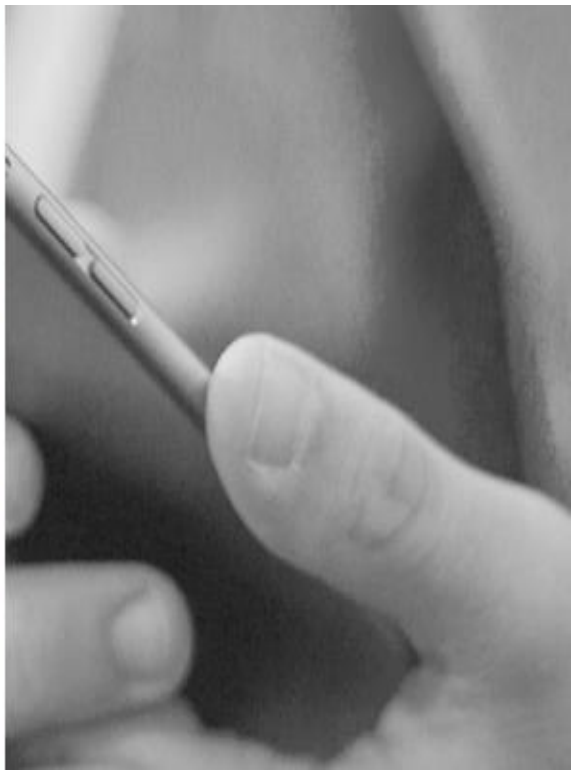
TRIAL INTERACTIVE - BEST PRACTICES V1.0



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1. Introduction

This document is intended to provide recommendations based on industry best practices for your TransPerfect eTMF and other related products.

It is meant to be a quickly accessible guide and a set of reminders to help you in the early setup phase, or at any point in the study's life cycle.

If you have suggestions, questions about processes or implementation, or change requests, your Trial Interactive Project team can assist you.

2. User Access

Configuring users correctly and keeping track of team changes throughout the activation/deactivation of user accounts is an important part of study management and can help you avoid possible audit and inspection findings.

Below are recommendations regarding managing user access:

- Initial users and their roles will be set out in the Configuration Manual, meaning you don't have to manually configure every single user.
- Correctly identifying users and their access requirements will mean that your team will enter the room with the access necessary to successfully complete their tasks.
    - **Note**: Only upon successful completion of relevant Trial Interactive Training will new users be provided with role-appropriate access to the eTMF.
- User access should be reviewed periodically to ensure users have the correct role to perform their job in the eTMF and to confirm any role changes.
- It is important that users no longer associated with the study have their access revoked promptly. It is possible to reactivate a user's access if they become active in your study again.
- We recommend defining what period of time being *inactive* will mean a user's access to the eTMF is revoked within your management system(s).
    - Note: Trial Interactive provides standard reports to help review user access.
- On top of having a solid periodic review procedure on access rights, we recommend that whenever a designated document owner (e.g. a site contact such as a Sub Investigator) stops working on a study, you deactivate their user profile so that Trial Interactive no longer expects documents from them which would otherwise show in the eTMF metrics.
- If you choose to restrict access to folders, User Groups can be leveraged to limit entire sets of users from access to specific folders.

- Make sure you have a full grasp of Folder Security options, as well as Users management settings. You will need to utilize both to leverage user access and document visibility in the eTMF.

- User access rights, such as 'Actions' and folder security settings, are more efficiently managed through user groups and we recommend that these be utilized, especially for large teams.

- When dealing with Regulatory Inspectors, Auditors, or other types of temporary-access users, make sure to revoke access to the users after the appropriate time window. You can also use the Expiration Date field in User configuration to automatically revoke a user's access after an indicated date.

3. Study Start-Up

Trial Interactive offers a Study Start-Up (SSU) module to handle site selection and activation, as well as other activities such as regulatory packet submissions.

The SSU module is able to be fully integrated with Trial Interactive's eTMF.

