing completion of required training should also be evaluated to assess if they need to be modified.

5.1.3 TMF Management Model Proposal

During the Initiation Phase, the user should identify the TMF RM Management Model. There are typically four different types of TMF management paradigms:

1. The Sponsor is solely responsible for TMF management
2. A Technical Vendor is primarily responsible for the TMF
3. A CRO is responsible for the TMF
4. TMF is a combined effort between the Sponsor and the CRO (Hybrid Model)

In all four cases, the most common flow of documents is towards the main TMF managing group (e.g. Sponsor, CRO, etc. – depending on the paradigm used). The sponsor should identify all TMF documents location/organisations.



Regardless of the operating model, it should be noted that the Sponsor retains overall responsibility over the TMF.

Dependent on the size of your organization, one or more options may be applicable.

Smaller organizations may be interested to rely on a partner with more experience and resources in line with TMF Management and partner with a CRO or a technical vendor to manage TMF related activities.

Larger organizations will have the resources and technologies to address TMF needs internally. They will also manage multiple studies in parallel and may be interested to choose a different model depending on their involvement in the study (e.g. Sponsor responsibility for key studies or therapeutic areas, CRO responsibility for externalized activities, Technical Vendor responsibility for supported studies, etc.)

It is required at the beginning of the study to indicate the essential documentation (artifacts) locations (for example, Sponsor TMF and CRO, Sponsor/CRO maintenance model) and set up Artifacts accountabilities and documents transferring procedures (where required) at the study end.

5.1.4 Stakeholders Overview

5.1.4.1 Identify all Stakeholders

If not already done so, you should identify the Project Owner as well as all the Stakeholders.

This is an important step and one that can be harder to manage than anticipated. The documentation of a clinical trial spans multiple processes and it is easy to overlook some impact, especially in big matrix organizations.

Stakeholders may include representation from Quality Assurance, Regulatory, SOP Administration as well as members of the Clinical Team, SME's from each of the 11 TMF RM Zones and any other group that creates or consumes content generated in support of a clinical trial.

A stakeholder should be identified for each department creating TMF content and/or for each part of the TMF (called Zones in the TMF RM). (**Note**: A stakeholder could very well be responsible for multiple TMF Zones).

5.1.4.2 Suggested Stakeholders per Zone

The table below gives a list of suggested stakeholders to invite to participate in the mapping per zone. This is not an exhaustive list. Study management who usually owns the TMF is key to a few zones but should ideally be kept in the loop of all mapping discussions.

Depending on your internal business processes, the list of stakeholders per zone could be longer.

11 Zones:	Functional Contributors (and their delegates)
Trial Management	Clinical Operations, Biostats, Clinical, ALL
Central Trial Documents	Clinical Operations. Medical Writing, Data Management
Regulatory	Regulatory Affairs, Safety Surveillance, Clinical Operations
IRB or IEC and other Approvals	Clinical Operations
Site Management	Clinical Operations, Legal, Finance
IP and Trial Supplies	Clinical Operations, Clinical Supplies, Manufacturing, CMC, GMP-QA,
Safety Reporting	Safety Surveillance, Clinical Operations
Central and Local Testing	Clinical Operations, Bio-Analytical
Third Parties	ALL (functions that delegate to vendors) Procurement, Legal, Finance
Data Management	Data Management
Statistics	Biostatistics, Programming

Please note that stakeholders of a zone will be responsible for defining the records that are part of their zone and to identify what processes are impacted.

Stakeholders will remain accountable for their part of the TMF even if they choose to delegate the responsibility of the day-to-day management to another party, internally (supporting department) or externally (e.g. CRO).

5.1.5 Suggested support material

5.1.5.1 Initiation Phase Checklist

Initiation	
	Review all of the material sent out in the Background Package
	Prepare the Business Case
	Prepare the project implementation plan/chapter and the resources required for the expected project
	Answer any questions and address any resistance
	Prepare the Change Management form (if required)
	Identify Stakeholders
	Identify the TMF RM Management Model