Below are our recommendations and advice regarding Study Start-Up:

- When setting up an SSU room, the required documents for the Country or IRB levels can be provided either at the Study or Site level. This means that, even though required documents are set up under the Country and IRB level, if the Provided By section has 'Investigative Site' selected, each site would have to provide the documents indicated. The required documents will appear as placeholders under the site.
- Pay careful attention to the list of documents required for site activation as including extra documentation may slow down the site activation process.
- When setting up Site-level required documents, take time to indicate whether or not they are specifically applicable to any particular role or contact at the site so that the placeholders can be automatically created whenever, for example, a new sub-investigator is added to the site and their profile indicates that they should provide documents.
- When creating a site contact, be sure to pay attention to the checkboxes at the bottom of the form to indicate whether or not the contact is considered to be a primary site contact and if they will be expected to submit documents to the study.
- Study Start-Up has a non-configurable two-step quality check workflow. In a standard setup, documents which are considered 'non-essential' for site activation can be stored in SSU and moved to the eTMF workflow upon activation of the site. However, the room can be configured to put *non*-essential documents through the SSU review process as well as essential documents.
- Generally speaking, we recommend that non-essential documents should be reviewed in the eTMF, as reviewing additional documents during the start-up process may slow down site activation.

- As a best practice recommendation, we suggest that all Regulatory Approvers should be set up in the system during configuration.
- In the sites module of SSU, when creating a site, it is mandatory to associate a Principal Investigator (PI) with the site. The PI can be changed if necessary but be prepared to enter the PI's information upon site creation.
- When setting up a PI or other Site Contact, be sure to set someone as the main contact. All communications, including the Regulatory Packet request would then go to this specified main contact. As an example: this should be the PI and Study Coordinator.
- Site communications are not automatically logged in the Communication Log section of the Site, Country, or IRB profile. A good practice is to enter communications into the **Communication Log** section (there is one for each Site, Country and IRB/EC), each time a communication event takes place.
- In the IRB/EC section, a good practice is to first understand what the approval cycle entails, especially for Central IRB/ECs, and then set-up time-specific options in the system (via Settings menu). This would allow the system to automatically calculate the projected timeline for site activation.
- In the Regulatory Review section, it is required that the Regulatory Reviewer enters a reason for rejection when rejecting a document. This allows the Start-Up Specialist to see why the document was rejected so they can make the necessary corrections.
- Likewise, in the Sites section, a reason for marking a document as ***Not Applicable*** should be specified clearly.
- There are several ways to move documents into the eTMF from SSU:
    - The first is before the site is activated - there is an option to publish the documents into the eTMF.
    - The other way is to retain the documents in the SSU and then push them into the eTMF, once they're required.
    - Our best practice recommendation is to move the documents into the eTMF upon site activation. Whether the system automatically moves all documents upon site activation or allows the Specialist to choose which documents should be moved to the eTMF is a matter of room configuration.

- Any documents, e.g. non-essential documents, that do **not** get reviewed in the SSU workflow, will have to be reviewed in the eTMF workflow.This would happen after moving the documents over (generally speaking, after site activation).

4. Site Management

Managing your sites and their status in the eTMF can impact how timely and complete your information is and can help you run your study as smoothly as possible.

Our best practice recommendations related to site management are:

- Define what you classify an active vs inactive site and assign the status accordingly in the eTMF.
- As you progress through a study's lifecycle, make sure you regularly review and update the status of your sites in the eTMF to ensure accurate TMF metrics.
- In the 'Settings/eTMF Health' menu, you have an option to exclude sites from eTMF completeness tracking based on site status. We encourage you to enable this option and set it for site statuses: **Closed** and **Non Participating**. Doing this will ensure your completeness tracking is indicative of the actual situation based on active sites.

5. Site collaboration/eISF

Trial Interactive's ***electronic Investigative Site File*** **(eISF) rooms** are built upon a collaborative platform, where study teams can upload working documents and prepare them for their final use.

eTMF integration allows you to easily move site files directly to the TMF, and signature workflows enable document control and approval. Remote site-monitoring capabilities are also built in, making your CRAs' tasks easier to perform.