5.1.6 Initiation Phase: Q&A

Considerations	**Best Practices and Suggestions**
What is the implementation purpose? Outline why you need to implement - initial or updating the tool.	For Initial – determine if this is a one-time process for a single study; moving forward with existing studies; or only for new studies. For Updates – determine what has changed and how it affects the current work structure and assigned responsibilities
Is the TMF RM going to be implemented to a paper TMF, electronic TMF, or a hybrid?	For each type of TMF (paper, electronic and hybrid) ensure that you are consistent in how it is implemented; create SOP for how Artifacts and corresponding documents will be managed using the hybrid model
How you will leverage the TMF RM? Will it be customized to your needs; this includes naming of Zone, Section & Artifact	Plan of approach or strategy – In what way did you leverage the TMF RM? Factors for consideration: implementing/adopting the TMF RM. Try and avoid a Zone by Zone way of working even when the mapping is split between Zone specific work groups. There should be consistency in the way the implementation work is handled across the Organization

Considerations	Best Practices and Suggestions
What areas of your Organization need to be involved? Clinical Operations, Regulatory, Data Management, etc.	Determine who your stakeholders are – TMF team, Clinical Study Team, all other functional areas. Don't hesitate to involve more people than fewer at first
Who should be part of the Core Team? Don't rule out IT, QA, etc.	Core team may be smaller and include those who will be testing/reviewing all information. Extended team may be more individuals from each functional area, as appropriate
Did you obtain Leadership Sponsorship?	Senior Management endorsement is key for a TMF RM implementation since many processes improvements activities may be initiated as a consequence of the TMF RM implementation
How to communicate from day one?	Each phase of the plan may have different levels and frequencies of communication. The scope of the TMF may be very large but not all stakeholders will be impacted at the same time and in the same way. Determine what works best for your Organization/departments and change, as appropriate.
What does your timeline look like?	Determine implementation milestone timelines – from planning, testing, delivery to go-live. Identify all milestones and determine the amount of time it will take to achieve each milestone.
What deliverables will be derived from each milestone?	Some milestones may have more than one, others none at all
Lessons Learned	Track your lessons learned for future updates. Retain all versions of your filing structure. If the decision was to not implement the new filing structure to all studies, keep in mind you may need to show how older, closed studies were filed to an auditor or inspector.

5.2 TMF RM Mapping

5.2.1 Requirements collection

As stated earlier, multiple stakeholders are involved in the TMF process. These many departments may have different expectations regarding the implementation of the TMF RM. It is important to liaise with all stakeholders to understand such expectations and determine the requirements, in line with the project objectives, that should be fulfilled for a successful implementation of the TMF RM across the organization.

5.2.2 Mapping Preparation

For organizations with their own existing TMF organization structure, it is recommended to prepare the mapping exercise. Although the TMF RM is recognized throughout the industry, it is preferable to prepare a Background Package to ensure all stakeholders are in agreement when they start the mapping exercise. The Background Package should consist of the following:

- Current TMF RM (which can be downloaded at https://tmfrefmodel.com/
- Description and background on the TMF RM
- Description (or sample) of the organization's current TMF to which the TMF RM is being mapped.
- If a business case has been developed and approved, it should be included in the Background Package. If a business case was not required, the Background Package should include a summary of the anticipated benefits to be realized along with any known obstacles to implementation. It is important to provide the extended team your organization's current TMF SOP(s) and TMF Expected Document List.
- Roadmap of the project
- List of Team Members including Project Owner and Stakeholders
- Clear expectations from all involved. An RACI or Resource and Responsibility Matrix(es)

The Background Package should include a description of the process through which the mapping will be realized.

5.2.3 Mapping Methods

The mapping itself can be done using different methods: Team meetings, brainstorming sessions, individual meetings, etc.

5.2.3.1 Mapping meetings only

If all your stakeholders for each zone are located in the same place, a mapping method consisting of multiple brainstorming or working group sessions with the appropriate stakeholders is probably the best approach. This will ensure the involvement of all stakeholders, promote a common understanding of the TMF structure and of the way the documentation is mapped with the model.

5.2.3.2 Individual Mapping with Consolidation Meetings

Larger companies, especially when spanning across multiple time zones, may find it difficult to organize the mapping only through brainstorming sessions due to the difficulty to gather all stakeholders within the same meetings and due to the potentially high number of attendees (which may lead to difficulties to reach a consensus).

To mitigate this situation, a proposed approach can be to ask all stakeholders to perform individual mappings of the documents they own. The mapping is then reviewed by all impacted stakeholders and remaining questions or remarks are discussed during a consolidation meeting.