Our best practice recommendations related to Site Collaboration are:

- Good user-access management is of paramount importance for running a secure and healthy ISF; make use of roles and of the specific Site-bound Users option to keep your study info secure.
- Best practice: limit most of your access designations to 'Site Users', which are natively restricted to only their assigned sites.
    - 'Room-level' access should be reserved for oversight/management personnel; only those who need complete visibility to correctly run the study.
- Trial Interactive's eISF can, and should, be leveraged throughout the study's lifecycle to create and edit documents. Users can do this through the Collaboration function for live documents, and templates.
    - To make the most of this, we recommend planning ahead regarding how sites will use the eISF. What templates do you want to deploy for sites? What is the go-to editing method for room users (ex: online/offline, individual/team collaboration)?
- You can implement site user assignment or user access restrictions (recommended) to handle different use cases, like running blinded/unblinded studies.
    - Example: To make sure only the appropriate personnel has access to restricted data, you can prevent entire sets of users from accessing folders using Groups management and folder security.

- Recommendation: By default, the eISF 'Staging' folder is accessible to everyone. Make sure only your internal study team the folder in order to avoid site personnel accidentally seeing each other's local content.
    - Individual Sites will have their own staging folder they can use when a document cannot be uploaded to its final location.

6. Events Management

The **Event Manager** allows you to create study events and milestones, associating a series of documents in the form of placeholders as a requirement.

The event's completion date will trigger the eTMF to classify the document placeholders as ***due*** and they will begin to show on the completeness tracking tools.

Our best practice recommendations related to Event Management are:

- You don't have to wait for a milestone's actual date to prepare an Event. You can act proactively and design your Events based on your Trial Management and TMF Plan.
- Filing a document against a placeholder requires less coding on the part of the uploader than other methods. It also prevents quality lapses that could occur due to coding mistakes.
    - We recommend training room users to leverage this placeholder fulfillment (adding documents directly to an existing placeholder) as opposed to uploading documents straight to folders.

7. Workflow Management

Document QC is a fundamental process for keeping a healthy eTMF. It helps you to get a grasp of the study's progress and reduces the likelihood of audit and inspection findings.

Whether you are a CRO or a Sponsor, you will want to make sure high-quality documents are filed in the eTMF. Designing your workflows during the study planning stage is key.

Our best practice recommendations related to Workflow Management are:

- The recommended **best practice** for eTMF rooms is to have a 2-step workflow to finalize documents. Each step of the review should be conducted by separate individuals, ensuring an independent review of the document(s).
    - Trial Interactive prevents the same person from reviewing the same document more than once in the same QC workflow.
- Decide early how you want your study team to handle QC. This includes confirming coding responsibilities, user-roles, and even *actions*[1]; as well as process determinations such as how to handle erroneous documents that could clog the workflow.
    - For example, you may not want duplicate documents to make it to the workflow stage in the first place, so a *coding team* member may be tasked with deleting or rejecting those as soon as possible.
- Trial Interactive allows you to flexibly process documents and when a document does not tell the whole story, your reviewers can pose questions to document submitter or an SME. This is done through queries (more on that in the next section).
    - Queries are best used when the reviewer of a document has a question which is preventing them from making a final determination regarding the status of the document.
    - If a new copy of the document should be submitted, it may be best to reject the existing item rather than open a query.

[1] *Actions* are additional user-bound features or access privileges that expand capabilities beyond the basic role profile. For example, an *Editor* may be granted the ability to rearrange document pages through the *Page Manipulations* action.

8. Query Process

Queries in Trial Interactive allow users to ask each other questions or work on clarifying aspects of document filing, audits, content, and more. *Query history* is tracked by the system from beginning to end.

Queries are organized into three types based on which function the question is related to. **Workflow** (created by a QC reviewer during the QC Workflow), **Audit** (created by an Auditor or Audit Responder as part of a Quality Review), and **General** (created by any user independent of any workflow or audit).

Our best practice recommendations related to queries are:

- Many clients tell us they want a more convenient way to monitor the ongoing and past queries for their study at a management level. For this, we recommend Admins use the *Queries Report*, available in Trial Interactive's **Reports** Module.
    - Another option is to use the **Queries Module**. Administrator users and Query Managers can see all open and resolved queries for the study from this location in the system. Other types of user will see their assigned queries only.
- Identify a Query Manager at the CRO and at the Sponsor level. This could be one user or a couple of users depending on the size of the study team. This allows the CRO and Sponsor users with a Query Manager addition to respond to queries on behalf of their respective teams.
- Queries should be monitored on a regular basis and not allowed to sit longer than necessary. Users should use the **My Queries** dashlet or the **Queries Module** for easy access to their queries (both received and sent).
- The quickest and, in many cases, best way for a responder to address a query is to simply reply to the initial mail alerting them to a Query having been assigned to them.