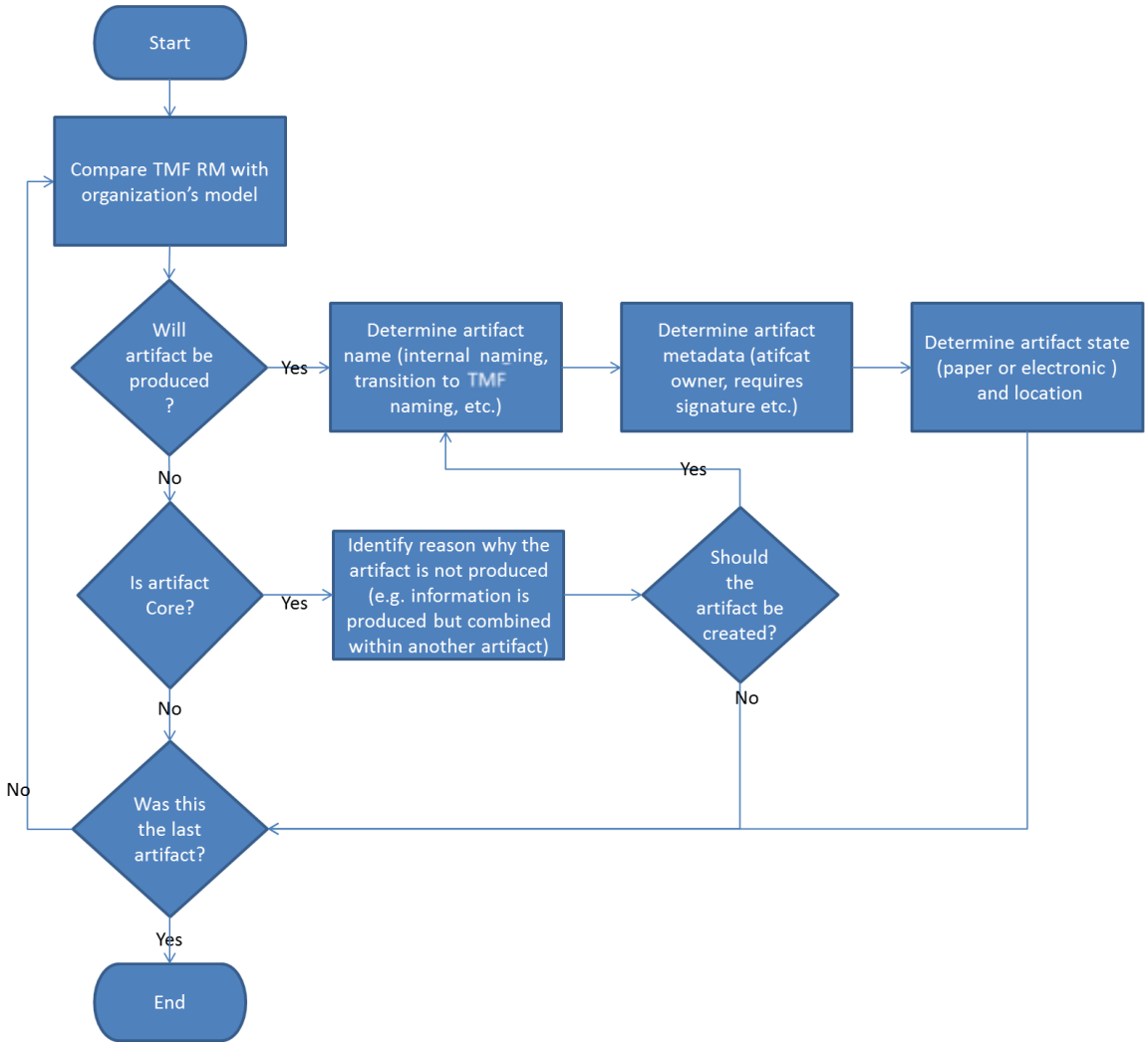
5.2.3.3 Individual Mapping with Central Team Validation

If collaboration is not perceived as the best option for your organization, this last method allows for more control on the end deliverable.

In this approach, key individuals are selected to represent their team/department and propose a mapping of the documents they own.

A central team reviews all individual mappings and addresses issues or discrepancies.

5.2.4 Proposed Mapping Flow



5.2.5 Metadata

5.2.5.1 TMF RM Metadata

Below is a list of metadata you may want to include in the TMF RM

- Artifact owner (what department/team manages this Artifact)
- Is the Artifact electronic or paper?
- Where is the Artifact stored? What system, what location?
- Does the Artifact have an approval process? Does it involve wet-ink signature?
- Should the Artifact be translated?

- Is the Artifact meant to part of a submission package (e.g. IND package)
- What type of QC process is applicable to the Artifact
- Should the visibility to the Artifact be limited on the consumer's blinded, unblended state?
- Should the Artifact be associated with another Artifact?
- Is the Artifact necessary to achieve a milestone (eg: Site Activation)?
- Does the Artifact have to be sent to sites?

5.2.5.2 TMF Artifact Metadata

Below is a list of metadata you may want to track at Artifact level, as part of your TMF process (some will only be applicable for electronic records)

- Date of the record (usually date of signature or date on which the document became effective)
- Creation date
- Author(s)
- Modification date(s)
- Modifier(s)/Reviewer(s)
- Rationale for change
- Approver(s)
- Version number/date
- QC date
- Site(s) Artifact is distributed to

5.2.6 TMF Mapping walk through

- Compare the TMF RM Artifacts with your Organization's current TMF Model. The Artifacts should be compared by Zone and by individual Artifacts within each Zone
- The TMF RM contains example Artifacts. These need to be assessed for appropriateness and relevance compared to the Organization's SOPs, business processes and workflow as well as outsourcing models
- If the Artifact on the TMF RM is listed as "Core" (required), the Artifact must be in the TMF whenever it is created in support of the clinical study. If such an Artifact does not exist in your current TMF Model, you will need to proceed to an analysis to determine why it is not generated. This analysis may uncover the need to add the Artifact generation to your processes.
- If the Artifact is listed as "Recommended", its presence in the TMF is not required. However, if it is produced during the brainstorming exercise, it is strongly recommended to include it to Organization-specific TMF Model.
- It is suggested for those Artifacts that are not used, the Model should indicate "Not Applicable". In the future, this may be helpful to determine whether the Artifact was just never filed as opposed to not applicable for the Organization. You may also choose to hide the row from your Organization TMF Model. Make this determination for each Artifact. However, it is prudent to keep all Artifacts on your Organization-specific TMF Model in the event that any Artifact will be required to be created in the future.

Note: Some Artifacts may be considered for deletion if they refer to processes your Organization will not manage (e.g. IP versus Devices)

- Determine the appropriate Artifact name that you will use for your Organization's TMF Model. Since implementation of the model is intended to introduce industry standardization, it is strongly recommended that you adopt the artifact name used within the model. If you choose instead to use a name that is different from the name defined in the TMF RM, capture the name that you are using on your Organization's TMF Model. The above process is iterative until you have considered all of the Artifacts listed in the TMF RM.
- It is very likely that as you review the RM, you will identify documents used within your Organization that appear to be new artifacts that are not included in the model. The RM has gone through extensive consultation and is based on globally applicable regulatory requirements for TMF content. For this reason, it is unlikely that your Organization is using an artifact that has not already been defined. It is recommended that you analyze the definition/purpose descriptions of the artifacts to see where your documents align. In almost all cases where a new artifact has been proposed, the document is a sub-artifact of an existing artifact, based on the definition/purpose included within the model.
- The TMF RM is organized into 3 levels: Trial, Country, and Site. Review the Artifacts within your Organization's TMF RM to understand how they can be applicable at any or all 3 levels. You can filter the TMF RM spreadsheet into the 3 distinct levels of Trial, Country, or Site to emphasize this point. Explain to the team members that they must consider each of the Artifacts at their multiple levels since responsibility for certain Artifacts may be different at each level. The RM provides the filing level that is typically seen within industry; it is important that within your Organization artifacts are filed at the appropriate level based on content of the record.
- During the review, also consider the location of the Artifact. The TMF is not necessarily all kept in the same location and many different systems (paper and/or electronic) may be used. For example, Monitoring Reports may be held in a system other than where the confirmation and follow-up letters are kept. This should be documented so that during a reconciliation, audit or inspection, you can determine where the records are located.
- Multiple iterations may be required to complete the finalized Organization's TMF Model and, as indicated previously, it may be efficient to conduct meetings for each Zone or groups of one-or-more Zones. Another option is to hold working group review sessions over the course of a few days to complete the review of the TMF RM filing structure to your Organization's TMF Model.