9. Email Correspondence

The **Communication module** provides a centralized point to review and classify communications that may be relevant to the study - such as key decisions, discussions, email approvals, etc. These can be sent via email to a designated study mailbox, named the *Communications Inbox*.

An assigned **Communications Reviewer** should access communications submitted to this inbox on a regular basis. This user should be tasked with deciding whether emails submitted to this inbox are relevant to the study or not. **Relevant Communications** are added as documents to the eTMF whereas those that are **Non-Relevant** are excluded from the eTMF.

Our best practice recommendations for the **Communication Inbox** are:

- Train your study teams on the purpose of the **Communication Inbox** and what constitutes relevant correspondence.
- Remember, even in rooms where TransPerfect document services are contracted, it is the Client's responsibility to identify users whose role will be to oversee the Communication Inbox and ensure that correspondence is marked accordingly.
- Designate multiple team members to this function in order to ensure coverage while avoiding excessive burdens on any given individual.
- Set up a recurring review period for this inbox to avoid buildup of un-reviewed emails, which can result in extra work particularly at the end of the study.
- When marked as **Relevant**, it will be the reviewer's responsibility to apply metadata to the document. Be sure to appoint personnel to this task who are capable of performing this task and who have been adequately trained.
- A room can be configured to only accept emails from addresses it recognizes (registered room users), designated domains (e.g. @example.net), or any specific email addresses you choose. Make use of this and plan ahead for what your study needs.

10. Quality Review

In Trial Interactive, the **Quality Review module** allows TMF Reviews and audits to be easily performed in the eTMF and for findings to be filed and tracked in-system.

Our best practice recommendations regarding the Quality Review module are:

- It is helpful to confirm which users will participate in a review before creating a quality review.
    - This includes defining which users are responsible for responding to and following up on any findings.
- Define the scope of each quality review.
    - For example, choosing between a risk-based approach vs overall review, to address which documents should be included.
- Documents in the eTMF should be regularly reviewed.
    - In Trial Interactive, you can review and export audit trails as well as action logs for processes and documents.
- As a best practice, your **minimum** TMF review frequency should be quarterly, and in the case of Study Start-Up documents, as soon as possible after **site activation**.
- Sites that have highest enrolment, or a high number of adverse events or protocol deviations, should be regularly reviewed. Expect regulatory authorities to be more demanding, in respect to these sites.

11. Inspection Readiness

When preparing to face an inspection, the key element to success is to have a clear plan thought out in advance. Make it accessible to your study team so that the inspection process moves smoothly and that potential findings are limited or avoided altogether.

Our best practice recommendations regarding Inspection Readiness are:

- Have an TMF Plan readily available and easily located. Expect to be required to show it at inspections.
- Keep documents current and in their expected location in TI – that is, where they can be accessed at a moment's notice when an inspector demands it.
- If TMF documents are stored in other eClinical systems, have a plan or matrix to indicate these locations.
- Use internal audits as a training experience and a preparedness tool. You can run a 'mock inspection' and gain insights into your own preparedness.
- You'll want contributors to upload documents in a timely manner. This helps with eTMF timeliness monitoring as well as inspection readiness.
- Be ready to provide direct access to Inspectors. It's a good idea to have the type of access confirmed ahead of time and an easy user-creation matrix ready.
- As a precaution, provide your own team members with a limited-access user profile in case an Inspector wants to see a user at work rather than access the platform themselves.
- When training inspectors to navigate the Trial Interactive eTMF, remember they don't need advanced system proficiency and expect to be trained within 30 minutes at most. Trial Interactive provides quick start guides and videos to reduce training time.
    - For the same reason, it is highly recommended to have prepared beforehand and provide to the inspectors easy-access materials, such as Quick Reference Guides.

- Only destroy paper originals following an established and documented process for certifying copies and paper destruction.
- After the inspection is complete, make sure that the access is revoked for all related “guest” users.