5.2.7 Organization Adaptations

Organizational adaptation to the TMF RM can be implemented to ease the transition between an existing TMF model and the TMF RM. For example, usage of Organization-specific artifact names instead of TMF RM names, adding of new sub-Artifacts to support changes in business processes, SOPs, business models etc. For instance, under 02.01.02 Protocol, the following sub-artifacts could be created:

02.01.02.01 Protocol
02.01.02.02 Protocol Checklist
02.01.02.03 Protocol QC Form
02.01.02.04 Protocol Approval Form
02.01.02.05 Protocol Correspondence

However, in any case, the Organization should keep a complete traceability matrix to the original TMF RM. It is also suggested that regular revisions of the adaptations are planned, to ensure the Organization specific adaptations that would no longer be required are removed.

5.2.8 Remaining Documents

Quite often, the mapping of documents between an organization's current TMF plan and the TMF RM raises questions and would appear to leave some documents behind.

In such cases, ask yourself the following questions:

- Does the Artifact help to tell the story of a clinical trial? If the answer is no, the document probably does not belong with the TMF.
- Can the document serve multiple purposes? If so, it may be that the document would fit in several Artifacts. In such case, it can be useful to review the processes governing this document in your organization and possibly split the document into smaller pieces with a clear mapping with the TMF.

If the document does belong in the TMF but does not seem to fit in any of the existing Artifacts, it may be needed to create a new Artifact for your organization. However, as stated previously, the creation of new artifacts is not recommended as this is contrary to a standardized industry approach. It is recommended that you identify the artifact whose definition/purpose most closely matches the purpose of the document in question. The creation of a sub-artifact, with a specific scope, may also help you overcome perceived gaps in the Reference Model. The "Recommended Sub-Artifacts" column includes a fully-customizable list of company-specific records that an organization might expect to file under a given artifact. This provides flexibility to help ensure the TMF Reference Model is aligned with an organization's SOPs and compliance needs.

Before creating a new artifact, you may want to liaise with the Global TMF RM community, through the TMF RM project group. The community may guide you into finding an appropriate mapping using the existing TMF RM version or, should the document indeed be left without a proper Artifact, will ensure an Artifact is added to the list of TMF Artifacts for a future version of the TMF RM.

5.2.9 Suggested support material

5.2.9.1 TMF RM Mapping Checklist

	Review the TMF RM Zones and their descriptions as captured in the TMF RM and determine if they are appropriate for the Organization
	The team should consider each Artifact or groups of Artifacts and how they have been organized in the Zones and Levels of the TMF RM
	With exception of the repeating Artifacts in the TMF RM, Artifacts should appear only once in the TMF to ensure clarity in filing procedures and accountability for placement of the content into the TMF

5.2.9.2 Suggested Deliverables List

Check list	Deliverables/Documentation
☐	Mapping document that shows current vs. new classification (keep these unless you plan on re-filing all documents from closed studies) **Objectives**: company TMF version control procedures and TMF harmonization mapping structure across all studies
☐	Map the Artifact to your functional areas – determine who the "content owner" is. **Objectives:** Stakeholders Management Engagement
☐	Map the Artifacts to the system/location in which they will reside. **Objectives**: TMF Master Model, study specific TMF Model, and transfer of essential documentation collection duties
☐	Update of internal SOPs as appropriate **Objectives**: company QA platform maintenance and sustainability
☐	Project Update communication/newsletter to keep all stakeholders and potential users up-to-date on the project status and timelines. **Objectives**: TMF Stakeholders Communication
☐	Training (including Work Instructions and tip sheets) for all users on classification, changes made from last filing model and practices and impacted processes.

Check list	Deliverables/Documentation
	Objectives: company QA/TMF platform maintenance and sustainability
☐	Transition plan between the previous Organization TMF Model and the new one. Plan for migration of current studies, if applicable. Determine if some studies will remain in the current structure based on timing, or other factors, and what studies will be migrated to the new model. **Objectives:** Change Management for TMF RM Implementation
☐	If moving from one electronic system to another – Prepare a Data Migration Plan. **Objectives**: Change Management for e-TMF RM Implementation

5.3 TMF RM Implementation

Now that you have produced a proposed TMF RM Mapping and related processes for your organization, it is time to implement it.

5.3.1 Training

Training on the new TMF RM should ideally include:

- In case your organization is new to the TMF RM, training on TMF RM history and why your organization decided to select it as its new Trial documentation management standard will help in embracing the change.
- Training on the TMF structure and how it is implemented in your Organization (paper, electronic, location, etc.)
- Training on the revised processes and procedures that were adapted in line with the adaption of the TMF RM.

The study teams will be the main population targeted by TMF RM training. However, many supporting processes may be impacted as well.

If a direct training is not required for all of these supporting teams, it is recommended to prepare awareness material to promote understanding of the TMF RM in supporting departments.

5.3.2 Pilot Phase

It is recommended to start with a pilot phase addressing a limited scope to confirm that the proposed mapping and process allows your organization to manage its trial documentation.

The objective of the pilot phase will be to:

- Confirm the completeness and adequacy of the TMF RM Mapping
- Validate the TMF process
- Validate the training material

6 Technical considerations

If your organization has decided to implement an electronic Trial Master File, there exist multiple technical vendors today who propose TMF Management solutions.

If you chose to implement the TMF on an existing record management system, the recommendation is to use the artifact unique ID as the key to your system. Indeed, the unique ID of the artifact is meant to remain constant whereas the artifact number could evolve over time.

7 Monitoring and Control

If you reached this phase, congratulations, you have successfully implemented the TMF RM within your organization.

Monitoring and control of your TMF are key activities that need to happen on a regular basis to ensure that:

- The TMF RM implementation meets the objectives of your organization
- You are and remain inspection ready at all times

More information on the TMF Monitoring and Control can be found at www.tmfrefmodel.com

8 Glossary

Term	Definition
Artifact	Records or documents which one would expect to find in a TMF at both Sponsor and Investigator site. It is important to note that Artifact "progeny records" such as approval/signature pages, amended records or translation documentation are not typically called out uniquely as they belong filed with their related Artifact.
Recommended Sub-Artifact	When an Artifact name does not explicitly refer to a single kind of record (Trial Management Plan, e.g.), Recommended Sub-Artifacts are intended to provide a means to list all Organization-specific records that an Organization would expect to file under a given Artifact. Examples are provided in the TMF RM but expected to be overridden as part of adopting the TMF RM for your Organization.
Sponsor	An individual, company, institution, or organization which takes responsibility for the initiation and management of a clinical study. Per 21 CFR Part 50, Sponsor means a person who initiates a clinical investigation, but who does not actually conduct the investigation, i.e., the test article is administered or dispensed to or used involving, a subject under the immediate direction of another individual. A person other than an individual (e.g., corporation or agency) that uses one or more of its own employees to conduct a clinical

	investigation it has initiated is considered to be a Sponsor (not a Sponsor-Investigator), and the employees are considered to be Investigators.
Metadata	Data that serves to provide context or additional information about other data.
Record	Records are documents [or more generally, information] created, received, processed and maintained as evidence and information assets by an organization or person, in pursuance of legal obligations or in the transaction of business.
Electronic Record; eRecord; Electronic Document	An electronic record is the combination of an electronic document plus additional metadata that defines the context and history of that content. An electronic document may be one or more document objects that as a collection represent the whole content and presentation of the document. Several examples of electronic documents that contain multiple objects are 1) SGML content and format files, or 2) compound documents that comprise many individual elements included in a structure. An electronic document may be a copy of a paper document that is an accurate representation or image of what content was contained on that original document.
Trial Master File (TMF)	The TMF contains those essential documents that individually and collectively permit the evaluation of the conduct of a trial and the quality of the data produced. These documents serve to demonstrate the compliance of the investigator, sponsor, and monitor with the standards of GCP and with all applicable regulatory requirements. (ICH Guideline for Good Clinical Practice, E6, Section 8).

Note: the updated glossary can be found in the latest version of the Trial Master File Reference Model

9 References

- ICH E6 (R2) Section 8
- ISO 14155:2011 Clinical Investigation of Medical Devices for Human Subjects – Good Clinical Practice
- Good Clinical Practice Guide, Medicines and Healthcare products Regulatory Agency (MHRA), 24 Sept 2012
- FDA Regulations 21 CFR Part 11
- FDA Regulations 21 CFR 312.57, 511.1(b)(7)(ii), and 812.140(d)
- Commission Directive 2005/28/EC (EU 2005/28/EC)
- EMA: Guideline on GCP compliance in relation to trial master file (paper and/or electronic) for content, management, archiving, audit and inspection of clinical trials
- https://tmfrefmodel.com/